PROGRAM

Convention Center Ribeirão Preto
Ribeirão Preto, SP
October 28 – 31, 2013

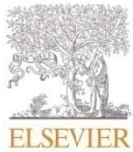
Financial Support

Ministério da Saúde


Enterprise Support

Remer Villaça & Nogueira


Exhibitors



Support

Sociedade Brasileira de Farmacologia e Terapêutica Experimental
sbfte@pratica.com.br / sbfte@sbfte.org.br
http://www.sbfte.org.br

Organization

Eventus Planejamento e Organização
eventus@eventus.com.br
http://www.eventus.com.br

Review, **Supervision**, **Layout**
Sandra Helena Rocha da Cruz

Message of the president

Dear Colleague,

On behalf of the Brazilian Society of Pharmacology and Experimental Therapeutics it is my great pleasure to welcome you to our 45th annual meeting. This year, we will focus our discussion on the development of new drugs and how to close the gap between pharmaceutical companies and academia in Brazil. This is certainly a long gap everywhere but we do need to work together for the benefit of our country.

This meeting is the result of a year of hard work by the Board of Directors, the Council, Executive Secretariat and Eventus. I very much thank all my colleagues for their efforts and dedication to the success of the event.

We are in debt to CNPq, CAPES, FAPERJ, FAPESP and the Ministry of Health (DECIT) for their financial support to our meeting. Special thanks also go to Biolab-Sanus Farmacêutica who supports the *José Ribeiro do Valle Award* and Remer Consultores who supports the *Innovation Award*.

Finally, I must thank the Abstract and Poster reviewers who have spent considerable time and effort to ensure that our standards are met. Do excuse our imperfections as I am certainly many things can indeed get better. In this regard, we very much appreciate your feedback, comments, criticisms and suggestions to the email sbfte@sbfte.org.br.

I wish you an excellent Congress and a very nice stay in Ribeirão Preto.

Enjoy the meeting and take your time to meet old and new friends.

Useful information

Secretariat
Congress Secretariat will be open from 8h to 18h.

Posters
Posters Sessions will happen on October 29 and 30 from 18h to 20h00 and October 31 from 10h00 to 12h00. Please display your poster from 08h00 at the day of your presentation and take it out after your presentation.

Certificates
The Certificates will be sent to the participant and lecturers in pdf

Media Desk
Media desk will be open from 8h to 18h. Please, leave your material at Media Desk at least two hours before your presentation. All rooms have *data show*. If you need any other equipment, please inform Media Desk as soon as possible. Lecturers presenting at 8h00 in the morning should leave your material at the day before

Badges
The use of badge is required for all activities and circulation areas

Abstracts
Abstracts presented at the poster session will be available at SBFTE site http://www.sbfte.org.br

Committees

Congress President
Mauro M. Teixeira (UFMG)

Organizing Committee
Mauro M. Teixeira (UFMG, Coordinator)
Fernando de Queiroz Cunha (USP)
Letícia Veras Costa Lotufo (UFC)
Yara Cury (IBu)
Maria Christina W. de Avellar (Unifesp)

Scientific Committee
Yara Cury (IBu, Coordinator)
Ana Marisa Chudzinski-Tavassi (IBu)
Fernando de Queiroz Cunha (USP)
Leticia Veras C. Lotufo (UFC)
Mauro M. Teixeira (UFMG)
Regina P. Markus (USP)

Fundraising Committee
Maria Christina W. de Avellar (Unifesp, Coordinator)
Cristoforo Scavone (USP)
Emer S. Ferro (USP)
Erick J. Ramo Silva (Unifesp)
Fernando de Queiroz Cunha (USP)
Regina P. Markus (USP)

Poster Committee
Leticia Veras Costa Lotufo (UFC, coordinator)
Emiliano Barreto (UFAL)
Maria Christina W. de Avellar (Unifesp)
Patricia M. R. Silva Martins (Fiocruz)
Rosely O. Godinho (Unifesp)

José Ribeiro do Valle Award Committee
Marco Aurélio Martins (Fiocruz, Coordinator)
João Ernesto de Carvalho (Unicamp)
Mauro M. Teixeira (UFMG)

Local Committee
Fernanda Castanheira (USP)
Fernando de Q. Cunha (USP)
Larissa Garcia Pinto (USP)
Sandra Fukada (USP)

Abstract Reviewers

Ana Leonor A. Nencioni
Ana Luisa Palhares de Miranda
André Sampaio Pupo
Andrea Grabe Guimarães
Arquimedes Gasparotto Junior
Áurea Elizabeth Linder
Candida Aparecida Leite Kassuya
Carlos Fernando de Mello
Carlos Renato Tirapelli
Carolina Baraldi Araujo Restini
Claudia Maria Padovan
Claudio Miguel Costa Neto
Cristóforo Scavone
Daniella Bonaventura
Diego Veras Wilke
Emiliano Barreto
Erick Jose R. Silva
Fernanda Regina de Castro Almeida
Fernando Mauricio F. Abdalla
Flavia Almeida Santos
Francisco Guimarães
François G. Noel
Glória E. P. Souza
João Ernesto Carvalho
Juliana Montani Raimundo
Lusiane Maria Bendhack
Marcellus Henrique L. Ponte de Souza
Marcelo Nicolas Muscara
Marco Aurélio Martins
Maria Martha Campos
Patrícia Martins
Patrícia Torres Bozza
Reinaldo Takahashi
Renata Grespan
Renata Mazaro
Roberto Cesar Pereira Lima Junior
Roberto Takashi Sudo
Sandra Helena P. Farsky
Soraia Katia Costa Pereira
Tania Araujo Viel
Teresa Cristina T. Dalla Costa
Thereza C. Barja-Fidalgo
Thiago Mattar Cunha
Valber Frutuoso
Vanessa de Paula Soares
Waldiceu Aparecido Verri Junior

Index

Schematic Scientific Program
28/10/2013 – Monday

Schedule	
09h00-12h00	Meeting of the Deliberative Council (only for Members of the Council and Society Board)
13h30-16h30	SBFTE Permanent Forum of Graduate Programs in Pharmacology (only for Heads of Pharmacology Graduate Programs, Council and Society Board)
14h00	Venue Secretariat and SBFTE Secretariat Opening
18h30-19h00	Opening ceremony
19h00-20h00	Opening Conference
20h00-22h00	Cocktail

09h00-12h00

Room Safira

Meeting of the Deliberative Council (only for Members of the Council and Society Board)

13h30-16h30

Room Safira

SBFTE Permanent Forum of Graduate Programs in Pharmacology (only for Heads of Pharmacology Graduate Programs, Council and Society Board)

14h00

Venue Secretariat and SBFTE Secretariat Opening

18h30-19h00 Opening ceremony

Room Rubi

19h00-20h00 Opening Lecture

Room Rubi

Sergio Ferreira Prize on Innovative Research
Cytokines: **from immune system hormones to mediators of pain and inflammation**
Stephen Poole (NIBSC, UK)
Chairperson: Mauro M. Teixeira (UFMG)

20h00-22h00

Cocktail

Schematic Scientific Program
Tuesday 29/10/13

Schedule	Room Topázio	Room Safira
08h00-08h50 *Courses* (class 1)	Building Biotechnology	*In silico*, *in vitro* and *in vivo* approaches in the Drug Development Process
	Room Topázio	**Room Rubi**
09h00-09h50 *Conferences*	Fatal or Crippling: New insights into cognitive dysfunction induced by cerebral malaria	Approaches targeting voltage gated channels open a novel window for diagnosis and therapy
	Room Esmeralda	
09h50-10h10	Coffee break	
	Room Topázio	**Room Rubi**	**Room Safira**
10h10-12h10 *Symposia*	University industry interaction: a new context for innovation	Ion channels	Mucosal Inflammation
	Room Rubi	
12h10-14h00	Desafios da Pesquisa e Pós-graduação em Farmacologia no Brasil Lunch	
	Room Topázio	**Room Rubi**	**Room Safira**
14h00-16h00 *Symposia*	Agents of innovation and development of drugs	New targets for brain vulnerability to injury and disease	New pathophysiological mechanisms of metabolic syndrome
16h00-17h00 Coordinated sessions	Respiratory, Urinary, Reproductive	Cardiovascular	Inflammation/pain
	Room Esmeralda	
17h00-17h30	Coffee break	
	Room Topázio	
17h30-18h20 Conference	Toll-like receptor activation: a novel mechanism linking vascular dysfunction in hypertension, erectile dysfunction and pre-eclampsia	
	Room Esmeralda	
18h20-20h15	Poster Session 1	
	Room Topázio	
20h30-21h30	SBFTE General Assembly	

08h00-08h50 Courses

Room Topázio

Building Biotechnology
Chairperson: Emer Suavinho Ferro (USP)
- *Class1: Introduction to biotechnology*
  Emer Suavinho Ferro (USP)

Room Safira

In silico, ***in vitro*** **and** ***in vivo*** **approaches in the Drug Development Process**
Chairperson: François G. Noël (UFRJ)
- *Class1: Drug Development:* in silico *approaches*
  Carlos Alberto Manssour Fraga (UFRJ)

09h00-09h50 Conferences

Room Topázio

Fatal or Crippling: **New insights into cognitive dysfunction induced by cerebral malaria**
Hugo Castro-Faria Neto (Fiocruz)
Chairperson: Maria Christina W. de Avellar (Unifesp)

Room Rubi

Approaches targeting voltage gated channels open a novel window for diagnosis and therapy
Walter Stuhmer (Max Planck Institute, Germany)
Chairperson: Cilene Lino de Oliveira (UFSC)

09h50-10h10 Coffee break

10h10-12h10 Symposia

Room Topázio

University industry interaction: **A new context for innovation**
Chairperson: Fernando de Queiroz Cunha (USP)
- *Entrepreneurship programs for university approach to the market*
  Aluir Dias Purceno
- *Cristália: A success case of pharmaceutical innovation*.
  Regina Scivoletto (Cristália Produtos Químicos Farmacêuticos Ltda)
- *Importance of HR training in the Innovation area*
  Linda Omar Alves Bernardes (Unifesp)
- *Bridging the Brazilian biotechnology gap through industry-industry and academia-industry interactions*
  Thiago Mares Guia (Bionovis)

Room Rubi

Ion channels
Chairperson: Andrea Grabe Guimarães (UFOP)

- *Development of new anti-arrhythmics derived from EPA and DHA*
  Jean-Yves Le Guennec (INSERM, France)
- *Efficacy of new drugs in the heart: effects on discrete events and concept of normalization ion channels function*
  Sylvain Richard (INSERM, France)
- *Chagasic Cardiomyopathy: An electrophysiological conundrum*?
  Jader dos Santos Cruz (UFMG)
- *Could nociceptors serve cardiovascular control*? *A neuroendocrine HNO-TRPA1-CGRP pathway*
  Peter Reeh (University of Erlangen-Nürnberg, Germany)

Room Safira

Mucosal Inflammation
Chairperson: José Carlos F. Alves Filho (USP)

- *Gastrointestinal mucositis during irinotecan-based cancer chemotherapy: Role of microbial sensing receptors*
  Roberto C. Lima Júnior (UFC)
- *The interplay between diet*, *the gut microbiota and the immune system determines the balance between inflammation and homeostasis*
  Angélica T. Vieira (UFMG)
- *The hypothalamus-pituitary-adrenal axis and glucocorticoids in the modulation of gut inflammation*
  Cristina Cardoso (USP)
- *Pro-resolution lipid mediators in intestinal inflammation*
  Allisson F Bento (UFSC)

12h10-14h00 Lunch / Symposia

Room Rubi

Desafios da Pesquisa e Pós-graduação em Farmacologia no Brasil.
Coordenador: Cristoforo Scavone (USP)

- *A trajetória do Fórum da Pós-Graduação em Farmacologia na SBFTE*
  Maria Christina W. de Avellar (Unifesp)
- *Evolução da Produção Bibliográfica em Farmacologia de Autores Brasileiros: Onde estamos e para onde queremos ir*?
  Carlos F. de Mello (UFSM)
- *Como pensar no Futuro da Farmacologia*
  Jamil Assreuy Filho (UFSC)
- *Discussão*

14h00-16h00 Symposia

Room Topázio

Agents of innovation and development of drugs
Chairperson: Ana Marisa Chudzinski-Tavassi (Butantan Institute)

- *Opportunities for companies in FINEP – Edital Inova Saúde*
  Igor Ferreira Bueno (FINEP)
- *Why investing (or not) in health biotechs in Brazil*
  Patricia Pellegrino (Wylinka)
- *FAPESP: Research Support for Innovation in Health*
  Sergio Queiroz (FAPESP)

Room Rubi

New targets for brain vulnerability to injury and disease
Chairperson: Cristoforo Scavone (USP)

- *TNFR2 as a target for therapeutics against neurodegenerative diseases*.
  Elisa Mitiko Kawamoto (NIH, USA)
- *New drug development for mood disorders*.
  Ana Cristina Andreazza (University of Toronto, Canada)
- *New insights in cholinergic system and Alzheimer's disease*.
  Tânia A. Viel (USP)
- *Rapid estrogen signaling GPER-1 and neuroprotection*
  Carolina Demarchi Munhoz (USP)

Room Safira

New pathophysiological mechanisms of metabolic syndrome
Chairperson: Eliana Hiromi Akamine (USP)

- *Metabolic syndrome-related hypertension: The contribution of perivascular adipose tissue (PVAT)*
  Theodora Szasz (Georgia Regents University, USA)
- *Metabolic syndrome*, *inflammation*, *and vascular consequences)*
  Eliana Hiromi Akamine (USP)
- *New immunological mechanisms involved in obesity-induced inflammation and type 2 diabetes: Role of NOD2 receptor*
  Daniela Carlos Sartori (USP)
- *Involvement of inflammatory mediators in the metabolic homeostasis*
  Adaliene Versiani Matos Ferreira (UFMG)

16h00-17h00 Coordinated sessions

Room Topázio

Respiratory, **Urinary**, **Reproductive**
Chairperson: Remo Castro Russo (UFMG)

- 08.002 *Effects of clonidine in the isolated rat testicular capsule*. Silva-Júnior ED, Rodrigues JQD, Souza BP, Jurkiewicz A, Jurkiewicz NH

- 08.011 *Acute aerobic exercise alters the contractile and relaxant responses on rat trachea*. Brito AF, Souza ILL, Pereira JC, Silva AS, Silva BA
- 08.013 *Inducible NO synthase plays a major role in obesity-associated overactive bladder*. Leiria LO[1], Augusto TM[2], Teixeira SA[3], Muscará MN[3], Carvalho HF[2], Antunes E[1] [1]UNICAMP – Farmacologia, [2]UNICAMP – Biologia Estrutural e Funcional, [3]USP – Farmacologia
- 08.006 *Mirabegron, a beta-3 adrenergic agonist relaxes rat corpus cavernosum and rabbit prostate*. Candido TZ, Antunes E, de Nucci G, Mónica FZ UNICAMP – Farmacologia

Room Rubi

Cardiovascular

Chairperson: José Eduardo da Silva Santos (UFSC)

- 06.058 *Mineralocorticoid receptor and G protein-coupled estrogen receptor mediate the vascular effects of aldosterone in female mice with type two diabetes*. Ferreira NS[1], Cau SBA[2], Manzato CP[1], Silva MAB[1], Tostes RC[1] [1]USP – Pharmacology, [2]UFJF
- 06.019 *Involvement of calcium on the positive inotropic effect produced by ATP and UTP right atria in hypertensive rats*. Rodrigues JQD, Silva-Junior ED, Camara H, Miranda-Ferreira R, Galvão KM, Caricati-Neto A, Jurkiewicz NH, Jurkiewicz
- 06.014 *Mitochondrial reactive oxygen species mediate the modulation of vascular contraction by periaortic adipose tissue*. Costa RM[1], Filgueira FP[2], Carvalho MHC[2], Akamine EH[2], Lobato NS[1] [1]UFG – Biological Sciences, [2]ICB-USP
- 06.047 *Norepinephrine-induced contraction of rat renal and femoral veins involves both α1 and α2-Adrenoceptors*. Rossignoli PS[1], Pereira OCM[2], Chies AB[1] [1]Famema-Unimar – Pharmacology, [2]IBB-UNESP – Pharmacology

Room Safira

Inflammation/pain

Chairperson: Thiago M. Cunha (USP)

- 05.001 *Neuropathic pain following spinal cord injury: A possible role of endothelin ETA and ETB receptors*. Forner S, Martini AC, Rae GA UFSC
- 04.038 *Aryl hydrocarbon receptor gene polymorphism isassociated with smoking-induced exacerbation of rheumatoid arthritis*. Talbot J[1], Peres RS[2], Oliveira RDR[3], Pinto LG[1], Almeida SCL[3], Silva JR[2], Franca RFO[1], Ryffel B[4], Cunha TM[1], Alves-Filho JC[1], Liew EY[5], Louzada-Junior P[3], Cunha FQ[1] [1]FMRP-USP – Farmacologia, [2]FMRP-USP – Imunologia, [3]HCFMRP-USP – Reumatologia, [4]CNRS-Orleans, [5]University of Glasgow
- 04.023 *TNFR1, but not TNFR2, is crucial to the development and progression of systemic inflammation and organ damage during experimental sepsis*. Melo PH, Nascimento CBD, Ferreira RG, Scortegagna GT, Borges VF, Cunha FQ, Alves-Filho JC FMRP-USP – Basic and Applied Immunology
- 04.012 *Endothelial cell P2Y[1] receptor purinergic signalling during chronic inflammation Oliveira SDS[1,2], Oliveira NF[1], Coutinho-Silva R[2], Savio LE[2], Meyer-*

Fernandes JR[3], *Silva CLM*[1] [1]IBCCF-UFRJ – Farmacologia Bioquímica e Molecular, [2]IBCCF-UFRJ – Imunologia, IBqM-UFRJ

17h00-17h30 Coffee break

17h30-18h20 Conference

Room Topázio

Toll-like receptor activation: **a novel mechanism linking vascular dysfunction in hypertension**, **erectile dysfunction and pre-eclampsia**
R. Clinton Webb (Georgia Regents University, USA)
Chairperson: Rita Tostes (USP)

18h20-20h15 Poster Session 1

Room Esmeralda

01. Cellular and Molecular Pharmacology	01.001-01.011
02. Neuropharmacology	02.001-02.011
03. Psychopharmacology	03.001-03.012
04. Inflammation	04.001-04.017
05. Pain and Nociception	05.001-05.014 and 05.030
06. Cardiovascular and Renal	06.001-06.021 and 06.064
09. Natural Products and Toxinology	09.001-09.021
10. Cancer and Cell Proliferation	10.001-10.014

20h30-21h30

Room Topazio

SBFTE General Assembly

Schematic Scientific Program
Wednesday 30/10/13

Schedule	Room Topázio	Room Rubi	Room Safira
08h00-08h50 *Courses* (class 2)	Building Biotechnology		*In silico*, *in vitro* and *in vivo* approaches in the Drug Development Process
	Room Topázio		**Room Rubi**
09h00-09h50 *Conferences*	Heteromerization of G protein-coupled receptors: impact on physiopathology and drug design		Cyclo-oxygenase-2/Vioxx and cardiovascular health and disease: Defining a new paradigm
	Room Esmeralda		
09h50-10h10	**Coffee break**		
	Room Topázio	**Room Rubi**	**Room Safira**
10h10-12h10 *Symposia*	José Ribeiro do Valle Award	Beyond dopamine in Parkinson's disease: Pathophysiology and treatment	Thrombosis and Homeostasis: Milestones and future prospects for the development of new tools and therapeutics
12h10-14h00	Lunch		
	Room Topázio	**Room Rubi**	**Room Safira**
14h00-16h00 *Symposia*	Great Development Themes in Brazil	Advances in the physiopathology and treatment of pain	Innovation on Natural Products in Brazil: Perspectives and challenges
16h00-17h00 Coordinated sessions	Cellular Signaling	Neuropharmacology	Natural Products
	Room Esmeralda		
17h00-17h30	Coffee break		
	Room Topázio		
17h30-18h20 Conference	Mining drugs from bugs: A blueprint of the mining field		
	Room Esmeralda		
18h20-20h15	Poster Session 2		

08h00-08h50 Courses

Room Topázio

Building Biotechnology
Chairperson: Emer Suavinho Ferro (USP)

- *Class2: How to start a small Biotech Company: Just do it!*
  Andrea Sterman Heimann (Proteimax Biotecnologia Ltda)

Room Safira

In silico, ***in vitro*** **and** ***in vivo*** **approaches in the Drug Development Process**
Chairperson: François G. Noël (UFRJ)

- *Class2: Drug Development:* in vitro *approaches*
  François G. Noël (UFRJ)

09h00-09h50 Conferences

Room Topázio

Heteromerization of G protein-coupled receptors: **impact on physiopathology and drug design**
Ralf Jockers (Institute Cochin, Paris)
Chairperson: Regina P. Markus (USP)

Room Rubi

Cyclo-oxygenase-2/Vioxx and cardiovascular health and disease: **defining a new paradigm**
Jane Mitchell (Imperial College, UK)
Chairperson: Gilberto de Nucci (UNICAMP)

09h50-10h10 Coffee break

10h10-12h10 Symposia

Room Topázio

José Ribeiro do Valle Award
Chairperson: Mauro M. Teixeira (UFMG)
Erika Cecon

- 04.032 *Amyloid beta peptide induces neuroinflammatory response in the pineal gland and impairs melatonin synthesis*. Cecon E[1], Fernandes PACM[1], Jockers R[2], Markus RP[1] [1]IB-USP, [2]Institute Cochin

Jaqueline Raymondi Silva

- 05.039 *Immune cell infiltration and production of inflammatory mediators in dorsal root ganglion*, *but not in spinal cord*, *are related to murine herpetic hyperalgesia*. Silva JR, Talbot J, Lopes AHP, Cunha TM, Cunha FQ FMRP-USP – Farmacologia

Natália Tabosa Machado

- 06.025 *Nitric Oxide as a target for the hypotensive and vasorelaxing effects induced by (z)-ethyl 12-nitrooxy-octadec-9-enoate in rats*. Machado NT[1], Marciel PMP[1], Alustau MC[1], Queiroz TM[1], Furtado FF[2], Silva TAF[1], Vasconcelos WP[1],

Santos PC[1], Oliveira-Filho AA[1], Veras RC[1], Araújo IGA[1], Athayde-Filho PF[1], Medeiros IA[1] [1]CCS-UFPB, [2]CFP-ETSC-UFCG

Ana Carla Zarpelon

- 05.009 *Role of Interleukin-33/ST2 receptor signaling in chronic constriction injury-induced neuropathic pain in mice*. Zarpelon AC[1], Rodrigues FC[1], Carvalho TT[1], Souza GR[2], Ferreira SH[2], Alves-Filho JC[2], Liew FY[3], Cunha TM[2], Cunha FQ[2], Verri WA Jr[1] [1]UEL – Departamento de Patologia, [2]FMRP – Farmacologia, [3]University of Glasgow – Immunology, Infection and Inflammation

Gabriela Trevisan

- 05.004 *TRPA1 receptor stimulation by hydrogen peroxide is critical to trigger pain and inflammation during acute gout attack*. Trevisan G[1], Hoffmeister C[1], Rossato MF[1], Oliveira SM[1], Silva MA[1], Silva CS[1], Nassini R[2], Materazzi S[2], Fusi C[2], Petri GP[3], Geppetti P[2], Ferreira J[4] [1]UFSM, [2]University of Florence, [3]UTFPR, [4]UFSC

Room Rubi

Beyond dopamine in Parkinson's disease: **Pathophysiology and treatment**.
Chairperson: Maria Aparecida Barbato Frazão Vital (UFPR)

- *Depression in Parkinson disease*
  Roberto Andreatini (UFPR)
- *Nitric Oxide and Parkinson's disease*
  Elaine Del Bel (USP)
- *Silencing genes by RNA interference – a promising therapy for Parkinson´s disease*.
  Ricardo Titze-de-Almeida (UnB)
- *Neuronal Death in Parkinson's disease*.
  Maria Aparecida Barbato Frazão Vital (UFPR)

Room Safira

Thrombosis and Homeostasis: **Milestones and future prospects for the development of new tools and therapeutics**
Chairperson: Aurea Elizabeth Linder (UFSC)

- *Potential therapeutic targeting of platelet-mediated cellular interactions*.
  Kenneth Clemetson (University of Berne, Switzerland)
- *From snake venom toxins to therapeutics--cardiovascular examples*.
  R. Manjunatha Kini (National University of Singapore, Singapore)
- *Developing a factor Xa inhibitor (Amblyomin-X) as a new antitumor molecule*
  Ana Marisa Chudzinski-Tavassi (Butantan Institute, Brazil)
- *Clinical use of antiplatelet agents*
  Dayse Maria Lourenço (Unifesp)

12h10-14h00 Lunch

14h00-16h00 Symposia

Room Topázio

Great Development Themes in Brazil
Chairperson: João Batista Calixto (UFSC)

- *National initiatives to promote drug development*
  Luiz Henrique Mourão do Canto Pereira (CGBS/SEPED/MCTI)
- *Drug and phytomedicines development – The role of the Academy*
  João Batista Calixto (UFSC)
- *INCT-INOFAR A Brazilian network for drug discovery*, *design & development*
  Eliezer J. Barreiro (UFRJ)

Room Rubi

Advances in the physiopathology and treatment of pain
Chairperson: Thiago M. Cunha (FMRP)

- *Comparative study of cold allodynia in animal models of neuropathic pain: Different etiologies*, *distinct pathophysiologic mechanisms*
  Joice Maria da Cunha (UFPR)
- *Aldehyde Dehydrogenase-2 activation induces analgesia in rodents: implication for the Human East Asian with ALDH2*2 mutation*
  Vanessa Olzon Zambelli (Butantan Institute)
- *The role of inhibiting glycogen synthase kinase-3 in the treatment of painful diseases*
  Adair Roberto Soares dos Santos (UFSC)
- *Chemotherapy-induced peripheral neuropathy – role of DNA damage and repair*
  Djane Braz Duarte (UnB)

Room Safira

Innovation on Natural Products in Brazil: **perspectives and challenges**
Chairperson: Claudia do Ó Pessoa (UFC)

- *New Lead Molecules For Cancer Chemotherapy*
  Cláudia do Ó Pessoa (UFC)
- *CPQBA-Unicamp: 25 years of research and development of natural products*
  João Ernesto de Carvalho (UNICAMP)
- *The use of drug delivery systems seeking to improve chemical and pharmacological properties of natural compounds*
  Lucindo Quintans Júnior (UFS)

16h00-17h00 Coordinated sessions

Room Topázio
Cellular Signaling
Chairperson: Lusiane M. Bendhack (USP)

- 01.012 *Bufalin promotes epithelial to mesenchymal transition in LLC-PK1 cells*. Martins-Ferreira J, Laczynski-Braz L, Cunha-Filho G, Quintas LEM, Noël F ICB-UFRJ

- 01.011 *G-Protein coupled estrogen receptor-1 traffics between plasma membrane and nucleus and activates MEK-ERK-CREB signaling in primary cortical culture*. Lopes DCF, Novaes LS, Santos NB, Duque EA, Wiezel G, Scavone C, Munhoz CD USP – Farmacologia
- 01.029 *ERK serves as a converging point in atenuation of skeletal muscle proteolysis induced by Gs and Gi-coupled adenosine receptors*. Figueiredo LB, Duarte T, Godinho RO Unifesp – Pharmacology
- 01.022 *Effect of atorvastatin on oxidative stress induced by lysophosphatidylcholine in human endothelial cells*. Fernandes VA[1], Navia-Pelaez JM[1], Diniz TF[2], Cortes SF[1], Lemos SV[2], Capettini LSA[1] [1]UFMG – 2Farmacologia, [2]UFMG – Fisiologia

Room Rubi

Neuropharmacology

Chairperson: Leonardo Resstel Barbosa Moraes (USP)

- 02.001 *Time-course analysis of prostaglandin E2 receptor immunoreactivity following pilocarpine-induced status epilepticus*. Grigoletto J, Funk VR, Oliveira CV, Grauncke ACB, Souza TL, Guerra GP, Oliveira MS UFSM – Physiology and Pharmacology
- 02.022 *μ and κ opioid-receptors in the prelimbic cortex have a facilitatory influence on the cardiovascular responses to acute restraint stress in rats*. Fassini A, Scopinho AA, Resstel LBM, Corrêa FMA FMRP-USP – Farmacologia
- 02.012 *Fenofibrate promotes neuroprotection in a model of rotenone-induced Parkinson's disease*. Barbiero JK[1], Santiago R[1], Tonin F[1], Boschen S[1], Bassani T[1], Gradowski R[1], Da Cunha C[1], Lima MMS[2], Vital MAVF[1] [1]UFPR – Farmacologia, [2]UFPR – Fisiologia

Room Safira

Natural Products

Chairperson: Emiliano de Oliveira Barreto (UFAL)

- 09.054 *Investigation of tocolytic effect of Lippia microphylla Cham*. *essential oil (Verbenaceae) and its major compounds*, *thymol and carvacrol*, *on rat uterus*. Silva MCC, Medeiros MAMB, Souza ILL, Ferreira PB, Sampaio RS, Martins IRR, Calvacante FA, Tavares JF, Silva BA – UFPB
- 09.049 *Rat isolated right atrial responses to Vitalius dubius (Araneae*, *Theraphosidae) venom and a purified polypeptide*. Tamascia ML[1], Rennó AL[1], Zelanis A[2], Serrano SMT[2], Hyslop S[1] [1]FCM-UNICAMP – Farmacologia, [2]CAT-CEPID-IBu – Toxinologia
- 09.013 *Rhamnogalacturonan from Acmella oleracea (L.) R.K. Jansen: gastroprotective and ulcer healing properties*. Ferreira DM[1], da Silva LM[1], Mendes DAGB[1], Nascimento AM[2], Iacomini M[2], Cipriani TR[2], Santos ARS[3], Werner MFP[1], Baggio CH[1] [1]UFPR – Pharmacology, [2]UFPR – Biochemistry and Molecular Biology, [3]UFSC – Physiological Sciences

- 09.014 *Effect of hesperidin methyl chalconhe in acute lung injury induced by LPS*. Domiciano TP[1], Staurengo-Ferrrari L[1], Casagrande R[2], Verry Jr WA[1] [1]CCB-UEL – Ciências Patológicas, [2]CCS-UEL – Ciências Farmacêuticas

17h00-17h30 Coffee break

17h30-18h20 Conference

Room Topázio

Mining drugs from bugs: **A blueprint of the mining field**
Jose M.C. Ribeiro (NIH, EUA)
Chairperson: Fernando de Q. Cunha (USP)

18h20-20h15 Poster Session 2

Room Esmeralda

01. Cellular and Molecular Pharmacology	01.012-01.022
02. Neuropharmacology	02.012.02.022
03. Psychopharmacology	03.013-03.023
04. Inflammation	04.018-04.033
05. Pain and Nociception	05.015-05.028
06. Cardiovascular and Renal	06.022-06.042
07. Endocrine and Gastrointestinal	07.001-07.007
09. Natural Products and Toxinology	09.022-09.042
11. Clinical Pharmacology, Pharmacokinetics, Pharmacogenomics and Preclinical Toxicology	11.001-11.014

Scientific Schematic Program
Thursday 31/10/2013

Schedule	Room Topázio	Room Safira
08h00-08h50 *Courses* (class e)	Building Biotechnology	*In silico*, *in vitro* and *in vivo* approaches in the Drug Development Process
	Room Topázio	**Room Rubi**
09h00-09h50 *Conferences*	Completing the circle in drug development: Discovery and applications of cyclotides	Polypharmacy of osteoarthritis: The Perfect Intestinal Storm
	Room Esmeralda	
10h00–12h00	Poster Session 3 with Coffee break	
	Room Topázio	
12h00-12h50 Closing Conference	The relevance of toxins and other natural products for drug discovery	
12h50-13h30	Closing ceremony and Awards	

08h00-08h50 Courses

Room Topázio

Building Biotechnology
Chairperson: Emer Suavinho Ferro (USP)

- *Class3: Legal aspects for building biotechnology in Brazil*
  Ricardo Remer (Remer Consultores)

Room Safira

In silico, ***in vitro*** **and** ***in vivo*** **approaches in the Drug Development Process**
Chairperson: François G. Noël (UFRJ)

- *Class3: Drug Development:* in vivo *approaches*
  Roberto Takashi Sudo (UFRJ)

09h00-09h50 Conference

Room Topázio

Completing the circle in drug development: **Discovery and applications of cyclotides**
David Craik (The University of Queensland, Australia)
Chairperson: Yara Cury (Butantan Institute)

Room Rubi

Polypharmacy of osteoarthritis: **The Perfect Intestinal Storm**
John Wallace (University of Calgary, Canada)
Chairperson: Gilberto de Nucci (UNICAMP)

10h00-12h00 Poster Session 3 with Coffee-Break

Room Esmeralda

01. Cellular and Molecular Pharmacology	01.023-01.032
02. Neuropharmacology	02.023-02.033
04. Inflammation	04.034-04.049
05. Pain and Nociception	05.029 and 05.31-05.042
06. Cardiovascular and Renal	06.043-06.063
08. Respiratory, Urinary and Reproductive Pharmacology	08.001-08.015
09. Natural Products and Toxinology	09.043-09.063

12h00-12h50 Closing Conference

Room Topázio

The relevance of toxins and other natural products for drug discovery
Alan Harvey (Dublin City University, Ireland)
Chairperson: Mauro M. Teixeira (UFMG)

12h50-13h30

Closing ceremony and Awards

Poster session 1 – Tuesday 29/10/13

01. Cellular and Molecular Pharmacology

01.001 LDT3 and LDT5 prevent prostate contraction and have antiproliferative effect in human prostate cells. Nascimento-Viana JB[1], Carvalho AR[1], Chagas-Silva F[1], Romeiro LAS[2], Souza PAVR[3,4], Nasciutti LE[3], Noël FG[1], Silva CLM[1] [1]UFRJ – Farmacologia Bioquímica e Molecular, [2]UnB – Desenvolvimento de Estratégias Terapêuticas, [3]UFRJ – Biologia Celular e do Desenvolvimento, [4]Hospital Geral do Andaraí RJ – Urologia

01.002 Effects of neolignan 2,3-dihydrobenzofuran against *Leishmania amazonensis* **and its cytotoxicity in macrophages and hemolytic activity**. Oliveira LGC[1], Carvalho FAA[2], Amorim LV[3], Sobrinho Júnior EPC[3], Lima DS[1], Vieira MM[4], Sousa-Neto BP[3], Brito LM[3], Carvalho CES[3] [1]NPPM-UFPI, [2]UFPI – Bioquímica, [3]UFPI, [4]UFPI – Biotec

01.003 Towards the mechanism involved in telocinobufagin-induced cell death. Amaral LS, Cunha-Filho GA, Noël FG, Quintas LEM[1] ICB-UFRJ

01.004 New digoxin derivatives: **Effects on Na^+/K^+-ATPase**. Silva NP, Noël FG, Quintas LEM CCS-ICB-UFRJ

01.005 Snakebites envenomation and alternative serotherapy by camelid nanobodies. Prado NDR[1], Pereira SS[1], Moraes MSS[1], Moreira-Dill LS[2], Luiz MB[1], Kayano AM[2], Pereira-da-Silva LH[1], Soares AM[2], Stabeli RG[1], Fernandes CFC[1] [1]Fiocruz Rondônia, [2]UNIR – Estudos de Biomoléculas Aplicado a Saúde

01.006 The *N*-phenylpiperazine LDT66 is a competitive antagonist of alpha$_{1A}$-adrenoceptors and an inhibitor of human prostate cell proliferation. Chagas-Silva F[1], Nascimento Viana JB[1], Romeiro LAS[2], Souza PAVR[3,4], Nasciutti LE[3], Noël F[1], Silva CLM[1] [1]UFRJ – Farmacologia Bioquímica e Molecular, [2]UnB – Desenvolvimento de Estratégias Terapêuticas, [3]UFRJ – Biologia Celular e do Desenvolvimento, [4]Hospital Geral do Andaraí RJ – Urologia

01.007 Study of P2X7 antagonist treatment on wound healing process in rats. Castro AB, Magalhães JF, Souza BB, Raimundo JM, Bonavita AG UFRJ-Macaé

01.008 Characterization of new *N*-phenylpiperazine derivatives designed by homologation of the antipsychotic lead compound LASSBio-579. Pompeu TET[1], Moura BC[1], Alves FRS[2], Figueiredo CDM[1], Antonio CB[3], Herzfeldt V[3], Rates SMK[3], Barreiro EJ[2], Fraga CAM[2], Noël FG[1] [1]UFRJ – Farmacologia Bioquímica e Molecular, [2]LASSBio-UFRJ, [3]UFRGS – Ciências Farmacêuticas

01.009 Melatonin inhibits $P2Y_1$ receptor-mediated leukocyte adhesion to endothelial cell. Cardoso TC, Noël FG, Silva CLM UFRJ – Farmacologia Bioquímica e Molecular

01.010 ***In vitro*** **effects of relaxin in early and late steps of rat spermatogenesis**. Pimenta MT, Francisco RAR, Porto CS, Lazari MFM Unifesp – Pharmacology

01.011 G-protein coupled estrogen receptor-1 traffics between plasma membrane and nucleus and activates MEK-ERK-CREB signaling in primary

cortical culture. Lopes DCF, Novaes LS, Santos NB, Duque EA, Wiezel G, Scavone C, Munhoz CD USP – Farmacologia

02. Neuropharmacology

02.001 **Time-course analysis of prostaglandin E2 receptor immunoreactivity following pilocarpine-induced *status epilepticus***. Grigoletto J, Funck VR, Oliveira CV, Grauncke ACB, Souza TL, Guerra GP, Oliveira MS UFSM – Physiology and Pharmacology

02.002 **Characterization of behavior and cognitive alterations after pilocarpine-induced *status epilepticus* in C57BL/6 mice**. de Oliveira CV, Grigoletto J, Funck VR, Grauncke ACB, de Souza TL, Oliveira MS UFSM – Fisiologia e Farmacologia

02.003 **Potentiation of the effect of phenobarbital with Montelukast in pentylenetetrazol-induced seizures**. Jesse AC, Marafiga JR, Fleck J, Mello CF UFSM – Physiology and Pharmacology

02.004 **Decreased Na^+,K^+-ATPase activity after pilocarpine-induced *status epilepticus* in mice**. Grauncke ACB, Funck VR, de Oliveira CV, Grigoletto J, de Souza TL, Pereira LM, Guerra GP, Oliveira MS UFSM – Fisiologia e Farmacologia

02.005 **Long-term treatment with Cilostazol reverts the retrograde amnesia caused by chronic cerebral hypoperfusion in middle-aged rats**. Godinho J, Bacarin CC, Ferreira EDF, Zaghi GGD, Oliveira RMMW, Milani H UEM – Farmacologia e Terapêutica

02.006 **Effects of fish oil on ischemia-induced retrograde amnesia**, **oxidative stress**, **and neurodegeneration**. Bacarin CC[1], de Sá-Nakanishi AB[2], Bracht A[2], Ferreira EDF[1], Oliveira RMMW[1], Milani H[1] [1]UEM – Farmacologia e Terapêutica, [2]UEM – Bioquímica

02.007 **CysLTR antagonists decrease pentylenetetrazol-induced seizures**. Marafiga JR, Lenz QF, Jesse AC, Mello CF UFSM – Physiology and Pharmacology

02.008 **Fish oil reduces cognitive deficits after acute cerebral ischemia**, **but not after chronic cerebral hypoperfusion in middle-aged rats**. Ferreira EDF, Zaghi GGD, Romanini CV, Oliveira RMMW, Milani H UEM – Farmacologia e Terapêutica

02.009 **Oral and prolonged administration of rotenone in mice induces motor impairment and anxiogenic-like behavior**. Zaminelli T, Zilli TLS, Fabeni F, Ferreira FF, Gradowski RW, Bassani TB, Barbiero JK, Santiago RM[1], Vital MABF UFPR – Pharmacology

02.010 **Anxiolytic-like effect of acute podoandin administration in mice**. Bonato JM[1], Schiavon AP[2], Amoah SKS[3], Biavatti MW[2], Oliveira RMMW[1] [1]UEM – Pharmacology and Therapeutics, [2]UFSC – Pharmaceutical Sciences

02.011 **Antidepressant-like effect of curcumin in 6-hydroxydopamine model of Parkinson's disease**. Gradowski RW, Zaminelli T, Santiago RM, Bassani TB, Barbiero JK, Vital MABF UFPR- Farmacologia

03. Psychopharmacology

03.001 Chronic postnatal administration of methylmalonic acid provokes spatial memory deficits in rats. de Souza TL, Grauncke ACB, Della-Pace ID, Fiorin FS, de Castro M, Busanello G, Ribeiro LR, Royes LFF, Furian AF, Oliveira MS UFSM

03.002 Behavioral profile and brain molecular characterization of elastase 2A knockout mice. Diniz CRAF[1], Casarotto PC[1], Becari C[2], Guimarães FS[1], Guimarães AO[3], Salgado HC[2], Bader M[4], Pesquero JB[3], Salgado MC[1], Joca SRL[5] [1]FMRP-USP – Pharmacology, [2]FMRP-USP – Physiology, [3]Unifesp – Biophysics, [4]Max-Delbrück – Molecular Medicine, [5]FCFRP-USP – Physics and Chemistry

03.003 Involvement of PI3K-class I gamma in acute effects of antidepressant drugs in mice. Vaz GN[1], Campos AC[1], Teixeira AL[1], Lima IVA[2] [1]UFMG – Tropical Medicine and Infectious Diseases, [2]ICB-UFMG – Pharmacology

03.004 Cannabidiol pretreatment reverses amphetamine-disruptive effects in the prepulse inhibition test in *Swiss* mice. Pedrazzi JFC[1], Issy AC[2], Guimarães FS[2], Del Bel EA[3] [1]FMRP-USP – Neurociências e Ciências do Comportamento, [2]FMRP-USP – Farmacologia, [3]FORP-USP – Morfologia, Estomatologia e Fisiologia

03.005 Arcaine attenuates morphine-induced conditioned place preference in mice. Tomazi L[1], Mello CF[1], Schoffer AP[1], Girardi BA[2], Rubin MA[3] [1]UFSM – Pharmacology, [2]UFSM – Toxicological Biochemistry, [3]UFSM – Pharmacology

03.006 Spermine reverses LPS-induced memory deficit in mice. Frühauf PKS[1], Ineu RP[1], Rossato MF[2], Mello CF[1], Rubin MA[1] [1]UFSM – Pharmacology, [2]UFSM – Toxicological Biochemistry

03.007 Evaluation of the effect of acute administration of agomelatine on the behavior of female rats in the elevated plus maze and forced swimming tests. Mendes CRM[1], Andrade AS[1], André E[2], Gavioli EC[1], Maia JP[3], Soares-Rachetti VP[1] [1]UFRN – Biofísica e Farmacologia, [2]UFPR – Farmacologia, [3]UFRN – Clínica Médica

03.008 Depressive-like behavioral phenotype of galectin-1 and 3 knock-out mice. Sartim AG[1], Joca SRL[1], Baruffi MD[2] [1]FCFRP-USP – Física e Química, [2]FCFRP-USP – Análises Clínicas, Toxicológicas e Bromatológicas

03.009 Acute systemic administration of DNA methylation inhibitors induces antidepressant-like effects: **Involvement of cortical BDNF-TRKB-mTOR pathway**. Romano ACD, Pereira VS, Joca SRL USP

03.010 Environmental enrichment and its protective effect on stress-induced anxiety: **implications of glucocorticoid signaling**, **MAPK pathway and CREB in basolateral amygdale**. Novaes LS, Santos NB, Lopes DCF, Duque EA, Wiezel G, Munhoz CD ICB-USP – Farmacologia

03.011 Participation of κ and μ opioid receptors in aversive behavior elicited by electrical stimulation in the dorsal periaqueductal gray. Almeida CB[1], Rangel MP[1], Roncon CM[1], Zangrossi Jr H[2], Graeff FG[2], Audi EA[1] [1]UEM – Farmacologia e Terapêutica, [2]USP – Farmacologia

03.012 Involvement of induced nitric oxide synthase in anxiety-like effects during ethanol withdrawal in mice. Bonassoli VT, Milani H, de Oliveira RM UEM – Farmacologia e Terapêutica

04. Inflammation

04.001 Evaluation of involvement of B_1 and B_2 kinin receptors in systemic inflammation induced by Periodontitis. Prestes AP, Machado WM, Olchanheski Junior LR, Fernandes D UEPG – Pharmaceutical Sciences

04.002 The effect of mirtenol in models of acute inflammation carrageenan-induced in rats. Gomes BS, Sousa-Neto BP, Sousa DP, Oliveira RCM, Oliveira FA NPPM-UFPI

04.003 Chronic administration of methylmalonate induces neuroinflammation in young rats. Ribeiro LR, Ferreira APO, Funck VR, de Oliveira CV, Furian AF, Oliveira MS, Royes LFF, Fighera MR UFSM

04.004 Role of hydrogen sulfide on apoptotic proteins expressions in allergic mice lungs. Mendes JA[1], Ribeiro MC[2], Ferreira HHA[2] [1]Unicamp – Farmacologia, [2]USF – Alergia e Inflamação

04.005 Anti-inflammatory activity of a new pyrazole derivative – LQFM 021. Florentino IF[1], Galdino PM[2], Oliveira LP[2], Sousa LV[2], Menegatti R[1], Costa EA[2] – [1]FF-UFG, [2]ICB-UFG

04.006 Inosine effects on inflamed skin: **Purine P1(A_{2A}) receptor as a target**. Oliveira BDV[1], Lapa FR[2], Otuki MF[1], Santos ARS[2], Cabrini DA[1] [1]UFPR – Farmacologia, [2]UFSC – Farmacologia

04.007 New strain of Proteus sp. potentiates LTC_4 expression in lung inflammatory response induced by LPS. Ferreira RR[1,2], Tambellini VY[1], Silva RC[3], dos Santos LA[2], Balbino AM[2], Vasconcellos SP[4], Fernandes L[2], Landgraf MA[2,5], Landgraf RG[2] [1]ICB-USP – Biotério Central, [2]Unifesp-Diadema – Inflamação e Farmacologia Vascular, [3]Unifesp – Medicina Translacional, [4]Unifesp-Diadema – Ciências Biológicas, [5]ICB-USP – Farmacologia

04.008 Investigation of topical photodynamic effect of cationic porphyrin. Carrenho LZB[1], Vandresen CC[1], Dallagnol JCC[1], Gonçalves AG[1], Noseda MD[2], Noseda MED[2], Ducatti D[2], Orsato A[2], Cabrini DA[3], Barreira SMW[1], Otuki MF[3] [1]UFPR – Ciências Farmacêuticas, [2]UFPR – Bioquímica, [3]UFPR – Farmacologia

04.009 Standardization of animal model for screening of wound healing substances. Souza BB, Magalhães JF, Castro AB, Raimundo JM, Bonavita AG UFRJ

04.010 Preventive and therapeutic anti-TNF-α therapy with pentoxifylline decreases arthritis and the associated periodontal co-morbidity in mice. Queiroz-Junior CM[1], Bessoni RLC[1], Costa VV[2], Souza DG[2], Teixeira MM[3], Silva TA[1] [1]UFMG – Oral Pathology, [2]UFMG – Microbiology, [3]UFMG – Biochemistry and Immunology

04.011 Tumor necrosis factor-alpha reduces adenosine diphosphate-induced platelet aggregation. Bonfitto PHL, Marcondes S, Antunes E FCM-Unicamp

04.012 Endothelial cell P2Y1 receptor purinergic signaling during chronic inflammation. Oliveira SDS[1,2], Oliveira NF[1], Coutinho-Silva R[2], Savio LE[2], Fernandes JRM[3], Silva CLM[1] [1]UFRJ – Farmacologia Bioquímica e Molecular, [2]UFRJ – Imunologia, [3]IBqM-UFRJ

04.013 Anti-inflammatory effect of methanolic extract and guanidine alkaloid N-1, **N-2**, **N-3-triisopentenylguanidine from alchornea glandulosa in mice**. Iwamoto RD[1], Formagio Neto F[1], Formagio ASN[2], Sarragiotto MH[3], Vieira MC[2], Kassuya CAL[1] [1]UFGD – Health Science, [2]UFGD – Agricultural Science, [3]UEM – Chemistry

04.014 Nitroxyl donor reduces septic arthritis inflammation in mice. Staurengo-Ferrari L[1], Miyazawa KWR[1], Domiciano TP[1], Ribeiro FAP[1], Pelayo JS[2], Miranda K[3], Casagrande R[4], Verri Junior WA[1] [1]UEL – Patologia, [2]UEL – Microbiologia, [3]University of Arizona, [4]UEL – Ciências Farmacêuticas

04.015 Role of glucocorticoid receptors on the transcription of genes related to LPS(*iv*)-induced effect on rat pineal gland. Fernandes PACM, Tamura EK, da Silveira Cruz-Machado S, Marçola M, Carvalho-Sousa CE, Muxel SM, Markus RP IB-USP – Fisiologia

04.016 Inhibitory effects of staphylococcal enterotoxin type A (SEA) and B (SEB) on mice bone marrow eosinophil adhesion *in vitro*. Ferreira-Duarte AP[1], Torres ASP[1], de Souza IA[1], Mello GC[2], Antunes E[2], Squebola-Cola DM[2] [1]FMJ – Biology and Physiology, [2]FCM-Unicamp

04.017 Dipyrone and its active metabolites produce antipyretic effect by acting at central nervous system. Malvar DC, Vaz LLV, Assis DCR, Melo MCC, Aguiar FA, Clososki GC, Souza GEP FCFRP-USP – Física e Química

05. Pain and Nociception

05.001 Neuropathic pain following spinal cord injury: **A possible role of endothelin ET_A and ET_B receptors**. Forner S, Martini AC, Rae GA UFSC – Farmacologia

05.002 TRPA1 receptor agonist sensitizes peripheral nociceptors from rats with painful peripheral mononeuropahty to mechanical stimuli. Scarante FF, Schreiber AK, Jesus CHA, Justa HC, Cunha JM UFPR – Pharmacology

05.003 Inflammatory mechanisms by which the sustained isometric contraction induces hyperalgesia in rats. Melo B[1], Santos DF[1], Jorge CO[1], Garcia J[1], Parada CA[2], Oliveira-Fusaro MCG[1] [1]FCA-Unicamp, [2]IB-Unicamp

05.004 TRPA1 receptor stimulation by hydrogen peroxide is critical to trigger pain and inflammation during acute gout attack. Trevisan G[1], Hoffmeister C[1], Rossato MF[1], Oliveira SM[1], Silva MA[1], Silva CS[1], Nassini R[2], Materazzi S[2], Fusi C[2], Petri GP[3], Geppetti P[2], Ferreira J[4] [1]UFSM, [2]University of Florence, [3]UTFPR, [4]UFSC

05.005 Muscle hyperalgesia is mediated by neutrophils and P2X3 receptors. Jorge CO[1], Melo B[1], Santos DF[1], Parada CA[2], Oliveira-Fusaro MCG[1] [1]FCA-Unicamp, [2]IB-Unicamp

05.006 Development of a new model of muscle hyperalgesia. Santos DFS[1], Melo B[1], Jorge CO[1], Garcia J[1], Parada CA[2], Oliveira-Fusaro MCG[1] [1]FCA-Unicamp, [2]IB-Unicamp

05.007 Involvement of TRPV-1 and TRPA-1 channels in the antinociceptive and antiedematogenic effects of hydroalcoholic extract from *Machaerium hirtum* (Vell.)Stellfeld (Barks). Lopes JA[1], Nishijima CM[1], de Souza Maria NCV[2], Sannomiya M[2], Rocha LRM[1], Hiruma-Lima CA[1] [1]IBB-Unesp-Botucatu – Fisiologia, [2]EACH-USP

05.008 New muscarinic agonist reversed thermal hyperalgesia and mechanical allodynia signs in model of morphine-induced tolerance in rats. Monteiro CES[1], Nascimento-Júnior N[2], Zapata-Sudo G[1], Fraga CAM[2], Barreiro EJ[2], Sudo RT[1] [1]ICB-UFRJ – Desenvolvimento de Fármacos, [2]FF-UFRJ

05.009 Role of interleukin-33/ST2 receptor signaling in chronic constriction injury-induced neuropathic pain in mice. Zarpelon AC[1], Rodrigues FC[1], Carvalho TT[1], Souza GR[2], Ferreira SH[2], Alves-Filho JC[2], Liew FY[3], Cunha TM[2], Cunha FQ[2], Verri Junior WA[1] [1]UEL – Patologia, [2]FMRP-USP – Farmacologia, [3]University of Glasgow – Immunology, Infection and Inflammation

05.010 Thalidomide reduces delayed-onset muscle soreness (DOMS) induced by intense acute swimming in mice. Borghi SM[1], Pinho-Ribeiro FA[1], Zarpelon AC[1], Cardoso RDR[1], Casagrande R[2], Verri Junior WA[1] [1]UEL – Ciências Patológicas, [2]UEL – Ciências Farmacêuticas

05.011 Depot dexamethasone delays allodynia development and inhibits dorsal root ganglion NF-kappa B translocation in sciatic nerve-injured rats. Bastos LFS[1], Vago JP[2], Caux TR[2], Costa BL[3], Godin AM[4], Menezes RR[4], Pena RR[1], Machado RR[4], Fialho SL[3], Sousa LP[2], Moraes MFD[1], Coelho MM[4] [1]UFMG – Fisiologia e Biofísica, [2]UFMG – Análises Clínicas e Toxicológicas, [3]FUNED – Desenvolvimento Farmacotécnico, [4]UFMG – Produtos Farmacêuticos

05.012 Evaluation of the antinociceptive effect of Y-terpinene and possible mechanisms of action in mice. Freitas FFBP[1], Souza RDS[1], Reis Filho AC[1], Sousa SEL[1], Sousa DP[2], Almeida FRC[1] [1]NPPM-UFPI, [2]UFS – Pharmacy

05.013 Antinociceptive activity of the ethanolic extract from the flowers of *Acmella oleracea* (L.) R.K. Jansen in mice. Corso CR[1], Nomura EO[1], Hocayen PAS[1], Nascimento AM[2], Cipriani TR[2], Baggio CH[1], Werner MFP[1] [1]UFPR – Farmacologia, [2]UFPR – Bioquímica

05.014 Antinociceptive effect of dipyrone and its metabolites on hyperalgesia induced by carrageen and prostaglandin E_2. Assis DCR[1], Malvar DC[1], Vaz ALL[2], Melo MCC[1], Rae GA[3], Clososki GC[2], Souza GEP[1] [1]FCFRP-USP – Física e Química, [2]FCFRP-USP – Química Organic, [3]UFSC – Farmacologia

05.030 Effects of the pro-resolving lipid mediator lipoid A4 on neuropathic pain following spinal cord hemi section in rats. Martini AC, Forner S, Rae GA UFSC – Farmacologia

06. Cardiovascular and Renal

06.001 Effect vascular of ethanolic extract of leaves *Vitex polygama* Cham. (Lamiaceae). Vidal MC, Carneiro A, Ferreira LLDM, Konno TUP[1], Guimarães DO[1], Leal ICR[1], Muzitano MF[1], Raimundo JM[1] [1]UFRJ

06.002 New agonist of adenosine receptor reduces cardiac and vascular dysfunction in rats with monocrotaline-induced pulmonary hypertension. Pereira SL[1], Alencar AKN[1], Ferraz EB[2], Tesch R[1], Nascimento JHM[2], Maia R[1], Fraga CAM[1], Barreiro EJ[1], Sudo RT[1], Zapata-Sudo G[1] [1]ICB-UFRJ, [2]IBCCF-UFRJ

06.003 Estrone acutely relaxes rat aorta through an endothelium-dependent mechanism: **role of nitric oxide**. Oliveira TS, Oliveira LM, Filgueira FP, Ghedini PC UFG – Fisiologia e Farmacologia

06.004 Evaluation of cardiac and renal markers function in Wistar rats treated with different clozapine-loaded nanosystems. Güllich AAC[1], Coelho RP[1], Pereira MP[1], Mezzomo J[1], Pilar BC[1], Ströher DJ[1], Galarça LASL[1], Piccoli JCE[1], Haas SE[1], Puntel RL[2], Manfredini V[1] [1]Unipampa – Estresse Oxidativo, [2]Unipampa – Nutrição, Saúde e Qualidade de Vida

06.005 Cardioprotective activity of subcutaneously administered pyridostigmine. Souza ACM[1], Barcellos NMS[1], Frezard FJG[2], Guimarães HN[3], Castro QJT[1], Pereira SC[1], Grabe-Guimarães A[1] [1]UFOP – Farmácia, [2]UFMG – Fisiologia e Biofísica, [3]UFMG – Engenharia

06.006 Effect of ethanolic extract the fruit peel from *Platonia insignis* on the cardiovascular system in rats. Mendes MB, Santos MEP, Azevedo PSS, Sabino CKB, Arcanjo DDR, Chaves MH, Oliveira AP UFPI – Plantas Medicinais

06.007 Hypotensive effect of ethyl acetate fraction the fruit peel from *Platonia insignis* Mart. in rats. Mendes MB, Silva-Filho JC, Arcanjo DDR, Chaves MH, Oliveira RCM, Oliveira AP, Moura LHP, Campelo RT, Resende-Junior LM UFPI – Plantas Medicinais

06.008 Vasorelaxant effect induced by thymol in porcine coronary artery rings. Mendes-Neto JM[1], Nascimento RS[1], Diniz JM[1], Guedes DN[1], Medeiros IA[2], Costa KVMC[1], Gonçalves IGA[3], Albuquerque KLGD[1], Correia NA[1] [1]UFPB – Fisiologia e Patologia, [2]UFPB – Biotecnologia, [3]UFPB – Ciências Farmacêuticas

06.009 Reduction in CINC-2 and IL-18 expression is related to improvement of renal function, in intrauterine undernourished rats. Landgraf MA[1,2], Hirata AE[3], Landgraf RG[2], Correa-Costa M[4], de Marco DTK[3], Semedo P[5], Gil FZ[3], Câmara NOS[4] [1]Unifesp – Pharmacology, [2]Unifesp – Inflammation and Vascular Pharmacology, [3]Unifesp – Physiology, [4]USP – Immunology, [5]Unifesp – Nephrology

06.010 Compensatory cardiac leptin receptor upregulation and P-Type ATPases modulation in rats submitted to neonatal leptin treatment. Marques EB, Silva RM, Graça RO, Scaramello CBV UFF – Farmacologia Experimental

06.011 Effects of the selective TRPV4 Modulators GSK1016790A and HC-067047 in isolated arteries from several species. Silva JDP, Alves Filho FC, Ballejo G FMRP-USP – Pharmacology

06.012 Acute ethanol intake induces endothelial dysfunction in rat aorta. Hipolito UV[1], Callera GE[2], Touyz RM[2], Batalhao ME[3], Carnio EC[3], Tirapelli CR[3] [1]FMRP-USP – Farmacologia, [2]Universidade de Ottawa, [3]EERP-USP

06.013 Short pre-exposure to sodium nitrite does not induce tolerance in rat aorta. Banin TM, Bendhack LM FCFRP-USP – Física e Química

06.014 Mitochondrial reactive oxygen species mediate the modulation of vascular contraction by periaortic adipose tissue. Costa RM[1], Filgueira FP[2], Carvalho MHC[2], Akamine EH[2], Lobato NS[1] [1]UFG – Biological Sciences, [2]ICB-USP

06.015 Nitroglycerin but not the new nitric oxide donor RuBPY phosphorylates eNOS-Ser1177. Paulo M, Grando MD, Vercesi JA, da Silva RS, Bendhack LM FCFRP-USP – Física e Química

06.016 Evaluation of cardioprotection ipriflavone in rats submitted to the left coronary ligature. Castro QJT[1], Albuquerque K[1], Carneiro CM[1], Guimarães HN[2], Leite R[1], Mosqueira VCF[1], Grabe-Guimarães A[1] [1]CiPharma-UFOP, [2]DEE-UFMG – Engenharia

06.017 Evaluation of the mechanism of action of Riparin I, II and III of relaxation in mice mesenteric artery. Garcia DCG[1], Barbosa-Filho JM[2], Lemos VS[3], Cortes SF[1] [1]UFMG – Pharmacology, [2]UFPB – Pharmaceutical Technology, [3]UFMG – Physiology and Biophysics

06.018 Characterization of cardiovascular function and anthropometric parameters with aging in rats. Marques EB, Barros RB, Rocha NN, Scaramello CBV MFL-LAFE-UFF

06.019 Involvement of calcium on the positive inotropic effect produced by ATP and UTP right atria in hypertensive rats. Rodrigues JQD, Silva-Junior ED, Câmara H, Miranda-Ferreira R, Galvão KM, Caricati-Neto A, Jurkiewicz NH, Jurkiewicz A Unifesp – Pharmacology

06.020 New anti-inflammatory prototypes present anti-atherosclerotic effects through NF-kB inhibition. Vieira TBQ[1], Motta NAV[1], Fumian MM[1], Barreiro EJ[2], Maia RC[2], Kummerle AE[3], Brito FCF[1] [1]LAFE-FF-UFF – Fisiologia e Farmacologia, [2]LASSBio-UFRJ, [3]UFRRJ – Química

06.021 Immunological tolerance to cardiac antigens improves healing after myocardial infarction. Ramos ERB, Ramos GC, Rezende Junior E, Bicca MA, Assreuy F UFSC – Farmacologia

06.064 Oxidation of DHA is responsible for its anti-arrhythmic effects on mouse ventricular myocytes. Roy J, Olivia TM, Roussel J, Oger C, Galano JM, Pinot E, Durand T, Le Guennec JY INSERM – Physiology cardiovascular

09. Natural Products and Toxinology

09.001 Evaluation of kinetics in the cell cycle of lymphocytes *Cebus apella* exposed to carcinogen N-methyl-N-nitrosourea (MNU) and treated with Canova®. Feio DCA[1], Muniz JAPC[2], Burbano RMR[1], Brito Junior LC[3], Lima PDL[4] [1]ICB-UFPA – Citogenética Humana, [2]MS – Primatas, [3] ICB-UFPA – Patologia Geral, Imunopatologia e Citologia, [4]CCBS – Biologia Molecular

09.002 Evaluation of the mechanisms of action involved in the gastroprotection of *Serjania marginata* in rodents. Périco LL[1], Beserra FP[1], Ganev EG[1], Heredia Vieira SC[2], Vilegas W[2], Rocha LRM[1], Hiruma-Lima CA[1] [1]Unesp-Botucatu – Fisiologia, [2]Unesp-Araraquara – Química Orgânica

09.003 Effects of the essential oil of *Croton zehntneri* and its major components, **anethole and estragole**, **on the rat *corpora cavernosa***. Cabral PH[1], Campos RM, Fonteles MC[1], Santos CF, Lessa LMA, Cardoso JHL, Nascimento NRF[2] [1]UFC – Physiology and Pharmacology, [2]UECE

09.004 Beneficial effects of dicaffeoylquinic acid-rich fraction from leaves of *Arctium lappa* on gastrointestinal complications associated with *Diabetes mellitus*. da Silva LM[1], Ferreira-Maria D[1], Carlotto J[2], Cipriani TR[2], Souza LM[2], Baggio CH[1], Werner MFP[1] [1]UFPR – Farmacologia, [2]UFPR – Bioquímica

09.005 Spleen morphology and splenic corpuscles morphometry in diabetic rats induced with streptozotocin and treated with *Azadirachta indica*, a. Juss and streptozotocin 6CH. Corsini TB[1], Pacheco MR[1], Amoroso L[1], Baraldi-Artoni SM[1], Machado MRF[1], Santos E[1], D'Angelis FHF[1], Rivera GG[1] [1]FCAV-Unesp-Jaboticabal – Morfologia e Fisiologia Animal

09.006 Evaluation of the antioxidant mechanism of ethanolic *Azadirachta indica* (Neem) extract. Takayama KS[1], Souza CR[1], Baracat MM[1], Casagrande R[1], Georgetti SR[1] [1]UEL – Ciências Biológicas

09.007 The NO/sCG pathway involvement in vasorelaxant effect of *Lippia origanoides* ethanol extract on rat mesenteric artery. Campelo RT[1], Carvalho GD[1], Moura LHP[1], Sousa TO[2], Citó AMGL[2], Arcanjo DDR[1], Oliveira AP[1] [1]NPPM-UFPI, [2]UFPI – Química

09.008 Vasorelaxant effect of the ethyl acetate fraction from *Mimosa caesalpiniifolia* flowers extract in rat mesenteric artery. Moura LHP[1], Campelo RT[1], Santos MEP[1], Rezende Junior LM[1], Silva-Filho JC[1], Monção NBN[2], Citó AMGL[2], Oliveira RCM[1], Arcanjo DDR[1], Oliveira AP[1] [1]NPPM-UFPI, [2]UFPI – Química

09.009 *Vochysia bifalcata*: Biological activity for a reforestation species. Horinouchi CDS, Mendes DAGB, Soley BS, Cabrini DA, Otuki MF UFPR – Farmacologia

09.010 Active fractions of *Celtis iguanaea* (Jacq.) Sargent (Cannabaceae). Sousa LV, Oliveira LP, Silva DPB, Florentino IF, Nascimento MVM, Costa EA UFG – Farmacologia de Produtos Naturais

09.011 Effect of ethyl acetate fraction of *Harpagophytum procumbens* on cell viability *in vitro*. Schaffer LF[1], Peroza LR[2], Alves SH[1], Fachinetto R[1,2], Wagner C[1] [1]UFSM – Farmacologia, [2]UFSM – Ciências Biológicas: Bioquímica Toxicológica

09.012 Evaluation of crude extracts of Norte-Fluminense plants in the process of cutaneous wound healing in rats. Rodrigues AAM[1], Magalhães JF[1], Castro AB[1], Leal ICR[2], Muzitano MF[2], Raimundo JM[1], Bonavita AG[1] [1]UFRJ – Laboratório Integrado de Pesquisa, [2]UFRJ – Produtos Naturais

09.013 Rhamnogalacturonan from *Acmella oleracea* (L.) R.K. Jansen: gastroprotective and ulcer healing properties. Ferreira DM[1], da Silva LM[1], Mendes DAGB[1], Nascimento AM[2], Iacomini M[2], Cipriani TR[2], Santos ARS[3], Werner MFP[1], Baggio CH[1] [1]UFPR – Pharmacology, [2]UFPR – Biochemistry and Molecular Biology, [3]UFSC – Physiological Sciences

09.014 Effect of hesperidin methyl chalconhe in acute lung injury induced by LPS. Domiciano TP[1], Staurengo-Ferrari L[1], Casagrande R[2], Verri Junior WA[1] [1]UEL – Ciências Patológicas, [2]UEL – Ciências Farmacêuticas

09.015 *In vitro* antioxidant activity of ethanol extract of pods from *Samanea tubulosa* (Benth). Sales PAB, Oliveira JMG, Nogueira Neto JD, Oliveira MS, Sousa MRSC, Moura ER, Costa APR NPPM-UFPI

09.016 Possible involvement of calmodulin and PI3K on endothelium-dependent relaxation evoked by butanolic fraction of *Caryocar brasiliense* Camb. leaves in rat thoracic aorta. Oliveira LM, Oliveira TS, Costa EA, Filgueira FP, Ghedini PC UFG – Ciências Fisiológicas

09.017 The inhibitory effect of crotoxin on the functionality of bone marrow neutrophils contributes to its long-lasting anti-inflammatory properties. Lima TS[1,2], Oliveira RBB[1], Neves CL[1], Sampaio SC[1], Cirillo MC[1] [1]IBu – Pathophysiology, [2]IB-USP – Physiology

09.018 Oxidative stress markers after acute treatment with fumonisin B1 and pentylenetetrazol in liver of mice. Poersch AB, Lima CO, Trombetta F, Souto NS, Ribeiro LR, Furian AF UFSM – Physiology and Pharmacology

09.019 Effect of *Ocimum americanum* L essential oil effect on the leukocyte behavior evaluated by *in vivo* microcirculation technique. Bastos RL, Yamada AN, Grespan R, Bersani-Amado CA, Cuman RKN UEM – Pharmacology and Therapeutic

09.020 Chemical composition and *in vitro* antimicrobial activity of the essential oil of *Nectandra grandiflora*. Murari AL[1], Heinzmann BM[2], Beutinger D[3], Peres MM[3], Gressler LT[4], Vargas APC[4], Silva DT[5], Longhi SJ[5] [1]UFSM – Farmacologia, [2]UFSM – Farmacologia / Engenharia Florestal, [3]UFSM – Farmácia, [4]UFSM – Medicina Veterinária, [5]UFSM – Engenharia Florestal

09.021 Myocardial protective effects induced by the ethanol extract of leaves of *Alpinia speciosa* (Zingiberaceae) in infarcted rats with isoproterenol. Tenório EP[1], Ferreira AKB[1], Barbosa DP[2], Brandão RAB[3], Smaniotto S[3], Araújo-Júnior JX[4], Ribeiro EAN[1] [1]UFAL – Enfermagem e Farmácia, [2]UFAL – Química e Biotecnologia,

[3]UFAL – Ciências Biológicas e da Saúde, [4]UFAL – Enfermagem e Farmácia / Instituto de Química e Biotecnologia

10. Cancer and Cell Proliferation

10.001 Cytotoxic activity of thiophene derivative on pancreatic carcinoma cell line (Panc). Carvalho MS[1], Rocha HAO[2], Moura RO[3], Mendonça FJB[3], Aguiar ACV[1] [1]UFRN – Biofísica e Farmacologia, [2]UFRN – Bioquímica, [3]UEPB – Ciências Biológicas

10.002 Evaluation cytotoxic of thiophene derivative in PANC and PC3 cells. Aguiar ACV[1], Câmara RBG[1], Rocha HAO[1], Mendonça Junior FJB[2], Moura RO[2], Carvalho MS[3] [1]UFRN – Bioquímica, [2]UEPB – Ciências Biológicas, [3]UFRN – Biofísica e Farmacologia

10.003 Evaluation of antitumoral activity of canthinone alkaloid. Torquato HFV[1], Paredes-Gamero EJ[2], Buri MV[2], Ribeiro-Filho AC[2], Martins DTO[1] [1]UFMT – Pharmacology, [2]Unifesp – Biochemistry

10.004 Evaluation of antitumor activity of the hexane extract of *Calophyllum brasiliense* Camb. Torquato HFV[1], Buri MV[2], Paredes-Gamero EJ[2], Ribeiro-Filho AC[2], Martins DTO[1] [1]UFMT – Farmacologia, [2]Unifesp – Biochemistry

10.005 Mebendazole induces citotoxity, apoptosis and reduce metaloproteinases expression in gastric cancer cell line (AGP-01). Pinto LG[1], Soares BM[1], Barreto LH[1], Assumpção PM[2], Riggins GJ[2], Burbano RMR[1], Montenegro RC[1] [1]UFPA – Citogenética Humana, [2]Johns Hopkins University – Medicine

10.006 Study of pterocarpanquinone LQB 118 effects on prostate tumor cell line. Martino T[1], Jordão FC[1], Justo GA[1], Coelho MGP[1], Costa PRR[2], Sabino KCC[1] [1]UERJ – Bioquímica, [2]NPPN-UFRJ

10.007 *In vitro* anticancer potential of essential oils from *Piper* species of the Amazon. Pinto AVU[1], Pinto LC[1], Soares BM[1], Barreto LH[1], da Silva JKR[2], Maia JGS[2], Andrade EHA[3], Burbano RMR[1], Montenegro RC[1] [1]UFPA – Laboratório de Citogenética Humana, [2]UFPA – Química

10.008 Comparison of antitumor activity of *Blechnum occidentale* L. (Blechnaceae) between native and cultivated plants. Nonato FR[1], Ruiz ALTG[1], Silva EB[2], Oliveira LM[2], Veiga LF[3], Melo PS[3], Alencar SM[3], Carvalho JE[1] [1]CPQBA-Unicamp – Farmacologia e Toxicologia, [2]UEFS – Ciências Biológicas, [3]ESALQ-USP – Agroindústria, Alimentos e Nutrição

10.009 RNA interference with nNOS reinforces the IFN-γ injury in glioma cell lines. Resende FFB[1], Silva SS[1], Caldeira FMC[1], Pardo L[2], Stühmer W[2], Del Bel EA[3], Titze-de-Almeida R[1] [1]FAV-UnB – Tecnologias para Terapia Gênica, [2]Max-Planck-Institute – Molecular Biology of Neuronal Signals, [3]FORP-USP – Neurofisiologia e Biologia

10.010 Toll-like receptor 4 (TLR4) regulates signaling proliferation on human melanoma cells. Souza MJ, Ribeiro-Pereira C, Barja-Fidalgo C UERJ – Biologia Celular

10.011 Silencing EAG1 enhances temozolomide effects on glioblastoma cells in culture. Sales TT[1], Resende FFB[1], Rocha WS[1], Del Bel EA[2], Pardo L[3], Stühmer W[3], Titze-de-Almeida R[1] [1]FAV-UnB – Terapia Gênica, [2]FORP-USP – Neurofisiologia e Biologia Molecular, [3]Max-Planck-Institute – Molecular Biology of Neuronal Signals

10.012 Effects of the calcium channels blocker verapamil on surgically damaged liver under the biological curative amniotic membrane (homogenous) in rats: **Immunohistochemistry study**. Vilela-Goulart MG, Gomes MF, Bastos-Ramos WP CEBAPE-Unesp-São José dos Campos

10.013 Evaluation cytotoxic of compound thiophenic 6CN-10 in pancreatic carcinoma. Aquino ACQ[1], Carvalho MS[1], Aguiar ACV[1], Rocha HAO[2], Moura RO[3], Mendonça Junior FJB[3] [1]UFRN – Biofísica e Farmacologia, [2]UFRN – Bioquímica, [3]UEPB – Ciências Biológicas

10.014 Production of melatonin by Glioma cell lines. Kinker GS[1], Marie SK[2], Oba-Shinjo SM[2], Muxel SM[1], Carvalho-Sousa CE[1], Fernandes PA[1], Markus RP[1] [1]IB-USP – Fisiologia, [2]FM-USP – Neurologia

Poster session 2 – Wednesday 30/10/13

01. Cellular and Molecular Pharmacology

01.012 Bufalin promotes epithelial to mesenchymal transition in LLC-PK1 cells. Martins-Ferreira J, Ferreira LLB, Cunha-Filho GA, Quintas LEM, Noël FG ICB-UFRJ

01.013 Relaxin and Follicle-Stimulating Hormone (FSH) differentially affect signaling pathways and cell cycle gene expression in prepuberal rat sertoli cells. Nascimento AR, Lucas TFG, Porto CS, Lazari MFM Unifesp – Farmacologia

01.014 Effect of hydrogen peroxide in the metabolic activity and viability of adults stem cells. Machado AK[1], Cadoná FC[2], Homrich SG[3], Treichel TLE[3], Aramburú Jr JS[3], Pippi NL[3], Rodrigues CCR[3], Duarte MMMF[3], Saldanha JRP[3], Duarte T[3], Cruz IBM[1,2,3] [1]UFSM – Pharmacology, [2]UFSM – Toxicology Biochemistry, [3]UFSM – Biogenomics

01.015 New surgical procedure using permissive hypoxia in reperfusion decreases inflammation and edema from ischemia-reperfusion syndrome in hind limb of sheep. Neves DQ[1], Massucati-Negri M[1], Grees MAK[2], Castro DS[2], Ascoli FO[1], Marostica E[1] [1]UFF – Physiology and Pharmacology, [2]UFF – Veterinary Medicine

01.016 Effect of multifactorial malnutrition in rat vas deferens: **Ca^{2+} Modulators of alfa1-adrenergic signaling**. Bezerra CGP[1], Muzi-Filho H[2], Silva AMS[3], Zapata-Sudo G[3], Sudo RT[3], Einicker-Lamas M[2], Vieyra A[2], Lara LS[1], Cunha VMN[1] [1]UFRJ – Farmacologia e Inflamação, [2]IBCCF-UFRJ, [3]UFRJ – Pesquisa e Desenvolvimento de Fármacos

01.017 Daily variation of microRNAs expression in endothelial progenitor cells. Marçola M[1], Ramos CML[2], Parmigiani RB[2], Camargo AA[2], Markus RP[1] [1]IB-USP – Physiology, [2]IEP-HSL – Molecular Oncology

01.018 Activation of the Kinin B1 receptor modulates pathways involved in protein metabolism and skeletal muscle mass control. Parreiras-e-Silva LT[1], Reis RI[1], dos Santos GA[1], Pires-Oliveira M[2], Pesquero JB[3], Gomes MD[1], Godinho RO[2], Costa-Neto CM[1] [1]FMRP-USP – Bioquímica e Imunologia, [2]Unifesp – Farmacologia, [3]Unifesp – Biofísica

01.019 Effect of antipsychotic drugs on GSK-3β signaling in SH-SY5Y human neuroblastoma cells. Pompeu TET, Liquori DMS, Noël FG ICB-UFRJ

01.020 Nanobodies of camelid assets against crotoxin, **a neurotoxin of the snake *Crotalus durissus terrificus***. Luiz MB[1], Prado NDR[1], Pereira SS[1], Moreira-Dill LS[2], Kayano AM[2], Soares AM[2], Stabeli RG[1], Fernandes CFC[1] [1]Fiocruz-RO – Tecnologia de Anticorpos/Genética, [2]CEbio-Fiocruz,

01.021 Inhibition of NAD(P)H oxidase reverts the effects of chronic ethanol consumption on the contraction induced by Endothelin-1 in rat corpus cavernosum. Muniz JJ[1], Leite LN[2], Lacchini R[2], Tanus-Santos JE[2], Tirapelli CR[1] [1]EERP-USP, [2]FMRP-USP – Farmacologia

01.022 Effect of atorvastatin on oxidative stress induced by lysophosphatidylcholine in human endothelial cells. Fernandes VA, Navia-Pelaez JM, Diniz TF, Cortes SF, Lemos VS, Capettini LSA UFMG – Fisiologia e Farmacologia

02. Neuropharmacology

02.012 Fenofibrate promotes neuroprotection in a model of rotenone-induced Parkinson's disease. Barbiero JK[1], Santiago RM[1], Tonin F[1], Boschen SL[1], Bassani T[1], Gradowski RW[1], da Cunha C[1], Lima MMS[2], Vital MAVF[1] [1]UFPR – Farmacologia, [2]UFPR – Fisiologia

02.013 Effect of piroxicam in depressive-like behavior in animal model of parkinson's disease. Santiago RM[1], Barbiero J[1], Tonin FS[1], Zaminelli T[1], Boschen SL[1], Andreatini R[1], da Cunha C[1], Lima MMS[2], Vital MABF[1] [1]UFPR – Farmacologia, [2]UFPR – Fisiologia

02.014 GABAB receptor agonist only reduces ethanol drinking in light-drinking mice. Lima MR[1], Villas Boas GR[1], Silva AP[1], Trufini RF[1], Zamboni CG[2], Lacerda RB[2] – [1]Uniamerica – Farmacologia, [2]UFPR – Departamento de Farmacologia

02.015 Presynaptic M_1 and A_{2A} receptors play roles in facilitatory effect caused by methylprednisolone in neuromuscular transmission. Oliveira L[1], Costa AC[1], Noronha-Matos JB[1], Silva I[1], Ambiel CR[2], Corrado AP[3], Alves-do-Prado W[4], Correia-de-Sá P[1] [1]UP – Imuno-Fisiologia e Farmacologia, [2]UEM – Ciências Fisiológicas, [3]FMRP-USP – Farmacologia, [4]UEM – Farmacologia

02.016 Cannabidioltreatment reduces long term memory impairment promoted by aging process. Teixeira MFA[1], Rachid M[2], Teixeira AL[1,3], Campos AC[1,3] [1]UFMG – Imunofarmacologia, [2]UFMG – Patologia, [3]FM-UFMG – Clínica Médica

02.017 RNA interference with nNOS protects SH-SY5Y cells from interferon gamma injury. Silva SS[1], Lustosa CF[1], Ferreira NR[2], Del Bel EA[2], Titze-de-Almeida R[1] [1]FAV-UnB – Terapia Gênica, [2]FORP-USP – Neurofisiologia e Biologia Molecular

02.018 Alpha-melanocyte stimulating hormone (α-MSH) does not alter pilocarpine-induced seizures. Temp FR[1], Santos AC[1], Marafiga JR[1], Jesse AC[2], Guerra GP[3], Scimonelli TN[4], Mello CF[1] [1]UFSM – Fisiologia e Farmacologia, [2]UFSM – Fisiologia e Farmacologia, [3]UTFPR, [4]Universidade de Córdoba

02.019 Repeated cannabidiol administration results in antidepressant-like effect in mice. Schiavon AP[1], Bonato JM[1], Guimarães FS[2], Milani H[1], de Oliveira RMMW[1] [1]UEM – Farmacologia e Terapêutica, [2]FMRP-USP – Farmacologia

02.020 Alpha-melanocyte stimulating hormone (α-MSH) does not prevent pentylenetetrazol-induced seizures. Santos AC[1], Temp FR[1], Marafiga JR[1], Jesse AC[1], Guerra GP[2], Scimonelli TN[3], Mello CF[1] [1]UFSM – Fisiologia e Farmacologia, [2]UTFPR, [3]Universidade de Córdoba

02.021 Spinal cord trpv1 receptor activation by nitric oxide mediates nociception. Rossato MF[1], Beck VR[2], Hoffmeister C[2], Ineu RP[2], Funck VR[1], Oliveira

M[1,2], Ferreira J[1,2,3] [1]UFSM – Biochemical Toxicology, [2]UFSM – Pharmacology, [3]UFSC – Pharmacology

02.022 μ and κ opioid-receptors in the prelimbic cortex have a facilitatory influence on the cardiovascular responses to acute restraint stress in rats. Fassini A, Scopinho AA, Resstel LBM, Corrêa FMA FMRP-USP – Farmacologia

03. Psychopharmacology

03.013 Effects of ethanol withdrawal on anxiety and locomotor activity of mice evaluated in the open field and light/dark box tests. Coltri LP, Bonassoli VT, Milani H, de Oliveira RM UEM – Farmacologia e Terapêutica

03.014 Absence of IL-33 receptor alters behavioral responses to antidepressant and anxiolytic drugs in mice: **Involvement of hippocampal inflammation**. Lisboa SF[1], Montezuma K[2], Biojone C[2], Cunha FQ[1], Guimarães FS[1], Liew FW[3], Verri Junior WA[4], Joca SRL[2] [1]FMRP-USP – Farmacologia, [2]FCFRP-USP – Farmacologia, [3]University of Glasgow – Immunology, [4]UEL – Patologia

03.015 Antidepressant-like effect of melatonin in a rotenone-induced Parkinson's disease model. Bassani TB, Gradowski RW, Zaminelli T, Barbiero JK, Santiago RM, Boschen SL, Vital MABF UFPR – Pharmacology Department

03.016 Antimanic-like effects of PKC inhibitor myricitrin in animal models. Pereira M[1], Siba IP[1], Pizzolatti MG[2], Santos ARS[3], Ruani AP[2], Andreatini R[1] [1]UFPR – Dept of Pharmacology, [2]UFSC – Chemistry, [3]UFSC – Physiology

03.017 Role of IFN-alpha/beta receptors in the genesis of anxiety-like behaviors in mice. Cardoso BA, Teixeira AL, Campos AC FM-UFMG – Imunofarmacologia

03.018 Acute interactions of ayahuasca and antidepressants on apomorphine-induced hypothermia. Amaral WC, Mendes FR UFABC – Ciências Naturais e Humanas

03.019 Fluoxetine exposure during pregnancy and lactation induces anxiogenic-like effect on adult rat offspring. Estrada VB[1], Silva AS[1], Gomes MV[2], Moreira EG[1], Pelosi GG[1] [1]UEL – Ciências Fisiológicas, [2]Unopar – Ciências da Saúde

03.020 Effect of *Dioclea violacea* M. (Aqueous Extract) on general activity observed in the open-field arena and its dyskinetics movements after haloperidol acute treatment in rats. Mariani MP[1], Gemignani S[2], Pedroso-Mariani SR[2] [1]FM-PUCCamp – Pharmacology, [2]FMJ – Pharmacology

03.021 Beneficial effect of the antioxidant vitamin e on behaviors related to anxiety in normoglycemic and diabetic rats. Andrade EG, Souza CP, Rodrigues AB, Cunha JM, Zanoveli JM UFPR – Farmacologia

03.022 Serotonin regulation of anxiety-related defensive responses in the prelimbic cortex of rats. Yamashita PSM, Zangrossi Jr H FMRP-USP – Farmacologia

03.023 Pharmacologic manipulation of 5-HT1A receptors located in the dorsal sub-region of the dorsal raphe nucleus exerts opposed control on inhibitory

avoidance and escape behaviors. Pobbe RLH[1], Spiacci Jr A[1], Zangrossi Jr H[1] – [1]FMRP-USP – Pharmacology

04. Inflammation

04.018 Immunotoxin IL13-PE attenuates silica-induced lung fibrosis by a mechanism independent of epithelial cell damage. Ferreira TPT[1], Arantes ACS[1], Nascimento CVF[1], Olsen PC[1], Guimarães FV[1], Puri R[2], Hogaboam C[3], Martins MA[1], Silva PMR[1] [1]IOC-Fiocruz – Inflamação, [2]FDA-NIH – Biologics Evaluation and Research, [3]UMich – Pathology

04.019 Zymosan injected into rat air pouches induces fever dependent and independent on prostaglandins. Marquiafável FS, Melo MCC, Souza GEP FCFRP-USP – Física e Química

04.020 Antinociceptive properties of ethanolic extracts of plant species present in Restinga of Jurubatiba National Park. Mello RJ, Carmo PL, Bonavita AG, Muzitano MF, Leal ICR, Guimarães DO, Konno TUP, Raimundo JM UFRJ

04.021 Polyinosinic: **polycytidylic acid as a model of febrile response in rats**. Bastos-Pereira AL[1], Fraga D[2], Simm B[3], Ott D[3], Roth J[3], Zampronio AR[1] [1]UFPR – Pharmacology, [2]UFMS – Pharmacology, [3]JLU-UniGuiessen – Veterinary Sciences

04.022 Effect of CB1 and ETA receptors blockage in the survival rate and body temperature after cecal ligation and puncture (CLP) in rats. Leite MCG[1], Brito HO[1], Bastos-Pereira AL[1], Fraga D[2], Zampronio AR[1] [1]UFPR – Farmacologia, [2]UFMS

04.023 TNFR1, **but not TNFR2**, **is crucial to the development and progression of systemic inflammation and organ damage during experimental sepsis**. Melo PH, Nascimento CBD, Ferreira RG, Scortegagna GT, Borges VF, Cunha FQ, Alves-Filho JC FMRP-USP – Basic and Applied Immunology

04.024 Pulmonary Fibroblasts express CXCR4 and produce CCL3, **CXCL2**, **LTB4 and LTC4 after CXCL12 stimulation**. Danilucci TM, Oliveira SHP FOA-Unesp-Araçatuba – Basic Sciences

04.025 Preventive treatment with dexamethasone changes the progression and increase neuroinflammation in Experimental Autoimmune Encephalomyelitis. Santos NB, Lopes DCF, Novaes LS, Duque EA, Wiezel G, Munhoz CD USP – Farmacologia

04.026 Potential protective effect of silymarin on irinotecan induced steatohepatitis in mice. Sousa NRP[1], Assis-Junior EM[1], Lima-Júnior RCP[1], Moreira LS[1], Albuquerque RR[2], Almeida PRC[3], Malveira LRC[1], Oliveira CMG[1] [1]UFC – Physiology and Pharmacology, [2]UFC – Biomedicina, [3]UFC – Pathology and Forensic Medicine

04.027 Granulocytopoietic activity of satphylococcal enterotoxin type A (SEA) and B (SEB) in mice: **A possible mechanism to explain the pulmonary allergic exacerbation induced by these toxins in mice**. Torres ASP[1], Duarte APF[1], Squebola-Cola DM[2], Mello GC[2], Antunes E[2], De Souza IA[1] [1]FMJ – Fisiologia, [2]Unicamp – Farmacologia

04.028 Down-modulation of activated human neutrophil by LMW-fucoidan: Role of microparticles. Moraes JA[1], Frony AC[1], Barcellos-de-Souza P[1], Boisson-Vidal C[2], Barja-Fidalgo C[1] [1]UERJ – Biologia Celular, [2]INSERM U765

04.029 N-acylhydrazone derivative LASSBio-294 suppresses inhibits lung inflammation caused by intransal siica in mice. Sá YAPJS[1], Ferreira TPT[1], Arantes ACS[1], Ciambarella BT[1], Barreiro EJ[2], Fraga CAM[2], Martins MA[1], Silva PMR[1] [1]Fiocruz – Inflamação, [2]UFRJ – Avaliação de Substâncias Bioativas (LASSBio)

04.030 Female sexual hormones modulate the febrile response induced by prostaglandin but not by morphine. Brito H[1], Leite MCG[1], Simões FC[1], Brito LM[2], Zampronio AR[1] [1]UFPR – Farmacologia, [2]UFMA – Medicina

04.031 Anti-inflammatory effects of inosine in lung allergic inflammation: evidence for the involvement of A2 and A3 adenosine receptors. Costa FRL[1,2], Ligeiro de Oliveira AP[3], Accetturi GB[4], Martins OI[4], Domingos VH[4], Lima TW[4], Cabrini DA[5], Santos ARS[2] [1]UFSC – Pharmacology, [2]UFSC – Physiological Sciences, [3]Uninove, [4]USP – Pharmacology, [5]UFPR – Pharmacology

04.032 Amyloid beta peptide induces neuroinflammatory response in the pineal gland and impairs melatonin synthesis. Cecon E[1], Fernandes PACM[1], Jockers R2, Markus RP[1] [1]IB-USP, [2] Institute Cochin

04.033 Pharmacological activity of *Uncaria tomentosa* in an experimental model of cyclophosphamide-induced hemorrhagic cystitis. Benevides FT[1], Marques LM[2], Alencar NMN[2], Aragão KS[1] [1]Estácio – Pharmacology, [2]UFC – Physiology and Pharmacology

05. Pain and Nociception

05.015 Actions of Phα1β peptide purified from the Brazilian spider *Phoneutria nigriventer* venom on the adverse effects caused by morphine in mice. Tonello R[1], Rigo F[2], Gewehr C[2], Gomez MV[2], Ferreira J[1] [1]UFSM, [2]Santa Casa BH

05.016 Involvement of circulating platelets and neutrophils in the hyperalgesia induced by platelet releasate. Carrilho JM, Rosa JG, Santoro LM, Giorgi R IBu – Fisiopatologia

05.017 Superoxide anion induces mechanical hyperalgesia via spinal activation of MAP kinases and PI3K. Carvalho TT[1], Ribeiro FAP[1], Campos CC[1], Casagrande R[2], Verri Junior WA[1] [1]UEL – Ciências Patológicas, [2]UEL – Ciências Farmacêuticas

05.018 Antinociceptive and anti-inflammatory activity of *Condalia buxifolia* in mice. Simões RR[1], Junqueira SC[2], Maldaner G[3], Morel AF[3], Zanchet EM[1], Santos ARS[2] [1]UFSM – Fisiologia e Farmacologia, [2]UFSC – Ciências Fisiológicas, [3]UFSM – Química

05.019 Vitexin inhibits inflammatory pain in mice by targeting TRPV1, oxidative stress, and cytokines. Hohmann MSN[1], Borghi SM[1], Carvalho TT[1], Staurengo-Ferrari L[1], Pinge-Filho P[1], Casagrande R[2], Verri Junior WA[1] [1]UEL – Ciências Patológicas, [2]UEL – Ciências Farmacêuticas

05.020 Anti-hyperalgesic effect of World Health Organization (WHO) analgesics ladder in a model of paclitaxel-induced pain syndrome. Pinheiro KV[1], Rigo FK[2], Oliveira SM[3], Ferreira J[3] [1]UFSM – Farmacologia, [2]Santa Casa BH, [3]UFSM – Bioquímica Toxicológica

05.021 Differential nociceptive response induced by TRPM8 agonist in streptozotocin-diabetic rats. Jesus CHA, Scarante FF, Schreiber AK, Cunha JM UFPR – Farmacologia

05.022 Effects of warm water immersion therapy on persistent inflammatory pain model: **Analyze of action mechanism**. Britto RN[1], Stramosk J[1,2], Cesar-Martins T[2], Batisti AP[2,3], Santos ARS[4], Piovezan AP[2], Martins DF[1,2] [1]Unisul – Fisioterapia, [2]Unisul – Neurociência Experimental, [3]Unisul – Naturologia Aplicada, [4]UFSC – Neurobiologia da Dor e Inflamação

05.023 Anti-nociceptive effects of essential oil *Piper rivinoides* Kunth. Costa NF[1], Nascimento DD[1], Siqueira AM[1], Calheiros AS[1], Souza SP[2], Valverde SS[2], Frutuoso VS[1], Castro-Faria-Neto HC[1] [1]Fiocruz – Imunofarmacologia, [2]Fiocruz – Farmanguinhos

05.024 Quercetin attenuates tactile allodynia in rats with sciatic constriction injury. Lopes EM[1], Piauilino CA[1], Brandão DCBS[1], Gomes BS[1], Brito SMRC[1] [1]UFPI – Biochemistry and Pharmacology

05.025 Role of TRPV1 on the development of acute gout attacks. Hoffmeister C[1], Silva MA[2], Rossato MF[2], Trevisan G[2], Oliveira SM[2], Guerra GP[3], Silva CR[2], Ferreira J[4] [1]UFSM – Farmacologia, [2]UFSM – Química, [3]UTFPR – Alimentos, [4]UFSC – Farmacologia

05.026 Bioassay-guided fractionation of hexanic extract from *Pterodon polygalaeflorus* by its antinociceptive activity. Pinto FA, Vigliano MV, Velozo L, Sabino KCC, Coelho MGP UERJ – Bioquímica

05.027 Activation of P2X3 and P2X2/3 receptors in gastrocnemius muscle of rats induces pro-inflammatory cytokines release and neutrophil migration. Schiavuzzo JG[1], Melo B[1], Santos DFS[1], Teixeira JM[2], Parada CA[2], Fusaro MCGO[1] [1]FCA-UNICAMP, [2]IB-UNICAMP

05.028 NLCR4/ASC/caspase-1 inflammasome assembling participates in the genesis of inflammatory pain. Lopes AHP, Talbot J, Silva RL, França RFO, Zamboni DS, Ferreira SH, Cunha FQ, Cunha TM FMRP-USP

06. Cardiovascular and Renal

06.022 Vasodilatory activity of fractions from the ethanolic extract of leaves of *Kielmeyera membranacea casar* (Calophyllaceae). Paes BM, Carneiro LC, Faria PP, Ferreira LLDM, Konno TUP, Leal ICR, Muzitano MF, Guimarães DO, Raimundo JM UFRJ

06.023 P-Type ATPases modulation goes along with cardiac dysfunction observed in rats fed with a high fat diet. Silva RM, Marques, EB, Oliveira GF, Rocha NN, Scaramello CBV UFF

06.024 Activation of AT1-receptor by Angiotensin II modulates the release of nitric oxide in thoracic aorta of hamsters in the early stages of hypercholesterolemia. Pereira PC[1], Pernomian L[2], Franco JJ[2], Gomes MS[2], Uyemura SA[2], de Oliveira AM [1]FMRP-USP, [2]FCFRP-USP

06.025 Nitric Oxide as a target for the hypotensive and vasorelaxing effects induced by (z)-ethyl 12-nitrooxy-octadec-9-enoate in rats. Machado NT[1], Marciel PMP[1], Alustau MC[1], Queiroz TM[1], Furtado FF[2], Silva TAF[1], Vasconcelos WP[1], Santos PC[1], Oliveira-Filho AA[1], Veras RC[1], Araújo IGA[1], Athayde-Filho PF[1], Medeiros IA[1] [1]CCS-UFPB, [2]CFP-ETSC-UFCG

06.026 *In vivo* effects of spironolactone and eplerenone on the cardiac ischemia of rats. Amancio GCS[1], Alvarenga AC, Guimarães AG[2], Isoldi MC[1] [1]UFOP – Ciências Biológicas, [2]Cipharma-UFOP

06.027 Involvement of nitric oxide and oxidative stress in the modulation of blood pressure observed in late pregnancy of spontaneously hypertensive rats (SHR). Zancheta D[1], Souza GDS[2], Alves GA[1], Costa TCP[1], Antoniali C[1] [1]FOA-UNESP-Araçatuba – Basic Sciences, [2]FMRP-USP – Physiology

06.028 Hydrogen peroxide activates the endothelial enzymes NO-synthase (eNOS) and cyclooxigenase (COX) in renal hypertensive rat aorta. Silva BR[1], Grando MD[2], Bendhack LM[2] [1]FMRP-USP – Pharmacology, [2]FCFRP-USP – Physic and Chemistry

06.029 Use of ruthenium compounds as a Nitric Oxide scavenger in rat aortic rings: **Restoration of vascular tone**. Moura AL[1], Roveda Jr AC[2], Franco DW[2], Tfouni E[3], Cespedes IC[1], Spadari RC[1] [1]Unifesp, [2]IQSC-UNESP, [3]IQRP-UNESP

06.030 Atorvastatin downregulates vascular Nox expression and ameliorates oxidative stress-associated inflammatory process in type 2 diabetic db/db mice. Bruder-Nascimento T[1], Callera G[2], Montezano A[3], He Y[2], Antunes T[2], Cat AND[3], Tostes RC[1], Touyz RM[3] [1]FMRP-USP – Pharmacology, [2]University of Ottawa, [3]University of Glasgow – Cardiovascular and Medical Sciences

06.031 Acute modulatory effect of atorvastatin on nNOS/H_2O_2 pathway in aorta from normolipidemic mice. Mota GPC[1], Pelaez JMN[1], Lemos VS[2], Cortes SF[1], Capettini LSA[1] [1]ICB-UFMG – Pharmacology, [2]ICB-UFMG – Physiology and Biophysics

06.032 Effects of taurine supplementation upon adiposity, **glucose homeostasis and vascular reactivity in MSG rats**. Leão VF, Faria PP, Ferreira LLDM, Raimundo JM, Ribeiro RA UFRJ

06.033 High-salt (4%) plus high-fructose (6%) diet reduces the vascular reactivity to vasocontrictor *in vitro* but increases the systemic arterial pressure in rats. da Silva RCVAF[1], Souza P[1], da Silva-Santos JE[2] [1]UFPR, [2]UFSC

06.034 Endothelium abolishes the vasoconstriction induced by the calcium Ionophore A23187 in renal hypertensive (2K-1C) rat aorta. Feitoza PR[1], Silva BR[2], Bendhack LM[1] [1]FCFRP-USP – Físico-Química, [2]FMRP-USP – Farmacologia

06.035 Use of new selective oral and TRPC3 blockers for re-investigating the calcium permeable channels involved in endothelium-dependent relaxations. Silva JDP[1], Gonçalves MS[1], Alves Filho FC[1], Groschner K[2], Ballejo G[1] [1]FMRP-USP – Pharmacology, [2]MedUniv Graz – Biophysics

06.036 High salt intake impairs the responsiveness to diuretic drugs in rats. Crestani S[1], Souza P[2], Silva RCVAF[2], Marques MCA[2], Gasparotto Junior A[3], Cosmo MLA[3], Victório JC[3], Santos JES[1] [1]UFSC – Farmacologia, [2]UFPR – Farmacologia, [3]Unipar – Farmacologia

06.037 Evaluation of artemether cardiac toxicity. Grabe-Guimarães A[1], Karam S[2], Meschin P[2], Thireau J[2], Mosqueira VCF[1], Richard S[2] [1]CiPharma-UFOP, [2]INSERM U1046

06.038 Chronic treatment with fluoxetine induces oxidative stress and alters aortic contraction in rats. Simplicio JA[1], Resstel LBM[1], Tirapelli CR[2] [1]FMRP-USP – Pharmacology, [2]EERP-USP – Pharmacology

06.039 Reactive oxygen species are involved in the vascular relaxation induced by nitric oxide donor in mesenteric resistance artery from 2K-1C rats. Andrade FA[1], Silva RS[2], Bendhack LM[2] – [1]FMRP-USP – Pharmacology, [2]FCFRP-USP – Physics and Chemistry

06.040 Regulation of Angiotensin-II potency by metabolites derived from cyclooxygenases in carotid artery from rat exposed to repeated restrain stress. Côco H[1], Gomes MS[2], Pernomian L[2], de Oliveira AM[2] [1]FMRP-USP – Farmacologia, [2]FCFRP-USP – Farmacologia

06.041 Molecular mechanisms associated with reversion of proteinuria in hypertensive rats treated with RAS inhibitors. Corrêa JWN[1], Girardi ACC[2], Boaro KR[2], Salles T[2], Yogi A[3], Callera GE[3], Touyz RM[3], Bendhack LM[4], Krieger JE[2] [1]ICB-UFAM – Farmacologia, [2]InCor-HC-FMUSP, [3]University of Ottawa, [4]FCFRP-USP

06.042 The Nitric Oxide donor [Ru(terpy)(bdq)NO+]3+ (TERPY) does not alter the expression of endothelial Nitric Oxide synthase (eNOS) in SHR aortas. Potje SR[1], Perassa LA[1], Graton ME[1], da Silva RS[2], Bendhack LM[2], Antoniali C[1] [1]FOA-Unesp – Basic Sciences, [2]FCFRP-USP – Physics and Chemistry

07. Endocrine and Gastrointestinal

07.001 Diabetic neuropathy is ameliorated in streptozotocin-injected rats after treatment with sulfonylhydrazone derivative. Pereira SL, Souza BJ, Trachez MM, Monteiro CES, Costa FP, Romeiro NC, Lima LM, Barreiro EJ, Sudo RT, Zapata-Sudo G ICB-UFRJ

07.002 Acute toxicity and gastroprotective activity of *Cissampelos sympodialis* Eichl.(Menispermaceae). Sales IRP, Formiga RO, do Nascimento RF, Lúcio ASSC, Barbosa-Filho JM, Batista LM UFPB

07.003 Acute toxicity and protective effect of *Maytenus erythroxylon* Reissek (Celastraceae) against ethanol/HCl-induced gastric ulcers in mice. Formiga RO, Caldas Filho MRD, Paulo LL, Quirino ZGM, Batista LM UFPB

07.004 Protective effect of *Nanuza plicata* (Mart.) L. B. Smith & Ayensu (Velloziaceae) against NSAID and stress-induced gastric ulcers in mice. Sousa TM, Lima GRM, Tavares JF, Batista LM UFPB

07.005 Evaluation of participation of sulfhydryl compounds and nitric oxide in the gastroprotective effect of *Maytenus distichophylla* mart. ex Reissek (Celastraceae). Caldas Filho MRD, Jesus NZT, Machado FDF, Duarte MC, Silva MS, Tavares JF, Batista LM UFPB

07.006 The effects of a *Baccharis trimera* hydroethanolic extract in alcoholic hepatic steatosis in mice. Lívero FR[1], Alves de Souza CE[1], Oliveira LG[1], Diettrich RL[2], Werneck MC[1], Strapasson RLB[3], Stefanello MEA[3], Botelho EL[4], Acco A[1] [1]UFPR – Farmacologia, [2]UFPR – Medicina Veterinária, [3]UFPR – Química, [4]Unipar – Farmácia

07.007 Gastroprotective effect of ethanolic extracts of the roots and stem from *Pilosocereus gounellei* (Cactaceae). Sousa GA[1], Oliveira IS[1], Viana AFSC[1], Carvalho CS[1], Souza MFV[2], Oliveira RCM[1], Oliveira FA[1] [1]UFPI – Medicinal Plants, [2]UFPB – Pharmaceutical Technology

09. Natural Products and Toxinology

09.022 Effect of acute exposition to Fumonisin B1 on oxidative stress markers in liver of mice. Lima C, Poersch AB, Trombetta F, Naieli S, Furian AF UFSM – Physiology and Pharmacology

09.023 Phytochemical and anti-inflammatory analysis of *Agave sisalana* extracts. Palacios JL, Da Quinta ARM, Kuruiwa D, Santos L UNESP-Assis – Ciências Biológicas

09.024 Antinociceptive and anti-inflammatory effects of β-glucan isolated from the *Kluyveromyces marxianus*. Oliveira RFA[1], Valasques Jr GL[1], Assis AS[1], Villarreal CF[2], Lima FO[1] [1]UEFS – Saúde, [2]UFBA – Farmácia

09.025 Synergic effect of Brazilian nut ingestion and superoxide dismutase (MnSOD) polymorphism on blood oxidative stress biomarkers. Barbisan F, de Rosso Motta J, Frescura Duarte MMM, Duarte T, Dal Berto M, Jung IEC, CRUZ IBM UFSM

09.026 Evaluation of cytoprotective and healing gastric ulcers activity of bark extract from *Himatanthus sucuuba*. Lobato AMV[1], Batista LS[1], Marcondes HC[2], Silva MN[3], Sena CBC[1], Silva MCF[1], Hamoy M[1], Jóia VM[1] [1]ICB-UFPA, [2]Dequi-ICEB-UFOP, [3]ICEN-UFPA

09.027 Effect of methanol extract of *Baccharis dracunculifolia* in pancreatic islets of obese mice. Hocayen PAS[1], Grassiolli S[2], Pochapski MT[3], Silva LA[4], Malfatti CRM[4] [1]UFPR – Farmacologia, [2]UEPG – Biologia, [3]UEPG – Odontologia, [4]Unicentro – Educação Física

09.028 Investigation of the activity of *Maytenus obtusifolia* (Celastraceae) on gastrointestinal motility. Machado FDF, Sales IRP, Sousa TM, Gomes IF, Tavares JF, Batista LM UFPB

09.029 Antibacterial activity of the ethanol extracts from *Terminalia fagifolia* Mart & Zucc (Combretaceae). Araujo AR[1], Quelemes PV[2], Perfeito MLG[2], Nunes PHM[3], Soares MJS[4], Leite JRSA[1] [1]UFPI – Medicinal Plants [2]UFPI – Biodiversity and Biotechnology, [3]UFPI – Physiology and Biophysics, [4]UFPI – Veterinary Morphophysiology, Teresina

09.030 Gastroprotective effect of essential oil of *Croton argyrophylloides* Muell Arg. Gama CS, Silva TFS, Araújo SA, Estevam CS, Batista JS UFS – Fisiologia

09.031 Study of the cytotoxic effect of *Bothrops jararacussu* and *Apis mellifera* venom in renal tubular cells (LLC-Pk1) and antagonism by polyanions. Teixeira-Cruz JM, da Silva Amaral L, da Silva Gonçalves T, Monteiro-Machado M, Amorim-Tomaz M, Melo PA, Quintas LEM ICB-CCS-UFRJ – Farmacologia e Química Medicinal

09.032 *Piper spp*. Amazon: antimicrobial activity of extracts and essential oils. Soares-Mota MR[1], Batista AC[1], Cunha ALB[1], Santos SM[2], Souza DJF[2], Pohlit AM[3], Fernandes OCCF[4], Chaves CMC[1] [1]EMBRAPA – Medicinal Plants, [2]Literatus, [3]INCA – Natural Products Research, [4]Fiocruz – Biodiversity

09.033 Gastroprotective effect of hydroalcoholic extracts of croton *Argyrophylloides* Muell Arg. Silva TFS, Gama CS, Araújo SA, Estevam CS, Batista JS UFS – Fisiologia

09.034 Anti-allergic activity of *Stephanolepis hispidus* skin aqueous extract in an allergic pleurisy model in mice. Ferraris FK[1], Costa TEMMC[2], Penido C[2], Fernandes LDA[3], Amendoeira FC[1] [1]INCQS-Fiocruz – Farmacologia, [2]Farmanguinhos-Fiocruz – Farmacologia Aplicada, [3]IEAPM – Oceanografia

09.035 Antioxidant and vasodilatory activities and chemical evaluation of the ethanolic extract of aerial parts of *Stachytarpheta schottiana* (Verbenaceae). Moreira AP, Leal MCR, Ferreira LLDM, Zanetti GD, Leal ICR, Guimarães DO, Muzitano MF, Carmo PL, Raimundo JM UFRJ

09.036 Participation of the TRP channels in vasorelaxant effect induced by carvacrol in vascular tissue from spontaneously hypertensive rats. Ramos-Reis M[1], Almeida MM[2], Alves QL[1], Ferreira JM[1], Albuquerque JM[1], Simões LO[1], Silva DF[1] [1]UFBA – Biorregulação, [2]UFPB – Biotecnologia

09.037 Carvacrol induces vasorelaxant effect by inhibiting calcium influx in vascular tissue from spontaneously hypertensive rats. Ferreira JM, Ramos-Reis M, Alves QL, Albuquerque JM, Silva DF UFBA – Biorregulação

09.038 *Yerba mate* extract increase *in vitro* biomineralization in osteogenic differentiation model of rat bone marrow-derived mesenchymal stromal cell. Brito VGB, Barros TL, Nakamune ACMS, Chaves Neto AH, Oliveira SHP FOA-Unesp – Ciências Básicas

09.039 Cardiovascular responses to *Lachesis muta* (South American bushmaster) snake venom in anesthetized rats: No cholinergic involvement. Dias L[1], Rodrigues MAP[1], Soubhia PC[2], Brunieri LVP[1], Brunieri LVP[1], Rennó AL[1],

Melgarejo AR[3], Hyslop S[1] [1]FCM-Unicamp – Farmacologia, [2]Unicamp – Controle de Intoxicações, [3]IVB – Zoologia Médica

09.040 Anxiolytic-like effects of acute and repeated treatment with *Cissussicyoides* (Vitaceae) extract. Souza TS[1], Froza MG[1], Silva JD[1], Duarte RP[2], Scarpelim OJ[3], Baretta IP[4] [1]Unipar – Biomedicine, [2]Unipar, [3]Unipar – Nursing, [4]Unipar – Pharmacology

09.041 Antiedematogenic effect of Carvacrol in histamine-, dextran- and substance P-induced edema in mice. Silva FV[1], Sousa-Neto BP[1], Arcanjo DDR[1], Machado FDF[1], Quintans-Júnior LJ[2], Guimarães AG[2], Oliveira FA[1], Oliveira RCM[1] [1]UFPI – Medicinal Plants Research, [2]UFS – Physiology

09.042 Gastroprotective effect of (-)-myrtenol against gastric ulcer induced by ibuprofen and cold restraint-stress, in rodents. Viana AFSC[1], Carvalho EF[1], Lima GS[1], Oliveira IS[1], Silva FV[1], Reis Filho AC[1], Sousa DP[2], Oliveira RCM[1] [1]UFPI – Medicinal Plants, [2]UFPB

11. Clinical Pharmacology, Pharmacokinetics, Pharmacogenomics and Preclinical Toxicology

11.001 Analysis of the postnatal development of mice offspring exposed to yellow fever vaccine during intrauterine life. Marianno P, Costa GA, Salles MJS UEL – Biological Sciences

11.002 Evaluation of therapeutic association's effect on digoxin pharmacokinetics. Souza FC, Baptista TM, Neri JS, Scaramello CBV UFF – Farmacologia Experimental

11.003 A novel *in vivo* model for evaluation of vaginal permeability test applied to fenticonazole. Campos RM[1], Pissinatti L[1], Rojas-Moscoso JA[1], Chen LS[2], Porto M[1], Gagliano TJD[3], de Nucci G[1] [1]Unicamp – Pharmacology, [2]Galeno Research Unit, [3]IBCCF-UFRJ

11.004 Simvastatin treatment increases nitrite levels in obese women: Modulation by T-786 polymorphism of NOS3. Andrade V[1], Sertorio J[2], Fernandes K[1], Sandrim V[1] [1]IEP-SCBH, [2]Unicamp – Farmacologia

11.005 Robotic simulation used to optimization of teaching applied pharmacology to medicine. Fagundes Junior LH[1], Aguiar ARA[2], Suassuna FAB[1], Câmara PRS[1] [1]UnP – Medicina, [2]UnP – Enfermagem

11.006 Evaluation of ozonized sunflower oil in skin healing in rats. Figueiredo M, Miara LC, Anater A, Ribeiro DR, Rodrigues Filho JG, Michelotto Junior PV, Farias MR, Pimpão CT FCAV-PUCPR – Animal Science

11.007 Pharmacokinetics profile of thalidomide on the doses 200 mg and 400 mg in healthy male volunteers. Sales LC[1], Leite ALAS[1], Nascimento DF[1], Kerr LRFS[2], Costa IF[1], Freire LM[1], Rocha MBS[1], Pontes AV[1], Frota Bezerra FA[1], Moraes MO[1], Moraes MEA[1] [1]UFC – Fisiologia e Farmacologia, [2]UFC – Saúde Comunitária

11.008 Influence of food on bioavailability of venlafaxine administered in extended release capsules. Freire LM, Rocha MBS, Leite ALAS, Nascimento DF,

Pontes AV, Sales LC, Sena KS, Costa IF, Lopes BB, Frota Bezerra FA, Moraes MO, Moraes MEA UFC – Fisiologia e Farmacologia

11.009 Inosine via adenosine receptors prevents MeHg-induced motor impairment: **behavioral and biochemical aspects**. Macedo-Junior SJ[1], Cerutti ML[2], Nascimento DB[3], Farina M[4], Santos ARS[2], Cardozo AM[5] [1]UFSC – Farmacologia, [2]UFSC – Ciências Fisiológicas, [3]UFSM – Química, [4]UFSC – Bioquímica, [5]UFSC – Patologia

11.010 Haematological responses in *Rhamdia quelen* sedated with propofol. Gressler L[1], Spall S[2], Sutili F[1], da Costa S[3], Parodi T[1], Baldisserotto B[1] [1]UFSM – Fisiologia e Farmacologia, [2]UFSM – Farmácia Industrial, [3]CESNORS-UFSM – Zootecnia,

11.011 Evaluation of the plasma kinetics and biodistribution of association of paclitaxel with a cholesterol-rich nanoemulsion in *Cebus apella*. Feio DCA[1], Oliveira NCL[1], Morikawa AT, Muniz JAPC, Burbano RMR, Maranhão RC, Lima PD [1]UFPA

11.012 Pharmacokinetic evaluation of sulfamethoxazole + trimethoprim in rats as a tool for predictive bioequivalence / bioavailability studies in humans. Hoffmann FI[1], Pritsch MC[1], Postali M[1], Santos MB[1], Manfio JL[1], de Lima TCM[2] [1]Biocinese – Biopharmaceutical Studies, [2]UFSC

11.013 Preclinical toxicology studies of LASSBIO-788, **a potential antiatherogenic compound**, **on the male rat reproductive tract**. Alfradique VAP[1], Motta NAV[1], Kummerle AE[2], Barreiro EJ[2], Brito FCF[1], Ribas JAS[1], Marostica E[1] [1]UFF – Physiology and Pharmacology, [2]UFRJ – LASSBio

11.014 Evaluation of safety of cyclosporin used in dogs. Anater A, Ribeiro DR, Rebello AP, Solomon S, Souza Netto A, Farias MR, Pimpão CT FCAV-PUCPR

Poster session 3 – Thursday 31/10/13

01. Cellular and Molecular Pharmacology

01.023 Modulatory effects of atorvastatin on nitric oxide pathway in oxidative stress and inflammatory response induced by oxidized LDL in human endothelial cells. Navia-Pelaez JM[1], Diniz TF[2], Capettini LSA[1], Lemos VS[2], Cortes SF[1] [1]UFMG – Farmacologia, [2]UFMG – Fisiologia e Biofísica

01.024 Synthesis and functional analysis of novel AT1 receptor ligands with potential biased agonistic properties. Duarte DA, Prando EC, Oliveira EB, Costa-Neto CM FMRP-USP – Biochemistry and Immunology

01.025 Involvement of channels in the vasorelaxant effect of AAL 195. Silva JCG[1], Costa CDF[2], Herculano EA[3], Ferreira AKB[1], Araújo-Júnior JX[3], SILVA DL[3], Ribeiro EAN[1] [1]ESENFAR-UFAL, [2]RENORBIO-UFAL, [3]IQB-UFAL

01.026 *Tityus serrulatus* venom and its toxins Ts1 and Ts5 increase cytosolic Ca^{2+} concentration in isolated vascular smooth muscle cells. Neto Filho MA[1], Vasconcelos F[2], Bendhack LM[3], Arantes EC[3] [1]UNINGA – Pharmacology, [2]UFPA – Toxicology, [3]FCFRP-USP – Physics and Chemistry

01.027 Quercetin induces autophagy, apoptosis and cell cycle arrest in human tumor xenograft model. Maso V[1], Calgarotto AK[1], Franchi Jr GC[2], Nowill AE[2], Vasallo J[3], Latuf Filho P[3], Saad STO[1] [1]Unicamp – Hemocentro, [2]CIPOI-Unicamp, [3]CIPED

01.028 Structural insight on Angiotensin II Type 1 and Type 2 receptors in the light of the CXCR4 structure. Martin RP, Rodrigues ES, Silva RF, Shimuta SI Unifesp – Biophysics

01.029 ERK serves as a converging point in attenuation of skeletal muscle proteolysis induced by Gs and Gi-coupled adenosine receptors. Figueiredo LB, Duarte T, Godinho RO Unifesp – Pharmacology

01.030 Role of arginine1 residue of bradykinin in the activation of kinin B2 receptors. Silva RF, Martin RP, Rodrigues ES, Oliveira L, Shimuta SI Unifesp – Biofísica

01.031 Label-free quantitative proteomic analysis revealed the molecular profiling of Imatinib Mesylate and 5-Azacytidine treatment in lung cancer. Sousa JCC, Abdelhay E, Pizzatti L CEMO-INCa

01.032 Kinin B1 function on insulin resistance and control of weight gain. Sales VM[1], Gonçalves-Zillo T[1], Batista C[1], Silva ED[1], Barros CC[2], Mori MAS[1], Pesquero JB[1] [1]Unifesp – Biofísica, [2]UFPEL – Nutrição

02. Neuropharmacology

02.023 Influence of music therapy on cognitive and behavioral aspects of rats at different stages of developing central nervous system. Cavalcanti PP[1], Sampaio WCM[2], Silva PCO[2], Pereira DL[1], Lima VS[1], Siqueira JP[1], Ferreira VM[2] [1]UFMT – Ciências da Saúde, [2]UnB – Ciências da Saúde

02.024 Investigation of anti-anxiety-antidepressive-like property of oleanolic acid and development of new analogs. Fajemiroye JO[1], Pollepally PR[2], Rocha FR[3], Zjawiony JK[2] [1]UFG – Ciências Fisiológicas, [2]University of Mississippi – Pharmacognosy, [3]UFRRJ – Ciências Fisiológicas

02.025 Purinergic neurotransmitter triggers P2 / P1 receptors in the rat pineal gland according to daily variation of ectonucleotidases. Ornelas FGI[1], Souza-Teodoro LH[1], Dargenio-Garcia L[1], Fernandes PACM[1], Muxel SM[1], Stefanello N[2], Zanini D[2], Schetinger MRC[2], Markus RP[1], Ferreira ZS[1] [1]USP – Physiology, [2]UFSM – Toxicological Biochemistry

02.026 Exposure of adolescent rats to methylphenidate and cross-sensitization to ethanol: **Preliminary findings**. Gelain MAS[1], Gelain MS[1], Freese L[1], Pereira NSC[3], Costa PA[1], Caletti G[1], Bisognin KM[1], Souza MF[1], Nin MS[1], Gomez R[3], Barros HMT[1] [1]UFCSPA – Ciências Básicas da Saúde, [2]UFRGS

02.027 Anxiolytic-like effects of the benzodiazepine midazolam microinjected into distinct areas of the inferior colliculus of rats submitted to the elevated plus maze. Saito VM, Brandão ML FMRP-USP – Neuropsychopharmacology / INeC

02.028 Age-related changes induced by lipopolysaccharide on α2,3-Na,K-ATPase activity, cyclic GMP levels and oxidative status in rat hippocampus. Vasconcelos AR[1], Yshii LM[1], Böhmer AE[1], Lima LS[1], Alves R[1], Andreotti DZ[1], Marcourakis T[2], Scavone C[1], Kawamoto EM[1] [1]ICB-USP, [2]USP – Análises Clínicas e Toxicológicas

02.029 The influence of Na,K-ATPase isoforms in ouabain signaling cascade against LPS induced NF-kB activation in glial cells. Kinoshita PF, Yshii LM, Orellana AMM, de Sá Lima L, Kawamoto EM, Scavone C ICB-USP

02.030 Short-term sustained hypoxia increases the glutamatergic transmission in Nucleus *Tractus Solitarius* (NTS) neurons of juvenile rats. Accorsi-Mendonca D, Almado CEL, Machado BH USP – Fisiologia

02.031 Intrahippocampal injection of ouabain activates NF-kB and Wnt-beta-catenin signaling pathway in rats. Orellana AMM, Yshii LM, Böhmer AE, Kinoshita PF, de Sá Lima L, Andreotti DZ, Kawamoto EM[1], Scavone C USP – Farmacologia

02.032 Effects of reversible inactivation of the dorsal hippocampus on the cardiovascular responses activated by the chemoreflex and the possible involvement of NMDA receptors. Kuntze L B, Ferreira-Júnior NC, Lagatta DC, Resstel LBM FMRP-USP – Pharmacology

02.033 Medial prefrontal cortex cannabinoid CB1 receptors modulate autonomic responses in rats submitted to restraint stress. Moraes-Neto TB, Fassini A, Correa FMA, Resstel LBM FMRP-USP – Farmacologia

04. Inflammation

04.034 Animal model of intestinal damage induced by the compound SN-38, the active metabolite of the anticancer agent irinotecan. Wong DVT[1], Costa ELF[1], Bem AXC[1], Leite CAVG[1], Freire RS[1], Brito GAC[2], Lima AAM[1], Lima-Júnior RCP[1], Ribeiro RA[1] [1]UFC – Physiology and Pharmacology, [2]UFC – Morphology

04.035 Fibrinogen-induced experimental arthritis: **New method to sensitization**. Saraiva ALL, Talbot J, Veras FP, Peres RS, Lima KA, Cunha FQ, Alves-Filho JC FMRP-USP – Farmacologia

04.036 Is there a role for CXCR1/2 chemokine receptors in a model of OVA-induced allergic airway inflammation? Kraemer LR[1], Lima BHF[2], Lopes GAO[1], Garcia CC[2], Peixoto AC[1], Bertini R[3], Allegretti M[3], Teixeira MM[2], Russo RC[1] [1]UFMG – Fisiologia, [2]UFMG – Bioquímica e Imunologia, [3]Dompé

04.037 Effect of phosphodiesterase Type 4 (PDE4) inhibitors, **Rolipram and CILOMILAST ON the lung inflammatory response caused by silica particles in mice**. Souza ET[1], Ferreira TPT[1], Azevedo GBZ[1], Nunes IKC[2], Lima LM[2], Martins MA[1], Silva PMR[1] [1]Fiocruz – Inflammation, [2]LASSBio-UFRJ

04.038 *Aryl hydrocarbon receptor* gene polymorphism is associated with smoking-induced exacerbation of rheumatoid arthritis. Talbot J[1], Peres RS[2], Oliveira RDR[3], Pinto LG[1], Almeida SCL[3], Silva JR[2], Franca RFO[1], Ryffel B[4], Cunha TM[1], Alves-Filho JC[1], Liew EY[5], Louzada-Junior P[3], Cunha FQ[1] [1]FMRP-USP – Farmacologia, [2]FMRP-USP – Imunologia, [3]HCFMRP-USP – Reumatologia, [4]CNRS Orleans, [5]University of Glasgow

04.039 Galectin-3 increases mortality of mice submitted to polymicrobial sepsis. Ferreira RG[1], Nascimento DC[1], Melo PH[2], Kanashiro A[1], Borges VF[1], Mota JMSC[3], Cunha FQ[1], Alves-Filho JC[1] [1]FMRP-USP – Pharmacology, [2]FMRP-USP – Basic and Applied Immunology, [3]FMRP-USP – Internal Medicine

04.040 The anti-inflammatory and antinociceptive effects of β-caryophyllene, **a full agonist of cannabinoid receptor Type 2 (CB2)**, **in experimental arthritis**. Vieira R, Bento AF, Marcon R, Andrade EL, Calixto JB UFSC – Farmacologia

04.041 A novel monocyte subset contributes to clearance of damage tissue during sterile inflammation in the liver. Dal-Secco D[1], Jenne C[1], Yipp B[1], Wong C[1], Petri B[1], Kolaczkowska E[1], Ransohoff R[2], Charo I[3], Kubes P[1] [1]University of Calgary – Immunology, [2] Cleveland Clinic – Neurosciences, [3]University of California – Medicine

04.042 Evaluation of anti-inflammatory action of the hydroethanolic extract of *Macrosiphonia longiflora* (Desf.) Müll. **Arg on acute models of inflammation**. Silva AO[1], Almeida DAT[1], Martins DTO[1] [1]UFMT – Ciências Básicas em Saúde

04.043 Anti-inflammatory effects of aqueous extract of flowers from *Kalanchoe pinnata* and its flavonoid. Ferreira RT[1], Malvar DC[1], Coutinho MAS[2], Costa SS[2], Carvalho RRN[1], Vanderlinde FA[1] [1]UFRRJ – Ciências Fisiológicas, [2]UFRJ – Produtos Naturais

04.044 Selective effects of corticosterone pre-treatment in LPS-induced NFKB nuclear translocation in mixed primary cortical cultures. Duque EA, Lopes DCF, Novaes LS, Santos NB, Wiezel G, Silva NG, Scavone C, Munhoz CD [1]ICB-USP – Farmacologia

04.045 Effect of high-carbohydrate diet intake in metabolic and inflammatory response of mice IL18-/-. Yamada LTP[1], Oliveira MC[1], Lana JP[2], Batista NV[2],

Fonseca RC[2], Pereira RV[2], Cara DC[2], Ferreira AVM[3] [1]FF-UFMG – Ciência de Alimentos, [2]ICB-UFMG – Morfologia, [3]UFMG – Nutrição

04.046 Characterization of anti-inflammatory properties of passion fruit seed oil. Lima CKF[1], Moreira CC[1], Silva CS[1], Lima JA[2], Miranda ALP[1] [1]LEFEx-ICB-UFRJ, [2]Assessa

04.047 Role of B1 and B2 bradykinin receptors in sepsis induced by cecal ligation and puncture. Oharomari Jr LK, Trevisan SC, Cunha FQ FMRP-USP – Farmacologia

04.048 IL-10 exerts a dual effect on rat pineal melatonin production. Santos GC, Markus RP, Fernandes PA IB-USP – Fisiologia

04.049 Improvement of anti-edematogenic activity of friedelin with cyclodextrin complexes. Ferro JNS[1], Ferreira FR[2], Santos SL[1], Abreu FC[2], Conserva LM[3], Barreto EO[1] [1]ICBS-UFAL – Biologia Celular, [2]IQB-UFAL – Eletroquímica, [3]IQB-UFAL – Química de Produtos Naturais

05. Pain and Nociception

05.029 Antinociceptive activity of aggregatin D isolated from *Sinningia aggregata* in a model of mechanical hyperalgesia in mice. Souza GV[1], Bastos-Pereira AL[1], Ribas JLC[1], Stefanello ME[2], Zampronio AR[1] [1]UFPR – Farmacologia, [2]UFPR – Química

05.031 New method for evaluation of articular disability in experimental arthritis: **investigation the role of glial cells**. Quadros AU, Fonseca MD, Pinto LG, Ferreira SH, Cunha TM FMRP-USP – Farmacologia

05.032 Evaluation of the analgesic Effect of systemic and topical citral. Antunes AMP, Rocha NP IBB-Unesp – Pharmacology

05.033 Aldehyde dehydrogenase 2 activation reduces neuropathic pain in rats. Neto BS[1], Ferreira JC[2], Mochly-Rosen D[3], Cury Y[1], Zambelli VO[1] [1]IBu – Dor e Sinalização, [2]ICB-USP, [3]Stanford University – Chemistry and Systems Biology

05.034 FAR infrared emitted by bioceramics reduces hypernociception of inflammatory origin in mice. Emer AA[1], Lenfers B[2], Cidral-Filho F[1], Martins DF[1] [1]Unisul – Neurociência Experimental, [2]UFSC – Neurociências.

05.035 Effect of topical beta-myrcene in chronic neuropathic pain and acute inflammatory hyperalgesia. Dias MC, Rocha NP IBB-Unesp-Botucatu – Farmacologia

05.036 Analgesic and/or anti-inflammatory effects of two new compounds derived from pyrazole. Oliveira LP[1], Florentino IF[1], Sousa LV[1], Silva DPB[1], Menegatti R[2], Costa EA[1] [1]UFG – Fisiologia e Farmacologia, [2]UFG – Farmácia

05.037 Preliminary evaluation of the antinociceptive activity from bark of fruit of *Platonia insignis* Mart. (Clusiaceae). Souza RDS[1], Freitas FFBP[1], Nunes MGL[1], Santos BIS[1], Sousa SEL[1], Reis Filho AC[1], Costa ICG[2], Chaves MH[2], Almeida FRC[1] [1]UFPI – Plantas Medicinais, [2]UFPI – Química

05.038 Anti-inflammatory and antinociceptive activities of LQFM046 molecule. Silva DPB[1], Florentino IF[1], Galdino PM[1], Oliveira LP[1], Menegatti R[2], Costa EA[1] [1]UFG – Fisiologia e Farmacologia, [2]UFG – Farmácia

05.039 Immune cell infiltration and production of inflammatory mediators in dorsal root ganglion, **but not in spinal cord**, **are related to murine herpetic hyperalgesia**. Silva JR, Talbot J, Lopes AHP, Cunha TM, Cunha FQ FMRP-USP – Farmacologia

05.040 The role of NOD1 and NOD2 during peripheral neuropathy, **glial activation and release of pronociceptive cytokines**. Ferreira DW[1], Santa-Cecília FV[1], Cunha FQ[1], Ferreira SH[1], Zamboni DS[2], Cunha TM[1] [1]FMRP-USP – Farmacologia, [2]FMRP-USP – Biologia Celular e Molecular e Bioagentes Patogênicos

05.041 LASSBio-1247 is an effective prototype drug candidate to treat rheumatoid arthritis pain. Santos EAP[1], de Sá Alves FR[1], Lima CKF[1], Fraga CAM[2], Barreiro EJ[1], Miranda ALP[1] [1]UFRJ – Fármacos, [2]ICB-UFRJ

05.042 The medial plantar nerve ligation (MPNL) as a new model of neuropathic pain. Sant'Anna MBM, Souza GR, Bozzo TA, Ferreira SH, Cunha FQ, Cunha TM FMRP-USP – Farmacologia.

06. Cardiovascular and Renal

06.043 NAD(P)H oxidase inhibition with apocynin prevents the increase in blood pressure induced by chronic ethanol consumption Marchi KC[1], Tirapelli CR[2] [1]FMRP-USP – Farmacologia, [2]EERP-USP – Farmacologia

06.044 Chronic treatment with apocynin reduces arterial pressure and Angiotensin II *in vivo* effect in spontaneously hypertensive rats (SHR). Graton ME[1], Perassa LA[1], Potje SR[1], Lima MS[1], Antoniali C[1] [1]FOA-Unesp – Basic Sciences

06.045 Inhibition of NO-synthase does not normalize the contractile response to norepinephrine and epinephrine IB renal hypertensive rat aortas. Bocalon AC[1], Silva BR[2], Bendhack LM[1] [1]FCFRP-USP – Physics and Chemistry, [2]FMRP-USP – Pharmacology

06.046 Participation of Angiotensin II in oxidative stress, **vascular reactivity and neurohumoral alterations induced by chronic ethanol consumption**. Passaglia P[1], Mecawi AS[2], Antunes-Rodrigues J[2], Coelho EB[3], Tirapelli CR[4] [1]USP – Toxicologia, [2]USP – Fisiologia, [3]USP – Clínica Médica, [4]USP – Farmacologia

06.047 Norepinephrine-induced contraction of rat renal and femoral veins involves both α1 and α2-adrenoceptors. Rossignoli PS[1], Pereira OCM[2], Chies AB[1] [1]Famema-Unimar – Pharmacology, [2]IBB/-UNESP – Pharmacology

06.048 A Dual-NOX activation induced by Angiotensin II modulates vascular smooth muscle cells functions: **Role of alpha1beta1 integrin and ILK**. Moraes JA[1], Frony AC[1], Dias AM[1], Renovato-Martins M[1], Rodrigues G[1], Marcinkiewicz C[2], Assreuy J[3], Barja-Fidalgo C[1] [1]UERJ – Biologia Celular, [2]Temple University, [3]UFSC – Farmacologia

06.049 Cardioprotective effect of orlistat on arrythmias cardiac and lethal arising from rats' ischemia and reperfusion. Rodrigues FSM, Tavares JGP, Lima EPS, Miranda-Ferreira R, Jurkiewicz NH, Jurkiewicz A, Caricati-Neto A Unifesp – Farmacologia

06.050 Consequences elicited by stress restriction on the AT_1 receptor activation in diabetic rat carotid. Moreira JD[1], Pernomian L[2], de Oliveira AM[2] [1]FMRP-USP, [2]FCFRP-USP

06.051 Participation of NOX1/NADPH oxidase in the production O_{-2} in thoracic aorta of mice young undergoing cholesterol diet (1%). Moreira RP, Pernomian L, Gomes MS, de Oliveira AM FCFRP-USP – Física e Química

06.052 Effect of N-acetylcysteine on the purinergic and noradrenergic neurotransmission in smooth muscle of rat vas deferens. Lima EPS, Rodrigues FSM, Simões ACB, Sousa GL, Jurkiewicz NH, Jurkiewicz A, Caricati-Neto A Unifesp – Farmacologia

06.053 Evaluation of cavernous smooth muscle reactivity in rats with chronic heart failure: **Model of chronic volume overload**. Tartarotti PS[1], Silva FH[2], Rojas-Moscoso JA[2], Priviero FBM[1], Nucci G[2], Antunes E[2], Claudino MA[1] [1]USF, [2]Unicamp – Farmacologia

06.054 Oxidative stress impaired the vasorelaxation effect of nitric oxide-releasing indomethacin derived (NCX2121) in hypertensive rats aorta. Paula T D, Silva BR, Bendhack LM FCFRP-USP – Física e Química

06.055 Increase of contractile response in detrusor smooth muscle of rats with chronic heart failure: **Evaluating the development of overactive bladder**. Furquim SR[1], Silva FH[2], Rojas-Moscoso JA[2], Priviero FBM[1], de Nucci G[2], Antunes E[2], Claudino MA[1] [1]USF, [2]Unicamp – Farmacologia

06.056 Vasorelaxant effect of WE011 a derivative aminoguanidinic on mesenteric artery rings rats. Herculano EA[1], Silva JCG[2], Clementino-Neto J[2], Moura MTD[2], França PHB[1], Araújo-Júnior JX[1], Ribeiro EAN[2], Costa CDF[3] [1]IQB-UFAL, [2]ESENFAR-UFAL, [3]RENORBIO-UFAL

06.057 Participation of reactive oxygen species and metabolites derived from cyclooxygenase in the contractile response induced by Endothelin-1 in corpus cavernosum from ethanol-treated rat. Leite LN[1], Tirapelli CR[2] [1]FMRP-USP, [2]EERP-USP

06.058 Mineralocorticoid receptor and G protein-coupled estrogen receptor mediate the vascular effects of aldosterone in female mice with Type 2 diabetes. Ferreira NS[1], Cau SBA[2], Manzato CP[1], Silva MAB[1], Tostes RC[1] [1]USP – Pharmacology, [2]UFJF – Basic-Health

06.059 Chronic treatment with fluoxetine potentiates sympathetic neurotransmission and reduces alpha1-adrenergic contractile responses in rat mesenteric arterial bed. Pereira CA, Resstel LBM, Tostes RC USP – Farmacologia

06.060 Chemerin decreases insulin-induced vasodilation by reducing PI3K-AKT and MAPK signaling. Neves KB[1], Lobato NS[2], Lopes RAM[3], Mestriner FL[3],

Oliveira AM[1], Tostes RC[3] [1]FCFRP – USP – Pharmaceutical Sciences, [2]UFG – Biological Sciences, [3]FMRP-USP – Pharmacology

06.061 Maternal fluoxetine treatment during pregnancy and lactation increased the endothelium modulation of vasoconstriction in female adult offspring. Silva MA[1], Gerardin DC[1], Moreira EG[1], Pelosi GG[1], Akamine EH[2], Carvalho MHC[2], Ceravolo GS[1] [1]UEL – Fisiológicas, [2]ICB-USP – Farmacologia

06.062 Effects of dichloromethane extract of *Eugenia punicifolia* and derivatives in smooth muscle. Teixeira RGS[1], Pascual R[2], Araújo KGL[1], Gandía L[2], Silva CLM[3], Santos WC[1] [1]UFF, [2]Universidad Autónoma de Madrid, [3]UFRJ

06.063 Biophysical and pharmacological characterization of a new and efficient agonist of the high-conductance BK potassium channels. Duarte BO, Suarez-Kurtz G, Nascimento JHM, Ponte CG IFRJ – Biotecnologia

08. Respiratory, Urinary and Reproductive Pharmacology

08.001 Serotonin contracts the rat corpus cavernosum, but how? Berretta LM, Linder AE UFSC – Farmacologia

08.002 Effects of clonidine in the isolated rat testicular capsule. Silva-Júnior ED[1], Rodrigues JQD, Souza BP, Jurkiewicz A, Jurkiewicz NH Unifesp – Farmacologia

08.003 Soluble guanylate cyclase (sGC) degradation and impairment of nitric oxide-mediated responses in urethra from obese mice: Reversal by the sGC activator Bay 60-2770. Alexandre EC[1], Leiria LO[1], Silva FH[1], Davel APC[2], Mónica FZ[1], Antunes E[1] [1]Unicamp – Farmacologia, [2]IB-Unicamp

08.004 Increased prostate smooth muscle reactivity in middle-aged rats. Calmasini FB, Silva FH, Rodrigues RL, Báu FR, Antunes E FCM-Unicamp – Pharmacology

08.005 Bay 60-2770, a soluble guanylate cyclase activator relaxes corpus cavernosum from rabbit. Estancial CS, de Nucci G, Antunes E, Mónica FZ Unicamp – Farmacologia

08.006 Mirabegron, a beta-3 adrenergic agonist relaxes rat corpus cavernosum and rabbit prostate. Candido TZ, Antunes E, de Nucci G, Mónica FZ Unicamp – Farmacologia

08.007 Effect of opiates agonist in isolated corpus cavernosum from *Callithirx sp*. Rodrigues RL, Antunes E, de Nucci G, Mónica FZ FCM-UNICAMP – Pharmacology

08.008 Wistar audiogenic rat (WAR) displays erectile dysfunction: *In vivo* assessment. Rodrigues FL[1], Pereira MGAG[2], Garcia-Cairasco N[2], Tostes RC[1], Carneiro FS[1] [1]FMRP-USP – Pharmacology, [2]FMRP-USP – Physiology

08.009 Influence of adrenalectomy and dexamethasone treatment on testicular morphology and sperm parameters in adult rats. Silva EJR[1], Vendramini V[2], Restelli AE[3], Bertolla RP[3], Kempinas WG[4], Avellar MCW[1] [1]Unifesp – Farmacologia, [2]Unifesp – Morfologia e Genética, [3]Unifesp – Cirurgia, [4]Unesp – Morfologia

08.010 Treatment with ipriflavone improves the expression of neuronal nitric oxide synthase in genital tissue in the ovariectomized rat model of menopause. Rodovalho GV[1], Martins TA[1], Rezende J[1], Sá RG[2], Leite R[1] [1]CiPharma-UFOP, [2]UFOP – Ciências Biológicas

08.011 Acute aerobic exercise alters the contractile and relaxant responses on rat trachea. Brito AF, Souza ILL, Pereira JC, Silva AS, Silva BA UFPB

08.012 Evaluation of the in vitro response of human cells exposure to environmental pollution by polycyclic aromatic hydrocarbons. Mattos MS, Kraemer LR, Freire BHL, Teixeira MM, Resende RR, Russo RC UFMG

08.013 Inducible NO synthase plays a major role in obesity-associated overactive bladder. Leiria LO[1], Augusto TM[2], Teixeira SA[3], Muscará MN[3], Carvalho HF[2], Antunes E[1] [1]Unicamp – Farmacologia, [2]Unicamp – Biologia Estrutural e Funcional, [3]USP – Farmacologia

08.014 The NADPH oxidase inhibitor apocynin prevents sympathetic hyperactivity and down regulation of soluble guanylyl cyclase in corpus cavernosum from middle-aged rats. Silva FH[1], Leiria LO[1], Davel APC[2], Claudino MA[3], Toque HA[4], Antunes E[1] [1]Unicamp – Pharmacology, [2]Unicamp – Anatomy, Cellular Biology, Physiology and Biophysics, [3]USF – Laboratory of Multidisciplinary Research, [4]Georgia Health Sciences University – Pharmacology and Toxicology

08.015 Castration-induced impairment of rat internal pudendal artery reactivity is associated with vascular remodeling. Lopes RAM[1], Neves KB[2], Silva MAB[1], Carneiro FS[1], Tostes RC[1] [1]FMRP-USP – Pharmacology, [2]FCFRP-USP

09. Natural Products and Toxinology

09.043 Gastroprotective and healing activity of the hydroalcoholic fraction from leaves of *Cenostigma macrophyllum* Tul. var. Acuminata Teles Freire. Viana AFSC[1], Fernandes HB[1], Reis Filho AC[1], Lima GS[1], Santos MO[1], Chaves MH[2], Oliveira RCM[1] [1]UFPI – Medicinal Plants, [2]UFPI – Chemistry

09.044 A carvacrol synthetic derivative attenuates inflammatory and nociceptive responses. Bonfim RR[1], Paiva-Souza IO[1], Pereira DS[1], Moraes JP[1], Sousa DP[2], Barreto EO[3], Camargo EA[1] [1]UFS – Physiology, [2]UFS – Pharmacy, [3]UFAL – Cellular Biology

09.045 Influence of the route of administration on the cardiovascular responses to *Bothrops atrox* snake venom in anesthetized rats.

Rodrigues MAP, Dias L, Brunieri LVP, Rennó AL, Stroka A, Mello SM, Hyslop S Unicamp – Farmacologia

09.046 Resveratrol reduces maximum contractile response under alpha1-adrenoceptor stimulation in non-vascular smooth muscle. Vieira DFA[1], Domingos AO[2], Restini CBA[2] – [1]Unaerp – Ciências Farmacêuticas, [2]Unaerp – Medicina

09.047 Vasodilator effect of extract of *Cecropia glaziovi* in normotensive and hypertensive rats. Lobo KL[1], Carioletti GH[1], Santos TC[2], Campos AM[2], Linder AE[1] [1]UFSC – Pharmacology, [2]UFSC – Pharmaceutical Sciences

09.048 Capsaicin or eugenol treatment protects mice against some activities of *Apis mellifera* bee venom. Tavares-Henriques MS, Gonçalves TS, Monteiro-Machado M, Amorim-Tomaz M, El-Kik CZ, Passos-Guimarães, Melo PA ICB-CCS-UFRJ – Farmacologia e Química Medicinal

09.049 Rat isolated right atrial responses to *Vitalius dubius* (Araneae, Theraphosidae) venom and a purified polypeptide. Tamascia ML[1], Rennó AL[1], Zelanis A[2], Serrano SMT[2], Hyslop S[1] [1]Unicamp – Farmacologia, [2]CAT-CEPID-IBu – Toxinologia Aplicada

09.050 *Polygala cyparissias* induces vasorelaxation by inhibition calcium influx in rat isolated mesenteric artery. Albuquerque JM[1], Alves QL[1], Simões LO[1], Ramos-Reis M[1], Cechinel-Filho V[2], Silva DF[1] [1]UFBA – Biorregulação, [2]NIQFAR-CCS-UNIVALI

09.051 A role for adenosine in the hypotension caused by *Bothrops alternatus* snake venom in rats. Pereira EM, Tamascia ML, Hyslop S Unicamp – Farmacologia

09.052 Gestational toxicological evaluation of *Nepeta cataria* (Catnip) in rats by behavioral tests. Pereira MS, Mataqueiro MI, Moranza HG, Rizzo LF, Ferraz GC, Queiroz-Neto A FCAV-Unesp-Jaboticabal – Morfologia e Fisiologia Animal

09.053 Antihypertensive potential of extract from *Solanum sisymbriifolium* in spontaneously hypertensive rats – ethnopharmacological study. Simões LO[1], Silva AQG[2], Cechinel-Filho V[3], Silva DF[2] [1]UFBA – Ciências Farmacêuticas, [2]ICS – Biorregulação, [3]Univali

09.054 Investigation of tocolytic effect of *Lippia microphylla* Cham. essential oil (Verbenaceae) and its major compounds, thymol and carvacrol, on rat uterus. Silva MCC, Medeiros MAMB, Souza ILL, Ferreira PB, Sampaio RS, Martins IRR, Calvacante FA, Tavares JF, Silva BA UFPB

09.055 Gastroprotective properties of hydroalcoholic extracts and fractions from leaves of *Camellia sinensis* in rats. Borato DG[1], Ferreira DM[1], da Silva LM[1], Galuppo LF[1], Scoparo CT[2], Iacomini M[2], Werner MFP[1], Baggio CH[1] [1]UFPR – Pharmacology, [2]UFPR – Biochemistry and Molecular Biology

09.056 Antispasmodic effect of *Cardiospermum corindum* L. (Sapindaceae) on rat ileum. Silva VA[1], Andrade JR[1], Silva FL[2], Barbosa-Filho JM[3], Rigoni VLS[4,5], Nouailhetas VLA[4], Silva JLV[1] [1]Uninove – Farmácia-Bioquímica, [2]CCS-UFPB – Produtos Naturais e Sintéticos Bioativos, [3]CCS-UFPB – Ciências Farmacêuticas, [4]Unifesp – Biofísica, [5]Uninove – Medicina

09.057 Antimicrobial effect of the peppers *Capsicum baccatum var*. *Pendulum* and *Capsicum chinense* on *Staphylococus aureus* and *Pseudomonas aeruginosa* and its toxicity levels over *Artemia salina* Leach. Gontijo LS, Lima EA Pitágoras – Medicina

09.058 *Bidens pilosa* L. Root (Asteraceae) protects stomach against ulcer gastric in rats. Nascimento AJA[1], Nascimento PF[1], Santos JR[1], Costa DES[1], Silva FL[2], Barbosa-Filho JM[3], Silva JLV[1] [1]Uninove – Farmácia-Bioquímica/Saúde, [2]CCS-UFPB – Produtos Naturais e Sintéticos Bioativos, [3]UFPB – Ciências Farmacêuticas

09.059 Evaluation of the antimicrobial activity of *Agave sisalana*. Santos L, Santos HZT, Oliva Neto P [1]Unesp-Assis – Ciências Biológicas

09.060 Anticoagulant effect of chemically sulfated plant polysaccharides. Castro RR[1], Silva RO[1], Madeira JC[1], Pereira MG[1], Almeida RR[2], Ricardo MNPS[2] [1]UECE, [2]UFC

09.061 Antioxidant potential of extracts and fractions of *Agave sisalana*. Mazo GS, Zamaro HS, Santos L Unesp-Assis – Ciências Biológicas

09.062 Comparative toxinology of *Bothrops jararaca* and *Bothrops fonsecai* snake venoms. Collaço RCO[1], Silva IRF[1], Tamascia ML[1], Cogo JC[2], Randazzo-Moura P[3], Rodrigues-Simioni L[1], Hyslop S[1] [1]FCM-Unicamp – Farmacologia, [2]Univap – Pesquisa e Desenvolvimento, [3]PUC-SP – Farmacologia

09.063 Preliminary assessment of the bioactivity of ethanol extracts of parts of *Moringa oleifera* Lam. Nascimento JA[1], Santos AM[2], Nascimento AA[2] [1]UFPB – Ciência e Tecnologia de Alimentos, [2]Unifap – Ciências da Saúde

Lecture Abstracts

Courses:

Building Biotechnology. Ferro ES. Departamento de Biologia Celular e do Desenvolvimento, ICB-USP.

A biotecnologia é uma prática antiga, sendo utilizada desde o antigo Egito para a produção de pão e cerveja. No mundo contemporâneo, a biotecnologia tem sido utilizada de diversas formas, incluindo o tratamento de doenças. No universo acadêmico, a biotecnologia tem permiti-do um avanço rápido do conhecimento. Em nossa apresentação, faremos um breve resumo sobre o que é biotecnologia, sua relação com o processo de inovação e produção de biofármacos. No universo acadêmico, a biotecnologia tem contribuí-do de forma decisiva para a descoberta de novas moléculas bioativas. Suporte financeiro: CNPq, CAPES, FAPESP, Pró-Reitoria de Pesquisa USP (NAPPS)

How to start a small Biotech Company: **Just do it!** Heimann AS, Proteimax Biotecnologia Ltda.

Uma empresa de biotecnologia só necessita de uma ideia para ser aberta. No entanto, os riscos inerentes da biotecnologia são muito altos, e o retorno é sempre em longo prazo. Para dizer a verdade, o risco associado a pequenas empresas de biotecnologia é tão grande que é muito difícil confiar para fazer investimento financeiro. Mas, se o potencial de crescimento existe em uma pequena empresa de biotecnologia, podemos esperar um retorno impressionante sobre o valor investimento, por isso o risco pode valer a pena. Existem alguns cuidados para se ter na hora de iniciar o projeto que podem minimizar esse enorme risco, entre os quais verificar se há mercado para o produto e diante do investimento pretendido se haverá o retorno esperado. Em nosso curso tomaremos como exemplo a Proteimax Biotecnologia Ltda, que há 12 anos atua no mercado de nacional e internacional de biotecnologia. Suporte financeiro: CNPq, FAPESP e Proteimax Biotecnologia Ltda.

In silico, ***in vitro*** **and** ***in vivo*** **approaches in the Drug Development Process**.

Introdução: O principal objetivo deste curso é de oferecer uma visão crítica das primeiras fases do processo de descoberta e desenvolvimento de novos fármacos, baseado na literatura assim como na experiência própria dos docentes. O curso detalhará os objetivos, princípios, vantagens e desvantagens dos ensaios usados nas três seguintes etapas: *in silico*, *in vitro* e *in vivo*.

Drug Development: ***in silico*** **approaches** Fraga CAM. ICB-UFRJ.

Serão descritas brevemente as diferentes abordagens para o planejamento estrutural de novos protótipos candidatos a fármacos, dando ênfase as estratégias baseadas na estrutura do receptor alvo. Serão enumeradas as possíveis maneiras de se acessar a estrutura tridimensional de biomacromoléculas, *e.g*. difração de raios-X, RMN-H^1, modelagem por homologia, indicando suas principais vantagens e desvantagens. Os diferentes métodos *in silico* usados para compreender as interações moleculares associadas ao reconhecimento de uma micromolécula por uma biomacromolécula serão abordados, com ênfase nas ferramentas de docking e dinâmica molecular. Ademais, métodos modernos de triagem virtual de quimiotecas e a otimização estrutural de fragmentos

moleculares de baixo peso molecular, além do uso de ferramentas in silico para previsão de aspectos farmacocinéticos (absorção e metabolismo), também serão alvo de nosso curso. Enfatizaremos a vantagem da integração das abordagens *in silico*, *in vitro* e *in vivo*, *e.g*. em termos de busca de informações sobre afinidade e eficácia dos novos compostos em estudo, que permitam a validação dos modelos teóricos desenvolvidos e aplicados no planejamento de novos protótipos candidatos a fármacos. Apoio Financeiro: CNPq, FAPERJ, INCT-INOFAR.

Drug Development: ***In vitro* approaches**. Noël FG. ICB-UFRJ.

Após enumerar brevemente os modelos *in vitro* usados para avaliar aspectos particulares de farmacocinética (absorção, metabolização) e toxicologia, iremos dar mais ênfase nos aspectos farmacodinâmicos. Abordaremos os ensaios *in vitro* utilizados tanto para o *screening* quanto para determinação do mecanismo de ação de novos candidatos a fármacos. Discutiremos as vantagens e desvantagens dos modelos baseados no alvo molecular (ensaios de *binding*) *vs* modelos mais integrativos baseados em células e órgãos isolados. Enfatizaremos a vantagem da integração das abordagens *in silico*, *in vitro* e *in vivo*, *eg* em termos de busca de informações sobre afinidade e eficácia dos novos compostos em estudo. No caso dos ensaios de *binding*, discutiremos o ensaio de competição muito utilizado como méto-do de HTS (*High-through put screening*) para determinação da afinidade de um ligante para um deter-minado receptor. Mostraremos também como diferentes modalidades da técnica de *binding* podem servir para avaliar a eficácia intrínseca de uma substância (*binding functional*: GTP-*shift*, *binding* de [^{35}S]GTPγS para receptores metabotrópicos) e auxiliar no refinamento do mecanismo de ação molecular (ação no sítio ortostérico *vs* modulação alostérica; mecanismo bioquímica molecular, relacionado à cinética do efeito). Mencionaremos também o quanto o conceito de seletividade funcional desafia a avaliação da eficácia de um composto assim como a elaboração de HTS. Apoio financeiro: CNPq, FAPERJ, INCT-INOFAR

Drug Development: ***In vivo* approaches**. Sudo RT ICB-UFRJ.

Ensaio *in vivo* é etapa essencial e necessária na escalada de desenvolvimento de fármacos. Ausência desta etapa compromete, enfraquece e às vezes inviabiliza a inovação. Moléculas são planejadas para interagir com alvos específicos inte-grantes da fisiopatologia da doença. Testes em modelos computacionais, em células, em fragmentos de tecidos e em órgãos isolados podem demonstrar o sucesso do planejamento molecular. A comprovação da eficiência da nova substância proposta em diminuir sintomas, inibir o desenvolvimento da doença ou mesmo revertê-la em modelos animais é denominado prova de conceito. Este conceito é extremamente necessário pelo fato das informações obtidas *in vitro* não ter a forca suficiente para a translação da eficiência em doenças, principalmente as humanas. A atividade deste dia terá como objetivo central mostrar a importância e a necessidade da realização do ensaio *in vivo* no sentido de validar a inovação. Serão discutidos como selecionar os modelos experimentais e como desenhar os protocolos experimentais para diversas

situações que se aproximam da doença humana. Haverá discussão sobre vantagens e desvantagens dos principais modelos experimentais divididos por sistemas comprometidos pela doença, assim como, de apresentação de resultados pessoais. Além da prova conceitual será discutida a utilização de ensaios *in vivo* para avaliação pré-clinica da toxicidade aguda e subaguda dos fármacos, mostrando como estas etapas podem ser limitante no prosseguimento do desenvolvimento de fármacos. Apoio financeiro: CNPq, FAPERJ, INCT-INOFAR

Conferences

Cytokines: **from immune system hormones to mediators of pain and inflammation**. Poole S*, Ferreira S†, Cunha F†*. Biotherapeutics Group, NIBSC, UK †FMRP-USP – Farmacologia The characterization and subsequent cloning of cytokines that began in the early 1980's greatly improved our understanding of how the immune system uses the large number of chemical mediators that we now call cytokines. While immunologists began to investigate the autocrine, paracrine and endocrine functions of these molecules, Sergio Ferreira and his collaborators set out to investigate potential roles for cytokines in pain and inflammation. The rationale for this work was the finding that one of the first cytokines to be characterized and cloned, interleukin-1 (IL-1), was a potent inducer of prostaglanins (PGs), which Ferreira and colleagues had identified in the 1970s as important mediators of inflammatory pain [1]. The initially limited availability of recombinant IL-1 made it necessary for scientists wishing to generate immunoassays for IL-1 to use synthetic peptides with sequences derived from the published IL-1 sequence. These IL-1-related peptides were the starting point for Ferreira's investigation of the role of IL-1 in pain and inflammation, and structure-activity data for the peptides, and IL-1 itself when this became available, enabled the important role of IL-1 in inflammatory pain to be elucidated [2]. Subsequently, Ferreira, Cunha and others identified the role of the chemokine IL-8 in pain involving the sympathetic nervous system ("sympathetic pain") [3] and the important roles of tumour necrosis factor alpha, IL-6 and other cytokines in inflammatory pain [4] and the interactions of cytokines with bradykinin and other mediators [5]. The resulting body of work (some 300 publications) from Ferreira's laboratory on the roles of eicosanoids, other autocoids and cytokines in inflammatory pain represents the largest single contribution to our knowledge of this subject of any scientist in any country. References: [1] Moncada S, Ferreira SH, Vane JR. Prostaglandins, Aspirin-like Drugs and the Oedema of Inflammation. Nature, 1973, 246, 217-219. [2] Ferreira SH, Lorenzetti BB, Bristow AF, Poole S. Interleukin-1 beta as a potent hyperalgesic agent antagonized by a tripeptide analogue. *Nature*, 1988, 334 (6184), 698-700. [3] Cunha FQ, Lorenzetti BB, Poole S, Ferreira SH. Interleukin-8 as a mediator of sympathetic pain. *Br J Pharmacol*., 1991, 104(3), 765-7. [4] Cunha FQ, Poole S, Lorenzetti BB, Ferreira SH. The pivotal role of tumour necrosis factor alpha in the development of inflammatory hyperalgesia. *Br J Pharmacol*., 1992, 107(3), 660-4. [5] Ferreira SH, Lorenzetti BB, Poole S. Bradykinin initiates cytokine-mediated inflammatory hyperalgesia. *Br J Pharmacol*. 1993, 110(3), 1227-31.

Approaches targeting voltage-gated channels open a novel window for diagnosis and therapy. Stühmer W. MPI experimentelle Medizin, Göttingen, Germany).

Emerging evidence indicates that ion channels act in a variety of physiologic and pathologic processes beyond electronic signal transmission, including in cancer. Since this group of molecules has been successfully targeted for decades in other therapeutic areas, there is a significant body of knowledge on the pharmacology of potassium channels. Several groups of potassium channels with defined molecular identities have been proposed as candidates for therapeutic intervention. The strategies put forward range from classical small molecule blockade to gene therapy approaches, and include the use of potassium channels as targets for adjuvant therapy. We recently found that the potassium channel K(V)10.1 (or Eag1) can mediate cancer progression and that a monoclonal antibody, which inhibits K(V)10.1 action, can effectively restrict cancer cell proliferation. Due to its cell-surface accessibility, K(V)10.1 has a strong potential for tumor treatment and diagnosis. In addition, K(V)10.1 is confined to the central nervous system in physiological conditions. Therefore, this putative therapy would have few collateral effects once that the monoclonal antibody against K(V)10.1 has poor penetrability in the blood-brain-barrier. Given that its mode of action is likely independent of conventional cancer pathways such as tyrosine kinases, K(V)10.1 opens a novel window for treating cancer. We will give an overview of the current status of data linking K(V)10.1 to cancer, and propose techniques that could exploit K(V)10.1's properties for the management of cancer. References: 1- Pardo LA, Stühmer W. Eag1: an emerging oncological target. Cancer Res. 2008, 15;68(6):1611-3. 2- Stühmer W, Pardo LA. K(+) channels as therapeutic targets in oncology. Future Med Chem. 2010, 2(5):745-55. 3- Gómez-Varela D et al., Approaches targeting K(V)10.1 open a novel window for cancer diagnosis and therapy. Curr Med Chem. 2012;19(5):675-82. Financial support: Max Planck Society, Alexander von Humboldt Foundation.

Endoplasmic reticulum stress is a novel regulator of calcium signaling in the vasculature. Spitler KM., Giachini F, Tostes R, Webb RC. Georgia Regents University – Physiology

Dysfunctional calcium (Ca^{2+}) signaling contributes to the augmented vascular reactivity characteristic of hypertension. Upon agonist stimulation, vascular smooth muscle cells (VSMC) display a biphasic increase in cytosolic Ca^{2+}. First there is a transient increase due to inositol trisphosphate (IP_3)-mediated release of endoplasmic reticulum (ER) Ca^{2+} stores. Subsequently, activation of store-operated Ca^{2+} entry (SOCE) triggers plasma membrane Ca^{2+} entry into the cell resulting in a prolonged increase in cytosolic Ca^{2+} levels. Stromal interaction molecule 1 (STIM-1) is a resident Ca^{2+} sensor of the ER that triggers SOCE following ER store depletion through its interaction with Orai, a component of Ca^{2+} release-activated Ca^{2+} channels (CRAC). We demonstrated that increased VSMC Ca^{2+} influx via augmented STIM-1/Orai activity and enhanced ER Ca^{2+} release contribute to changes in vascular reactivity in hypertension. However, no studies have addressed the cellular mechanisms that underlie these observations. Thus, identification of new

signaling pathways that may lead to dysregulation of Ca^{2+} handling in the vasculature could unravel novel therapeutic targets. The ER is responsible for the synthesis, processing and folding of proteins, Ca^{2+} storage and lipid biosynthesis. A variety of cellular stresses (inflammation, oxidative, energy or Ca^{2+} depletion) interfere with the folding capacity which causes ER stress. The ER has a complex signaling cascade to cope with stress known as the unfolded protein response (UPR). Three ER membrane proteins initiate the signaling arms of the UPR: PKR-like ER kinase (PERK), inositol-requiring enzyme-1 (IRE1) and activating transcription factor-6 (ATF6). During ER stress the UPR signaling through these proteins works to restore ER homeostasis in part through the upregulation of ER chaperone proteins. Several ER chaperones require Ca^{2+} as a cofactor for their protein folding activity. Therefore the regulation of Ca^{2+} by the ER is not only critical for maintaining a low cytosolic Ca^{2+} concentration but is vital in maintaining proper ER function. Prolonged ER stress has been implicated as a key contributor to the development of cardiovascular disease. In this presentation we summarize evidence demonstrating that the ER is a major player in Ca^{2+} homeostasis and ER stress occurs in the vasculature during hypertension. We hypothesize that ER stress mediates the increased activation of STIM-1/Orai-1, Ca^{2+} influx and ER Ca^{2+} release in the vasculature. Consequently, inhibition of ER stress in a genetic model of hypertension should normalize Ca^{2+} signaling.

Heteromerization of G protein-coupled receptors: **Impact on physiopathology and drug design**. Jockers R. Institut Cochin, INSERM-CNRS, Université Paris Descartes

G protein-coupled receptors (GPCR) are involved in all physiological processes and are major drug targets. The idea that GPCR might form dimers or higher order oligomeric complexes has been formulated more than 20 years ago. Since then, this phenomenon has been confirmed with many different biochemical and biophysical techniques. Whereas receptor oligomerization is now widely accepted for class C GPCRs, it is still a matter of ongoing debate for class A GPCRs.

The more recent notion of GPCR heteromerization (association of two different GPCRs) is of primary importance, as these heteromers considerably expand the repertoire of functional GPCR units. Indeed, most GPCR heteromers have distinct functional properties compared to their corresponding homomers. Whereas GPCR heteromers have been first studied in heterologous expression systems, increasing evidence for the existence of GPCR hetermers in endogenous systems is emerging.

Mining drugs from bugs: **A blueprint of the mining field**. Ribeiro JMC. NIAID-NIH – Vector Biology.

Stealing vertebrate blood as a survival strategy requires a diverse set of skills including mechanical adaptations to lacerate the skin and sipping blood, as well as pharmacological innovations to antagonize their hosts' hemostasis, inflammation and immunity. The tripod of hemostasis, platelet aggregation, vasoconstriction and blood clotting, has to be properly antagonized for efficient blood feeding, and indeed saliva of blood sucking animals have at least one inhibitor of platelet aggregation, one vasodilator and one anti-clotting

component. Host behavioral defenses triggered by pain or itching can also prevent efficient blood feeding, opening up a large number of molecular targets that blood suckers attempt to disarm. Accordingly, all mediators of pain and itch are targeted, including bradykinin, histamine, serotonin, leukotrienes and ATP, as well as the nerve conduction itself. Complement activation and pro-inflammatory serine proteases are also targeted, as well as immune cell activation. The complex and redundant mechanisms of hemostasis, inflammation and immunity are thus counteracted by a complex potion of salivary compounds injected into the vertebrate skin while blood suckers attempt to feed.

The habit of blood feeding has evolved at least 21 times within animals including insects, ticks and mammals. A convergent evolution scenario is thus characteristic of the salivary composition of these animals. For example, ticks and triatomine bugs have completely different protein families or compounds to act as anticlotting or as vasodilatory substances. However, this diversity is also seen within animals that have a common blood feeding ancestor: While the anticlotting of *Aedes* mosquitoes is a member of the serpin family targeting Factor Xa, those of *Anopheles* are members of a novel peptide family targeting thrombin. Comparison of salivary proteins among species of the same mosquito subgenus shows that salivary proteins are at a fast pace of evolution, possibly driven by positive selection following chase by their hosts' adaptive immunity that creates a frequency dependent selection environment. The composition of the salivary potion of blood feeding animals is thus very large due to a convergent evolutionary scenario as well as the very fast pace of evolution of the salivary potion itself.

Advances in transcriptomic techniques allowed the description of the sialome (from the Greek sialo=saliva) from blood sucking insects, ticks and bats. It is estimated that sand fly (vectors of cutaneous leishmaniasis) saliva consists of ~40 different proteins, while those of mosquitoes near 100 and those from ticks reach 1,000 proteins. Ticks feed for several days or weeks and face their host's immunity in a protracted way different from the blitzkrieg preferred by mosquitoes or kissing bugs, which lasts less than 15 min. Ticks have many copies of the same protein family, sometimes with less than 50% identity, that they inject at different days of feeding, thus avoiding their host's immune response. There are near 15,000 species of blood sucking arthropods (ticks + insects), within 400 different genera of blood sucking arthropods. Analysis of the sialome of 25 different genera indicates that each reveals from 3-5 unique protein families, unique meaning there are no other known protein with similar primary sequence. Even closely related insects reveal novel salivary proteins. It is estimated that at least 2,000 novel protein families with unknown pharmacological activity remains to be discovered and characterized.

Because many blood suckers are also vectors of disease, and in the majority of cases the pathogen is injected at the site of the bite, it follows that the first encounter of the vertebrate immune system with the pathogen is in a site profoundly modified by the vector's saliva. Indeed the outcome of needle injection of pathogens is normally quite different from needle injection in the

presence of vector salivary homogenate, which normally potentiate infection in naïve hosts. These discoveries opened up another field of sialome research by targeting vector saliva as antigens to modify or prevent vector borne diseases, including leishmaniasis, Lyme's disease and arboviral diseases. Sialome research has also allowed fast identification of salivary antigens that may be used as immunological markers of vector exposure, many of which are now been tried in the field. Supported by the Intramural Research Program of the National Institute of Allergy and Infectious Diseases.

Completing the circle in drug development: **discovery and applications of cyclotides**. David J Craik. Institute for Molecular Bioscience, The University of Queensland, Brisbane, Australia

Cyclic peptides have a number of advantages over linear peptides and are, in particular, characterized by their higher stability. Over recent years more than 200 examples of ribosomally synthesized head-to-tail cyclised mini-proteins have been discovered in bacteria, plants and animals[1]. The cyclotides[2] are the largest family of these circular proteins and have applications in drug design[3] and agriculture[4]. They occur in plants from the Violaceae (violet), Rubiaceae (coffee) and Cucurbitaceae (cucurbit) families and have a diverse range of biological activities, including uterotonic, anti-HIV, antimicrobial, and insecticidal activities, the latter suggesting that their natural function is in plant defence. Individual plants express suites of 10-100 cyclotides. Cyclotides typically comprise ~30 amino acids, and incorporate three disulfide bonds arranged in a cystine knot topology. The combination of this knotted and strongly braced structure with a circular backbone renders the cyclotides impervious to enzymatic breakdown and makes them exceptionally stable. This presentation will describe the discovery of cyclotides in plants, their structural characterization, evolutionary relationships and their applications in drug design. Their stability and compact structure makes them an attractive protein framework onto which bioactive peptide epitopes can be grafted to stabilize them. Examples to be described include the development of lead molecules for cancer, infectious diseases, cardiovascular disease and autoimmune disease. Funding: this work was funded by a Fellowship and grants from the NHMRC (Australia). 1. Craik D J: *Science*, 2006, *311*, 1561. 2. Gruber C W, Elliot A, Ireland D C, Delprete P G, Dessein S, Göransson U, Trabi M, Wang C K, Kinghorn A B, Robbrecht E F, Craik D J: *The Plant Cell*, 2008, *20*, 2471. 3. Henriques S T, Craik D J: Cyclotides as templates in drug design. *Drug Discovery Today* 2010, 15, 57. 4. Barbeta B L, Marshall A T, Gillon A D, Craik D J, Anderson M A: *PNAS* 2008, *105*, 1221.

Polypharmacy of osteoarthritis: **The perfect intestinal storm**. Wallace JL. McMaster University, Canada

Osteoarthritis is an increasingly prevalent disorder with an incidence rate that rises sharply with age. Unfortunately, the most commonly used medications for providing symptomatic relief, nonsteroidal anti-inflammatory drugs (NSAIDs), can cause significant gastrointestinal (GI) ulceration. There is recent evidence that agents commonly employed to protect the upper GI tract actually increase the incidence and severity of ulceration and bleeding in the lower intestine. Intestinal injury is more difficult to diagnose and treat than upper

GI damage, and symptoms correlate poorly with the severity of tissue injury. Moreover, use of low-dose aspirin for cardioprotection (a common co-treatment with the selective cyclooxygenase-2 inhibitors) further augments intestinal damage, particularly when enteric-coated aspirin is used. Thus, by focusing entirely on prevention of NSAID-induced damage to the upper GI tract, physicians may be placing their patients at greater risk of serious, difficult to diagnose injury for which there are no proven-effective therapies, and that are associated with significantly higher rates of morbidity and mortality.

The relevance of toxins and other Natural Products for drug discovery. Harvey AL. University of Strathclyde, Glasgow and Dublin City University.

This presentation will address the question "How can a globally significant drug discovery operation be created in Brazil?" There are good reasons, both scientific and commercial, to focus on natural product-based drug discovery. Natural products have been the most successful source of medicines throughout history and they continue to provide leads for major classes of drugs, including antibiotics, anti-cancers, immunosuppressants and neurological agents. Many natural products have physicochemical properties suitable for drug development and their unmatched structural diversity allows them to interact with many different types of therapeutic targets. Surprisingly, major pharmaceutical companies have abandoned their use of natural products in drug discovery; also surprisingly, the vast majority of natural products have never been tested for relevant biological activity. There are clear opportunities for specialist ventures to exploit natural chemical diversity to discover novel leads that can be developed into valuable new medicines. The technologies required for natural product chemistry and for drug discovery bioassaying are becoming cheaper and more accessible. The key requirements for successful drug discovery are (1) outstanding chemical diversity in a sample collection that is in an "assay-ready" format and (2) sensible selection of therapeutic targets that are relevant to the diseases of interest, whether these are previously neglected illnesses endemic to the region or unmet therapeutic needs of large commercial markets. Given Brazil's rich biodiversity in land and sea and the quality of Brazilian scientific infrastructure, a drug discovery initiative based on natural products would be expected to produce valuable leads for significant new medicines.

Symposia

Entrepreneurship programs for university approach to the market. Purceno AD. Incubadora de Empresas INOVA, Coordenadoria de Transferência e Inovação Tecnológica – Universidade Federal de Minas Gerais – Belo Horizonte/MG – Brasil

Uma das maiores barreiras enfrentada pelas universidades brasileiras tem sido a dificuldade na vazão do conhecimento gerado nos centros pesquisa para o mercado, principalmente quando comparado às universidades internacionais, em especial as norte-americanas. As empresas de uma, maneira geral, tem tido uma visão burocratizada das universidades limitando muito o interesse de interação. Desenvolver maneiras inovadoras e dinâmicas para interação com as empresas é necessário caso queiramos alavancar a universidade ao nível de competitividade internacional.

Nesta apresentação Dr. Aluir Dias Purceno, Farmacêutico e coordenador da incubadora de empresas INOVA – UFMG apresentará as ferramentas desenvolvidas na UFMG para aproximação Universidade-Empresas. Entre as ferramentas, será apresentado o modelo NEXU de empreendedorismo, onde alunos da graduação desenvolvem estudos mercadológicos das tecnologias desenvolvidas na universidade, visando aumentar a atratividade para o mercado. Além do espaço NEXU, Aluir mostrará alternativas já praticadas pela UFMG onde as empresas juniores podem contribuir com o movimento empreendedor na geração de startups. Outra ferramenta, desenvolvida e praticada pela UFMG, é a formação de um núcleo de estudantes capacitados para consultoria de negócios. Esses estudantes, após treinamento, atuam no suporte ao desenvolvimento de novos negócios nas incubadoras universitárias. Além de contribuir com o ecossistema empreendedor da universidade, os alunos ganham qualificação diferenciada aumentando nitidamente sua empregabilidade. Todas as ferramentas apresentadas nesse trabalho têm a finalidade de aumentar a interação universidade-empresa e alavancar perfil gerador de novos negócios na universidade.

Um *case* de sucesso para Inovação Farmacêutica. Scivoletto R Cristália Produtos Químicos e Farmacêuticos, São Paulo, Brasil

A Cristália é uma empresa farmacêutica de capital inteiramente nacional. Fundada há 40 anos vem se destacando no cenário brasileiro por sua atuação na área de Inovação e Desenvolvimento. A empresa está estruturada pararealizar a cadeia completa de PD&I, em inovações radicais e incrementais que vai desde a prospecção e/ou concepção do projeto, passa pelo desenvolvimento do princípio ativo farmoquímico ou biotecnológico, desenvolve e/ou avalia a propriedade intelectual e industrial, conduz toda a tecnologia farmacêutica e Estudos de estabilidade, contrata, propõe e acompanha Estudos Pré-Clínicos e Clínicos para comprovação da eficácia e segurança, chegando à fabricação do produto e à disponibilização do medicamento no mercado. Seus projetos são propostos tanto pelos Pesquisadores funcionários da empresa quanto por Pesquisadores externos oriundos da academia. Na área de PD&I a ciência é discutida como o é num ambiente acadêmico e sua parceria com as Universidades e Institutos de Pesquisa é uma via de duas mãos. A interface com a academia é viabilizada através do Conselho Científico que é composto por Pesquisadores pertencentes a diferentes Universidades e que são profissionais de destaque em diversas áreas do conhecimento (multi e transdisciplinar), bem como por Pesquisadores internos à empresa. Esse Conselho avalia as propostas, propõe alterações quando necessárias e acompanha e seu desenvolvimento nas diferentes etapas. O destaque da empresa em Inovação Farmacêutica se deve à sua competência em ter estabelecido construtiva parceria com os cientistas do país.

Development of new anti-arrhythmics derived from EPA and DHA. Roy J*, Touzet-Mercier O*, Roussel J*, Thireau J*, Oger C+, Galano J-M+, Durand T+, Guennec J-Y Le*. *Inserm U1046 +UMR CNRS 5247

The cardioprotective effects through prevention of cardiac arrhythmias of long-chain polyunsaturated fatty acids of the n-3 series (PUFAs) have been

demonstrated over the last 40 years1. The main n-3 PUFAs are eicosapentaenoic acid (C20:5 n-3, EPA) and docosahexaenoic acid (C22:6 n-3, DHA) and both are highly peroxidable due to the presence of skipped dienes2. The effects of n-3 PUFA on cardiac function are still debated, notably because of the lack of information on the mechanisms involved3. Particularly, it is not well understood which is the active lipid: the PUFA or one of its oxygenated metabolites. A diet enriched in n-3 PUFAs (mainly fish-based), leads to enrichment in these fatty acids of cardiac cell membranes. Our hypothesis is that, after an infarct, the oxidative stress and the genesis of reactive oxygen species (ROS) cause an oxidation of membrane-bound PUFAs. Thus, the oxygenated metabolites generated could modulate the activity of ionic channels to exert anti-arrhythmic effects4. We thus decided to 1) produce oxygenated metabolites of EPA and DHA, isoprostanes (IsoPs) and neuroprostanes (NeuroPs) respectively5 and 2) investigate their anti-arrhythmic effects. We investigated, using a photometric system, calcium transients (using the ratiometric calcium fluorescent dye Indo-1) and cell shortening of electrically stimulated myocytes. By stimulating β-adrenergic pathways with 10 nM isoproterenol, it is possible to observe the occurrence of arrhythmic events. IsoPs and NeuroPs were applied on freshly isolated mouse ventricular myocytes. We observed that some molecules are anti-arrhythmics but not all suggesting a specificity of the effect. We are still screening IsoPs and NeuroPs and in parallel trying to unravel the signaling pathways likely involved. *Work founded by FRM (DCM2011112326047)*, *Inserm*, *CNRS*, *Universities 1 and 2*. 1 Bang H. et al. (1971) Lancet. 1: 1143-1145. 2 Jahn, U. et al. (2008). Angew Chem Int Ed Eng 47, 5894-5955 3 Saravanan P. et al. (2010). Lancet 376, 540-550. 4 Judé, S. et al. (2003). Br. J. Pharmacol. 139, 816-822. 5 Galano JM. Et al. (2013) Prostagl & Other Lipid Med, In Press.

Efficacy of new drugs in the heart: **effects on discrete events and concept of normalization of ion channels function**. Richard S, Thireau J, Le Guennec JY. INSERM U1046, Montpellier Universities 1&2, Montpellier

Arrhythmias are hard to control because they are complex, due to different types, causes and/or substrates. No really successful antiarrhythmic molecule has emerged over the last decades. However, there are new kids on the block. Among different options, novel strategies aiming at normalizing ionic homeostasis seem to be of particular interest. They are based on the fact that intracellular Na^+ and/or Ca^{2+} overload (the two can be linked) promoting spontaneous depolarization and action potentials during diastole are critically involved in the occurrence of common arrhythmias. For example, drugs that prevent excessive Na^+ entry (ranolazine) and aberrant diastolic Ca^{2+} release via the ryanodine receptor RyR2 (rycals, dantrolene, flecainide) demonstrate interesting antiarrhythmic properties. The key effect of ranolazine corresponds to the following underlying mechanistic concept: at concentrations that selectively block the "pathologic" persistent component of the Na^+ current (thereby preventing intracellular Na^+ overload), ranolazine has no effect on the global Na^+ current (in particular on peak amplitude). The Na^+ channels open normally, but the time spent in the open state is limited by the drug. Therefore,

ranolazine acts by normalizing rather than blocking (as does tetrodotoxin) the Na^+ current, which does not hamper the normal functioning of this current (excitability, and conduction). A similar "normalization" concept also applies to stabilizers of the binding of calstabin to leaky RyR2 (referred to as Rycals) that prevent only aberrant openings and Ca^{2+} leakage in diastole in diseased tissues, with no effect on normal function during systole (and therefore cardiac contraction). Interestingly, as evidenced for some local anesthetics or some Ca^{2+} channel blockers with vascular selectivity in the past, the blocking effect of flecainide on RyR2 in the open state also illustrates how the power of a drug may be in the details. In conclusion, the emergence of drugs that normalize the function of ion channels, with minimal interaction with the normal function of these proteins, may minimize potentially undesirable effects and provide more efficient and safer therapeutic options.

Chagasic Cardiomyopathy: **An electro-physiological conundrum**?
Roman-Campos D[1], Sales-Junior P[3], Duarte HL[1], Gomes ER[2], Lara A[2], Campos P[2], Rocha NN[4,5], Resende RR[1], Ferreira A[6], Guatimosim S[2], Gazzinelli RT[3], Catherine R[1], Cruz JS[1]. [1]ICB-UFMG – Bioquímica e Imunologia, [2]ICB-UFMG – Fisiologia e Biofísica, [3]CPqRR-Fiocruz – Imunopatolo-gia, [4]IB-UFF [5]Cenabio-UFRJ, [6]ICB-UFMG – Departamento de Morfologia.
Chagas' disease is one of the leading causes of heart failure in Latin American countries. Despite its great social impact, there is no direct evidence in the literature explaining the development of heart failure in Chagas' disease. Therefore, the main objective of the study was to investigate the development of the Chagas' disease towards its chronic phase and correlate with modifications in the cellular electrophysiological characteristics of the infected heart. Using a murine model of Chagas' disease, we confirmed and extended previous findings in this cardiomyopathy. The observed changes in the electrocardiogram were correlated with the prolonged action potential and reduced transient outward potassium current density. Reduced heart function was associated with remodeling of intracellular calcium handling, altered extracellular matrix content, and to a set of proteins involved in the control of cellular contractility in ventricular myocytes. Furthermore, disruption of calcium homeostasis was partially due to activation of the PI3Kinase/nitric oxide signaling pathway. Finally, we propose a causal link between the inflammatory mediators and heart remodeling during chagasic cardiomyopathy. Altogether our results demonstrate that heart failure in Chagas' disease may occur due to electrical and mechanical remodeling at the cellular level, and suggest that AKT/PI3K/NO axis could be an important pharmacological target to improve the disease outcome. Support: CNPq, FAPEMIG, PRONEX, Cristália, Fiocruz.

Could nociceptors serve cardiovascular control? **A neuroendocrine $NO^{\cdot}/H_2S$-HNO-TRPA1-CGRP pathway**.
Eberhardt M[1,5], Dux M[1,4], Namer B[1], Cordasic N[3], Miljkovic J[2], la Roche J[5], Fischer M[1], Leffler A[5], Lampert A[1], Jacobi J[3], Messlinger K[1], Ivanovic-Burmazovic I[2], Reeh P[1], Filipovic MR[2] [1]Institute of Physiology and Pathophysiology; [2]Department of Chemistry and Pharmacy; [3]Department of Nephrology and Hypertension, Friedrich-Alexander University Erlangen-Nuremberg, [4]Department of, University of Szeged – Physiology [5]Department of Anesthesiology

and Intensive Care, Medical School Hannover

Introduction: Nitroxyl, HNO, is the one-electon reduced congener of $NO^{\cdot}$, but follows an entirely distinct signaling pathway in mediating important cardiovascular functions. By inducing release of calcitonin gene-related peptide (CGRP), a potent and long-acting vasodilator, HNO combines general vasodilatation with positive inotropic and lusitropic effects [1]. HNO donors, thus, provide a great promise for the treatment of heart failure, without inducing nitrate tolerance [2]. However, the mechanism(s) by which HNO stimulates CGPR release and the biochemical pathway(s) for its *in vivo* production remained unknown. The CGRP neurosecretion is essentially controlled by the universal chemosensory receptor-channel TRPA1; its role in nociception and inflammatory diseases [3-4] has recently been elucidated, and endogenous activators emerging under pathological conditions have been identified [5]. But a constitutively produced intra- or intercellular signal that would activate TRPA1 and release CGRP from ubiquitous sensory nerves has not yet been encountered. Thus, a potential role of TRPA1 in cardiovascular physiology remained hypothesis. Recently, a new gasotransmitter emerged, hydrogen sulfide (H_2S). Several studies indicated that H_2S could interact with $NO^{\cdot}$, but only recently it was demonstrated that vasodilatory effects of H_2S directly depend on $NO^{\cdot}$ production [6], and it was shown, that HNO could be generated in the reaction of *S*-nitrosothiols and H_2S [7]. Here we provide evidence for endogenous HNO generation in a direct reaction of $NO^{\cdot}$ and H_2S and present a formerly unknown signaling cascade behind the well-documented physiological / pharmacological effects of HNO by introducing a new HNO-TRPA1-CGRP pathway as a route to neurovascular effects. Methods and results: Using biochemical techniques and fluorescent sensors [8] we provide evidence for a direct reaction of $NO^{\cdot}$ and H_2S and show that intracellular formation of HNO is dependent on $NO^{\cdot}$ and H_2S production, as it can be abrogaded by blocking pertinent enzymes, e.g. in dorsal root ganglion sensory neurons. Furthermore calcium imaging and patch-clamping provide that HNO - either applied by the donor Angeli's salt or by co-application of $NO^{\cdot}$ and H_2S – activates the irritant receptor TRPA1. Confirmed by biochemical techniques and peptide modeling, HNO, but not $NO^{\cdot}$ or H_2S alone, modulates TRPA1 channels by modifying critical cysteines [9-10] leading to formation of disulfide bonds which represent a novel mechanism for a remarkably sustained activation of the channel. As a consequence CGRP is released which is further investigated in knockout mouse studies using isolated heart and mesenteric blood vessels and an enzyme-linked immunosorbent assay. Drop in blood pressure in anaesthetized mice receiving HNO is dependent on TRPA1 and $NO^{\cdot}$-production and, furthermore, TRPA1 and CGRP substantially contribute to systemically and locally induced vasodilatation by H_2S. Finally, in a psychophysiological study on human volunteers we provide evidence for this new H_2S/NO-HNO-CGRP signaling cascade to be functional in the skin.

Interpretation: The body-wide representation of the neuroparacrine or neuroendocrine H_2S/ $NO^{\cdot}$-HNO-TRPA1-CGRP pathway could constitute an essential previously

unknown control element of blood pressure and cardiac contractility and explain some of the physiological effects of the new but also the old gasotransmitter, i.e. H_2S and $NO^{\cdot}$, respectively. Furthermore, combining vasodilatation with positive inotropic effects, HNO and H_2S donors could be considered a great promise for the treatment of heart failure. References: 1. Paolocci, N *et al*., *Proc*. *Natl*. *Acad*. *Sci*. *U*.*S*.*A*. 98, 10463 (2001) and 100, 5537 (2003). 2. Bullen, ML, *Antioxid*. *Redox Signal*. 14, 1675-1686 (2011). 3. Bautista, DM *et al*., *Cell*. 124, 1269-1282 (2006). 4. Engel, MA *et al*., *Gastroenterology*. 141, 1346-1358 (2011). 5.Eberhardt, MJ *et al*., *J Biol Chem*. 287, 28291 (2012). 6.Coletta, C *et al*., *Proc*. *Natl*. *Acad*. *Sci*. *U*.*S*.*A*. 109, 9161-9166 (2012). 7.Filipovic, MR *et al*., *J*. *Am*. *Chem*. *Soc*.134, 12016-12027 (2012). 8.Rosenthal, J *et al*., *J*. *Am*. *Chem*. *Soc*. 132, 5536 (2010). 9.Macpherson, LJ *et al*., *Nature* 445, 541-545 (2007). 10. Hinman, A *et al*., *Proc*. *Natl*. *Acad*. *Sci*. *U*.*S*.*A*. 103, 19564-19568 (2006).

Gastrointestinal mucositis during irinotecan-based cancer chemotherapy: **role of microbial sensing receptors** *Lima Júnior RCP* UFC – Fisiologia e Farmacologia.

The Colorectal Cancer (CRC) is one of the most prevalent neoplastic diseases in the world and is one leading cause of death. Irinotecan is a drug used as first line treatment for CRC and its liver metastases and has markedly improved the overall survival of patients. However, irinotecan-related side-effects, which include intestinal mucositis, have impacted negatively on therapeutic outcome, leading to delayed chemotherapy cycles, dose reductions and treatment interruption. Intestinal mucositis and life-threatening diarrhea may affect up to 80% of patients under irinotecan-based cancer chemotherapy regimens. The literature suggests, with our contribution, that intestinal mucositis is characterized by cell loss in the epithelial barrier lining the gastrointestinal tract which leads to cytokine release (TNF-alpha, IL-1beta, IL-18), activation of pro-inflammatory enzymes, including inducible nitric oxide synthase (iNOS), and increased risk of sepsis. Furthermore, data from our laboratory suggest that irinotecan induces functional alterations in the gut, bacteremia and bacterial translocation to peripheral organs. In addition, genetic deletion to microbial molecular patterns receptors, including Toll-like Receptor 2 (TLR2) and its adaptor protein MyD88, significantly prevent irinotecan-related diarrhea and intestinal damage. Besides, TLR9 and NOD1 deficiency are respectively protective only against inflammatory reaction and diarrhea development. On the other hand, TLR4 deficiency did not change the deleterious course of mucositis. Then, the precise role of these receptors and their downstream signaling pathways in irinotecan-associated toxicities merit further research which are currently been performed in our laboratory. This knowledge opens perspectives for improved clinical management of intestinal mucositis. Financial support: CNPQ, CAPES, FUNCAP.

The interplay between diet, **the gut microbiota and the immune system determines the balance between inflammation and homeostasis** [1,2]Vieira AT, [2]Macia L, [1,2]Canesso MCC, [1]Amaral FA, [3]Martins FS, [3]Nicoli J, [2]Mackay CR, and [1]Teixeira MM. [1]ICB-UFMG – Biochemistry and Immunology,

[2]Monash University – Immunology, [3]ICB-UFMG – Microbiology

Diet and the composition of gut microbiota represent new avenues to understand the basis of human diseases. Intake of fibre has beneficial effects on numerous inflammatory conditions, such as inflammatory bowel disease, colon cancer and obesity. Fiber is metabolized by commensal bacteria in the gastrointestinal tract, to yield high concentrations of short chain fatty acids (SCFAs), especially acetate. The molecular pathways by which SCFAs promote gut homeostasis are not fully understood, and SCFAs bind several receptors, including the G-protein coupled receptors GPR43. We show that a high fibre diet protects against DSS colitis in mice, in a process dependant in part on GPR43. A high fiber diet, acting through GPR43, were necessary for proper activation of the inflammasome pathway in gut epithelial cells, which is important for epithelial integrity and tissue repair. Levels of IL-18, an inflammasome related cytokine that promotes epithelial integrity, rose substantially in the colon and blood following intake of dietary fibre. GPR43 and circulating acetate also markedly affected inflammasome activation in peripheral leukocytes, production of IL-1β, and development of the inflammasome related condition, such as gout arthritis. SCFA treatment during an established inflammatory response promoted resolution of inflammation in an experimental model of gout. Elevated concentrations of IL-10 and TGFß cytokines and increased apoptosis's neutrophils were observed in the peri-articular knee tissue from the gout-mice treated with SCFA. Of note, mice feed with higher fiber diet showed reduced inflammatory cells infiltrate and reduced pro-inflammatory cytokines in knee tissue of mice with gout. These findings suggest, that endogenous microbiota shapes the host's ability to respond to inflammatory stimuli inside and outside the gut. SCFAs binding GPR43 provides a molecular link between diet, gastrointestinal bacterial metabolism, inflammatory responses and homeostasis. Financial support: FAPEMIG, CAPES e CNPq

The hypothalamic-pituitary-adrenal neuro-immunendocrine axis and glucocorticoids in themodulation of mucosal immunity. Cardoso CRB. FCFRP-USP

Inflammatory immune responses may be modulated by the hypothalamic-pituitary-adrenal axis (HPA) through neuroimmunoendocrine interactions and cortisol secretion. However, even in the presence of intact adrenal glands patients may develop chronic diseases such as Inflammatory Bowel Disease (IBD), caused by an imbalance between regulatory and effector responses in the gut. Adrenal glands are also involved in stress response, which may predispose to uncontrolled inflammatory diseases that may be treated with anti-inflammatory agents such as corticosteroids. However, many patients fail to respond to these treatments and their only option is colectomy. Then, we investigated the role of HPA axis and the efficacy of glucocorticoids (GC) in experimental IBD. C57BL/6 mice were subjected to bilateral adrenalectomy and colitis was induced by oral intake of water containing 3% Dextran Sulfate Sodium (DSS) in presence or absence of exogenous GC. Colitis was more severe in mice subjected to adrenalectomy, which showed greater weight loss, increased disease clinical score and earlier mortality when compared to colitis

group. The absence of adrenal glands was also related to augmented circulating neutrophils and eosinophils, increase in pro-inflammatory cytokines such as IL-1β, TNF-α, IFN-γ and IL-17 besides reduced NAG activity in the gut. GC replacement in adrenalectomized colitis mice resulted in an improvement in the *post-mortem* clinical score, with an attempt to repair the intestinal mucosa, reduced levels of proinflammatory cytokines and myeloperoxidase activity (MPO); however, it was not enough to prevent mice death. On the other hand, short-term treatment of non-adrenalectomizedcolitis mice with GC resulted in diminished circulating lymphocytes, reduced macrophages, neutrophils, IFN-γ, IL-17,TNF-α and IL-6 in the colon, besides local tissue repair. Otherwise, long-term administration of GCled to increased disease score that resulted in mice death, indicating that the efficacy of GCin colitis was dependent on the dose and schedule of the drug administration, as observed in IBD patients. Taken together, our results showed that endogenous and exogenous GC play an important role in the gut mucosal immunity, thus pointing to the HPA neuroimmunendocrine axis as an important pathway to modulate exacerbated inflammatory responses like in IBD. Financial support: CAPES / FAPESP/NAPDIN

Pro-resolution lipid mediators in intestinal inflammation. Bento AF, Marcon R, Claudino RF, Dutra R C, Bicca MA, Leite DFP, Calixto JB UFSC – Farmacologia

Omega-3 polyunsaturated fatty acids (n-3 PUFAs), such as eicosapentaenoic acid (EPA)- and docosahexaenoic acid (DHA)-derived mediators namely resolvins of D and E series, protectins and maresins are believed to exert beneficial roles in several inflammatory disorders, including inflammatory bowel diseases (IBD). Recently, our group has been investigating the anti-inflammatory and pro-resolution effects of some of those lipid mediators in different chemically induced mouse models of intestinal inflammation. We have reported that pharmacological treatment with EPA- and DHA-derived mediators, namely aspirin-triggered resolvin D1 (AT-RvD1) and its precursor (17*R*-HDHA), as well as resolvin D2 (RvD2) and maresin 1 (MaR1), in a nanogram range, greatly protected mice against dextran sulfate sodium (DSS)- or 2,4,6-*trinitrobenzene-sulfonic acid* (TNBS)-induced colitis. The treatment with these lipid mediators greatly improved disease activity index, body weight loss, colonic damage and polymorphonuclear infiltration in both colitis experimental models. Moreover, in vivo and in vitro experiments showed that these lipid mediators reduced several pro-inflammatory agents such as TNF-α, IL-1β, MIP-2, CXCL1/KC, IL-6 and INF-γ as well as the mRNA expression of adhesion molecules VCAM-1, ICAM-1 and LFA-1. Interestingly, AT-RvD1, 17*R*-HDHA, RvD2 and MaR1 abolished NF-κB activation, suggesting a common mechanism between these n-3 PUFA-derived mediators. Furthermore, we showed that the beneficial effects of AT-RvD1 on mucosal inflammation were depended on lipoxin A4 receptor (ALX/FPR2) activation. Moreover, we also demonstrated that MaR1 is able to switch macrophage phenotype from pro-inflammatory M1 to anti-inflammatory M2, suggesting an important mechanism of action on gut inflammation. Taken together, our findings showed for the first time the anti-inflammatory effects of resolvins of the D series, its precursor

17*R*-HDHA, as well as MaR1 in experimental colitis in mice. These studies suggest that those lipid mediators have the potential to be used for treating IBD. Financial support: CAPES, CNPq, FINEP, FAPESC.

Opportunities for companies in FINEP – Edital Inova Saúde. Bueno IF – FINEP

Será tratado quais as linhas de financiamento da FINEP, bem como os prazos para obtenção dos recursos. Além disso, abordarei uma avaliação prévia dos resultados alcançados com o Edital Inova Saúde, lançado no âmbito do programa Inova Empresa.

Why investing (or not) in health biotechs in Brazil. Pellegrino P. Associação Wylinka

The production of medical drugs in Brazil has increased in recent years, according to the Brazilian Association of Pharmaceutical Companies, however, investment in research and development (R&D) is still incipient. Research funding comes primarily from federal and state agencies, although some private laboratories begin focusing on partnerships with universities, which can minimize the lag of Brazil in relation to other countries. According to federal government, the public and private investments in health research should reach 13 billion over the next 4 years, equal to 0.3% of the gross domestic product.

One of the main areas of investment is the clinical research aiming to introduce new drugs, such as monoclonal antibodies against cancer, cell therapy using stem cells, tropical, chronic, cardiovascular and circulatory system diseases.

A study performed by Fiocruz points out that "the scientific and technological infrastructure, key to innovation in Economic-Industrial Health Complex is really weak, since companies, which hardly engage in R&D, don't ask for this type of work." Another point is that pharmaceutical companies have reduced investments in innovative activities in Brazil. Nowadays, in healthcare area increasingly aiming to financial results, the biotech and pharmaceutical companies cannot afford to adopt a strategy of research and development that seeks only to verify the effectiveness of a particular drug, "according to a biotechnology company's director. The main innovative companies are small businesses with annual revenues of up to R$ 140,000, and at least one-fifth have no profit, since their products are still in development and research step. "It takes at least 7 to ten years to develop a new drug and it is rare to find an investor or companies interested in invest in products that are in the initial phase. The risk is too high, even knowing that the profit can be even higher after it is in the market", guarantee investors. It is known that investments in R&D are under pressure because of government budget cuts, but the most important issue for the sector is to eliminate obstacles that prevent midsize companies to demonstrate to investors the return value of the products in development and the barriers to purchase supplies and equipments.

Curcumin Requires TNFα signaling to alleviate cognitive impairment elicited by innate immune activation. [1]Kawamoto EM, [1]Scavone C, [2]Mattson MP, [2]Camandola S [1]ICB-USP – Pharmacology, [2]NIA-NIH – Neurosciences

A decline in cognitive abilities is a typical feature of the normal aging process, and of neurodegenerative disorders such as

Alzheimer's, Parkinson's and Huntington's diseases. Although their etiologies differ, all of these disorders involve local activation of innate immune pathways and associated inflammatory cytokines. However, clinical trials of anti-inflammatory agents in neurodegenerative disorders have been disappointing, and it is therefore necessary to better understand the complex roles of the inflammatory process in neurological dysfunction. The dietary phytochemical curcumin can exert anti-inflammatory, anti-oxidant and neuroprotective actions. Here we provide evidence that curcumin ameliorates cognitive deficits associated with activation of innate immune responses by mechanisms requiring functional tumor necrosis factor-α (TNF-α) receptor 2 (TNFR2) signaling. *In vivo*, the ability of curcumin to counteract hippocampus-dependent spatial memory deficits, to stimulate neuroprotective mechanisms such as up-regulation of BDNF, to decrease glutaminase levels, and to modulate NMDA receptor activity, were absent in mice lacking functional TNF receptors. Curcumin treatment protected cultured neurons against glutamate-induced excitotoxicity by a mechanism requiring TNFR2 up-regulation. Our results suggest the possibility that therapeutic approaches against cognitive decline designed to up-regulate TNFR2 signaling might be more beneficial than use of anti-inflammatory drugs *per se*.

Lithium ameliorates rotenone-induced methylation and hydroxymethylation of DNA in cortical primary neurons. Scola G[1,2], Kim HH[1], Salvador M[2], Young LT[1], Andreazza AC[1] [1]University of Toronto – Psychiatry and Pharmacology, [2]UCS – Biotechnology

Background: Mitochondrial dysfunction, especially through down-regulation of complex I subunits and its subsequently oxidative stress damage have been strongly implicated in bipolar disorder (BD), which includes oxidative damage to DNA. DNA methylation alterations have also been implicated with BD. Emerging evidence suggests an interaction between oxidative stress and DNA methylation Therefore, in this study, we aimed to investigate whether oxidative stress induced by mitochondrial complex I dysfunction (induced by rotenone) leads to modulation of DNA methylation (5-methylcytosine; 5-mc) and 5-hydroxymethylcytosine (5-hmc) in rat cortical neurons. We also examined the ability of lithium to ameliorate rotenone-induced alterations to global of 5-mc and 5-hmc levels. **Methods**: Rat E18 cortical neurons were grown for 7 days and treated with 0.75mM lithium without B27 for another 7 days. Then cells were treated with rotenone (5nM, 10nM, and 50nM) for 30 minutes. To measure the levels of 5-mc and 5-hmc, we used immunocytoche-mistry. Complex I activity were evaluate by ELISA and cell viability by MTT assay and ATP levels were quantified. **Results**: We found that rotenone caused a dose dependent increase in 5-mc and 5-hmc, and lithium was able to ameliorate the levels of 5-mc and 5-hmc. Lithium also ameliorated rotenone-induced mortality, decreased in ATP levels, and complex I activity. **Conclusions**: The findings of this study suggest that rotenone increases methylation and hydroxymethylation of DNA in cortical primary neurons. Lithium was found to decrease rotenone-induced increase in 5mc and 5hmc levels, suggesting that lithium may ameliorate epigenetic aberrations produced by mitochondrial dysfunction.

New insights in cholinergic system and Alzheimer's disease. Viel TA. EACH-USP

Several physiological functions are altered in aging process. In central nervous system, the degree of decline in memory retrieval depends on the quantity and quality of stimuli received during life-time. The cholinergic system modulates long term potentiation and, therefore, memory processes. Our main interest is to understand how the aging brain or that one affected by neurodegeneration responds to environmental changes and how the cholinergic system modulates these processes. In this way, recently we showed that chronic infusion of amyloid-β peptide (Aβ) associated to attentional rehearsal altered the density of α7 nicotinic cholinergic receptor (nAChR) in the brain of male Wistar rats (Viel et al., Curr. Alzheimer Dis. 9(10):1210-1220, 2012. Animals received intracerebroventricular infusion of Aβ or vehicle (control – C) and their attention was stimulated weekly (Stimulated Aβ group: S-Aβ and Stimulated Control group: SC) or not (Non-Stimulated Aβ group: N-SAβ and Non-Stimulated Control group: N-SC), using an active avoidance apparatus. Conditioned avoidance responses (CAR) were registered. Chronic infusion of Aβ caused a 37% reduction in CAR for N-SAβ. In S-Aβ, this reduction was not observed. At the end, brains were extracted and autoradiography for α7 nAChR was conducted using [^{125}I]-α-bungarotoxin. There was an increase in α7 density in hippocampus, cortex and amygdala of SAβ animals, together with the memory preservation. These observations were reproduced in male C57Bl/6 mice also infused with Aβ. Moreover, with similar animals infused with Aβ and the α7 antagonist methyllycaconitine, and stimulated weekly in the same apparatus, it was observed that memory maintenance was abolished. Besides, these animals presented a significant increase of 3.2 times in number of senile plaques when compared to Aβ animals. We may conclude that sustained attention produced significant improves in memory in animal models of neurodegeneration. Blockade of α7 in mice infused with Aβ prevented the memory recover produced by this cognitive strategy and increased the number of senile plaques in the brain, which suggests the participation of this receptor in neuroprotection and maintenance of memory. Financial support: FAPESP, CAPES

Rapid estrogen signaling through GPER-1 and neuroprotection. Munhoz CD ICB-USP – Pharmacology

Estrogen (E2), the female sex hormone, plays an important role in homeostasis, protection, and plasticity in the central nervous system (CNS). E2 can act through classical, nuclear-initiated and/or non-classical, membrane-initiated mechanisms. These classical nuclear actions are well known and are mediated by the activation of nuclear receptors (ESR), which act as transcription factors. The membraneinitiated, rapid E2 actions are believed to be mediated by the G-protein coupled membrane receptor, GPER-1. In breast cancer cell lines, GPER-1 is thought to act through the activation of protein kinases, such as MAP kinase (mitogen activated protein, ERK) and AKT, however little is known about GPER actions in the CNS. In addition, GPER-1 signaling in the brain could potentially play a role in estrogenmediated neuroprotective effects in diseases such as stroke and

multiple sclerosis. The localization of GPER-1 in neuronal and glial cells is unknown and the role of glial cells in the development of neurodegenerative damage is a complex phenomenon that comprises neuronal survival. If in one hand, microglial and astrocytic activation during neuronal damage are sought to have detrimental effects and potentiate neuronal damage, on the other hand, a more recent view suggests that glial cells are involved in a variety of physiological functions, playing even a protective role in some neurodegenerative conditions. In a physiological context, we aimed to investigate the cellular mechanisms that support the protection through rapid estrogen signaling pathway via GPER-1 and the participation of neuronal and glial cells in these phenomena. FAPESP / CNPq / CAPES / PRP-USP

Metabolic syndrome-related hypertension: **The contribution of perivascular adipose tissue (PVAT)**

[1]Szasz T, [2]Matsumoto T, 1Webb RC. [1]Georgia Regents University Department of Physiology, [2]Hoshi University – Pharmacology

Vascular dysfunction is a common finding in hypertension and disorders associated with obesity, such as the metabolic syndrome. The perivascular adipose tissue (PVAT) produces a notable anti-contractile effect in physiological conditions. Increasing evidence demonstrates that paracrine action of PVAT also modulates other processes like vascular smooth muscle cell proliferation and migration and vascular inflammation. Metabolic and cardiovascular diseases alter the morphological and secretory characteristics of PVAT. In hypertension, the anticontractile effect of PVAT is diminished or lost and PVAT size is decreased. On the other hand, during obesity and diabetes, despite a significant increase in PVAT size, a similar loss of anticontractile effect is typically observed and PVAT dysfunction may contribute to the vascular insulin resistance. The mechanistic differences between the dysfunction of PVAT in hypertension and obesity are unclear, however immune cell infiltration, inflammation, oxidative stress and hypoxia may be common factors. The consequence on PVAT function of overlapping hypertension and obesity, a highly relevant situation for the human population, is unknown. We investigated the role of PVAT in vascular contraction in hypertension and obesity, separately and co-evolving, by using a young rodent model of diet-induced obesity (high fat high sucrose, HFHS) and angiotensin II-induced hypertension. Contrary to our expectations, HFHS diet-induced obesity alone did not produce PVAT dysfunction. Moreover, we observed that PVAT dysfunction present in angiotensin II-induced hypertension was ameliorated during co-exposure to the HFHS diet, possibly due to an increase in the PVAT activity of cystathionine gamma lyase, enzyme involved in the synthesis of the vasodilatory hydrogen sulfide. Future studies on PVAT function may provide novel therapeutical targets for vascular dysfunction in hypertension and obesity evolving independently or simultaneously. Financial support: American Heart Association, National Institute of Health.

Metabolic syndrome, **inflammation**, **and vascular consequences**. Akamine EH. ICB-USP – Farmacologia,

The prevalence of obesity and diabetes mellitus is on the rise and has become epidemic. Obesity is characterized by fat accumulation that negatively affects the

cardiovascular and endocrine system. The excessive accumulation of adipose tissue in the upper body is a risk factor for cardiovascular disease and insulin resistance. Diabetes, in turn, is associated to high mortality and incidence of cardiovascular complications. A chronic low-grade inflammation condition is present in both obesity and diabetes. A common feature of the cardiovascular complications is endothelial dysfunction, which is characterized by an imbalance in synthesis/bioavailability of endothelium-derived contractile and relaxing factors, which in turn leads to increased vascular tonus and vascular wall thickness, thrombosis, oxidative stress, vascular inflammation, and progression of atherosclerosis. Nevertheless, vascular alterations are not always observed in different models of obesity and diabetes in which inflammatory markers are increased. Increase in inflammatory markers, such as TNF-alpha and iNOS, has been observed in arteries of obese and diabetic animals, but endothelial dysfunction is not a rule, even though other alterations may be present. In obese mice, increased TNF-alpha is associated to senescence of endothelial cells, although changes of the endothelium-dependent relaxation have not been observed. In much the same way, expression of iNOS is increasedin arteries of diabetic rats; however, even in the presence of an increase in endothelium-derived contractile factors, vascular contraction is reduced.There is no algorithm whatsoever on how adipose tissuegrowth and hyperglycemia affect the vascular system. Indeed, most likely the response of the vascular system to fat accumulation and hyperglycemia is not an all-or-none phenomenon, and there are different adaptive responses to ensuing metabolic alterations. Financial support: FAPESP, CNPq, CAPES-DGU, Pró-Reitoria de Pesquisa/USP

New immunological mechanisms involved in obesity-induced inflammation and Type 2 diabetes: **Role of NOD2 receptor**. Sartori DC[1]; Zanetoni JJ[1]; Rocha FA[1]; Françozo MCS[1], Ramos SG[2]; Tostes RCA[3]; Zamboni DS[4]; Camara NO[5], Silva JS[1] [1]FMRP-USP – Biochemistry and Immunology, [2]FMRP-USP – Pathology, [3]FMRP-USP – Pharmacology, [4]FMRP-USP – Cell Biology, [5]ICB-USP – Immunology

Introduction: The pathophysiology of obesity, insulin resistance and type 2 diabetes (T2D) in rodents and humans is characterized by low-grade inflammation in adipose tissue and pancreatic islets. NOD-like receptors (NLRs) are innate immune receptors and new evidence is emerging with regard to their role in the regulation of metabolism and the activation of inflammatory pathways during metabolic disorders. Although one study observed high expression of NOD2 protein in spleen cells of obese mice feeding caloric diet, the importance of the NOD2 receptor in T2D remains unexplored. Objective: Thus, we addressed the role of NOD2 receptor in the obesity-induced inflammation and T2D onset. Methods and results: Metabolic and inflammatory properties were assessed in wild-type (WT) and NOD2 deficient mice fed a high-fat (HFD) or control diet (CTD). The metabolic parameters monitored were the body weight, food intake, total and visceral fat pad weight, fasting serum glucose or insulin concentrations and glucose tolerance. We also measured the systemic or tissue cytokine levels and lymphoid cell frequency in the spleen and pancreatic lymph nodes (PLNs). In this current study, we

observed that mice lacking NOD2 developed more weight gain, fat accumulation, adipocyte hypertrophy and hepatic steatosis compared to wild-type mice feeding HFD. These mice demonstrated elevated fasting insulin and glucose levels and glucose intolerance. We also observed a trend of increase in the triglyceride levels, but significant reduction in circulating TNF-α levels in these mice. In addition, the NOD2 deficiency caused an increase of IL-1β and decrease of IL-10 production into pancreatic tissue. In parallel, these mice had a significant increase of the regulatory T cell (Treg) frequency in the spleen associated with reduction in PLNs. Conclusion: These studies indicate that NOD2 receptor activation is important for regulation of obesity-induced inflammation and T2D development. Hence, NOD2 provides a novel link between innate immunity and metabolism. Financial support: São Paulo Research Foundation (FAPESP) Process nº 2012/10395-0.

Involvement of inflammatory mediators in the metabolic homeostasis. Menezes-Garcia Z; Oliveira M; Lima R; Soriani F; Cisalpino D; Botion LM; Teixeira MM; Souza DG; Ferreira AVM UFMG

Chronic, low grade inflammation has been observed during the development and maintenance of obesity. It has been proposed that adipose tissue is the primary source of proinflammatory mediators. Although many studies have been published in this field in the last two decades, the true nature of the inflammatory milieu in adipose tissue has yet to be clarified. In this respect, a question remains: why does adipose tissue become inflamed, and what is the physiological aspect involved in adipose inflammation upon nutrient overload? Here, we have used the platelet-activating factor (PAF) receptor deficient mice with a lower inflammatory response upon different stimuli, to evaluate the effect of nutrient overload on inflammatory and metabolic dysfunction. The present study has the following major findings: (i) the PAF receptor is important for containing diet-induced fat pad expansion; (ii) mice lacking the PAF receptor has a protective role in the development of insulin resistance induced by diet and (iii) the signaling pathway of the PAF receptor is involved in adipose tissue cytokine secretion induced by nutrient overload. Although the pathological features of inflammation in obesity are well understood, the physiological counterparts of such inflammation are unknown. Akin to what is observed in obesity, the acute inflammatory response triggered by infection or injury induces a state of insulin resistance. However, in such cases, there are concomitant reductions in body mass and adipose tissue weight. We, therefore, hypothesized that the inflammatory milieu in adipose tissue counteracts the fat pad expansion induced by nutrient overload. Consistent with this hypothesis, PAF receptor-deficient mice presented with low levels of inflammatory mediators in adipose tissue concomitant with the impairment of lipolysis, heightened lipogenesis and exacerbated expansion of adipose tissue mass. As noted for the PAF receptor-deficient mice, previous studies have shown that the absence of pro-inflammatory mediators or their signaling pathways causes an increase in the body weight and fat mass in humans and mice. Our study contributes to data considering the involvement of inflammation in the induction of insulin resistance and suggests that local

inflammation in adipose tissue may be related to tissue remodeling and, consequently, control of fat pad expansion. Financial assistance: Pró-Reitoria de Pesquisa da UFMG, Capes, FAPEMIG and CNPq.

Depression in Parkinson's disease. Andreatini R. UFPR – Pharmacology,

Depression is the most frequent psychiatric disorder occurring in 30-35% of patients with Parkinson's disease (PD). Depressive symptoms might appear in premotor stage and may be considered a prodromal symptomatology of PD. However, there are some differences between Major Depression patients with and without associated PD, such as lower frequency of suicide ideation, lesser feelings of guilt, and lower corticosterone level in depression associated with PD. Clinical and pre-clinical evidences suggest that monoamine changes and neuroinflammation contribute to depression associated with PD, which may have implications for its treatment. In this line, rats with parkinsonism induced by neurotoxin (e.g. 6-OHDA, MTPT or rotenone) show depressive-like behavior (e.g. decrease in sucrose preference and increase immobility time in forced swim test) which are related to monoamine depletion (e.g. serotonin) and neuroinflammation. L-dopa treatment may also contribute for depressive symptoms appearance in PD, since it reduced 5-HT in hippocampus of rats with parkinsonism induced by MPTP. Clinical evidence indicates that dual antidepressants (serotonergic and noradrenergic) are effective in depression associated with PD, while serotonin selective reuptake inhibitor show mixing results. Financial support: CNPq, CAPES, Fundação Araucária

Nitric Oxide and Parkinson's disease: **Pathophysiology and treatment**. Del Bel E. FORP-USP Physiology

Nitric oxide is a free radical that can also acts as an atypical neurotransmitter. It is a Janus-faced molecule and the exact role it plays in neurodegenerative disorders, neuroprotective or neurotoxic, is still ambiguous. Nitric oxide signaling plays a role in controlling motor behavior modulating the integration of information processed by the basal ganglia nuclei. In our laboratory we investigate the role of nitric oxide on motor control, in Parkinson's disease models, particularly a possible role in L-DOPA induced dyskinesia in rodents. High-resolution confocal laser scanning microscopy revealed nitric oxide synthase immunoreactive fiber boutons in submicrometer proximity to both the axon/dendrite and soma of tyrosine hydroxylase immunoreactive neurons and fibers of each studied region. The sequential staining for the enzymes nitric oxide synthase and tyrosine hydroxylase in the substantia nigra compacta indicated that these enzymes are colocalized in less than 1% of the neurons positive for either marker. Thus, such data provide grounds for a production of nitrergic by dopaminergic cells, together with an afferent nitric oxide input that could affect dopaminergic neurons through diffusion from neighbouring sources. Several pieces of evidence suggest that interference with nitric oxide could modify the neurodegenerative process involved in Parkinson's disease. Evidence has been produced in both animal models and in Parkinson's disease patients. Strikingly, nitric oxide synthase positive neuron numbers within the substantia nigra compacta and the basal ganglia in general are subject to

modification, for example nigral nitrergic neurons increase after intoxication with 6-hydroxydopamine (6-OHDA) administration. Up to date results show that nitric oxide synthase inhibition reduces L-DOPA-induced dyskinesia in rats and mice. The effect is dose-dependent and improved motor performance in rats (no interferes with L-DOPA positive motor effects). Especially noteworthy is also the evidence that nitric oxide synthase inhibitor sub-chronic administration was devoid of tolerance to the anti-dyskinetic effect differently from its cataleptic action. Nevertheless, the precise role of NO in the pathogenesis of such invalidating complications remains elusive. These preclinical findings suggest that nitric oxide is a promising therapeutic target for the reduction of L-DOPA-induced dyskinesia. FAPESP, CNPQ, CAPES and USP support this work.

Neuronal death in Parkinson's disease. Vital MABF UFPR – Farmacologia

In the past few decades several studies originating from clinical, autopsy material, and in vitro and in vivo experimental models of Parkinson' disease (PD) has been accumulated, which led us to begin to have some level of understanding of the pathogenesis of idiopathic PD.

The reason by which PD patients present a massive loss of dopaminergic neurons of the substantia nigra pars compacta (SNpc) is until now unknown. However, experimental data have been crucial for understanding the molecular mechanism involved in the events that result in neuronal death of PD. *Postmortem* analysis of brains from patients (dying) with PD shows that cytokines (TNF-alpha, interleukin IL-1beta, IL-2, IL-6) are increased in the nigrostriatal system. Moreover, the vulnerability of the DA-ergic neurons is also considered to be a result of oxidative stress caused by increased generation of reactive oxygen species with aging, the reduced capacity of the antioxidant system and changes in the microglial activation pattern. We have shown that the administration of some neurotoxins (MPTP, 6-OHDA, LPS and rotenone) directly into the SNpc of rats causes a partial loss of dopaminergic neurons, depletion of striatal (DA), upregulation of the pro-inflammatory enzyme cyclooxygenase-2 and glutathione (GSH) reduction. These changes resulted in memory and motor deficits with temporary impairment mimicking the early phase of PD. Moreover, it was demonstrated that these animals exhibited a depressive-like behavior besides the hippocampal serotonin reduction. Some neuroprotective drugs (melatonin, curcumin, ibuprofen, pioglitazone) were effective in restore the dopaminergic neuronal function in these animal models of PD. Apoio Financeiro: CNPq, Capes, Fundação |Araucária

Potential therapeutic targeting of platelet-mediated cellular interactions. Kenneth J. Clemetson University of Berne – Haematology

Cardiovascular diseases remain the major cause of death and disablement in developed countries and are rapidly increasing in other countries that have adopted Western life styles. Thrombosis or embolism often leads to life threatening conditions such as cardiac infarction and stroke. Platelets have critical roles in the physiological function of haemostasis and its pathological equivalent, thrombosis. For many years aspirin was the only efficient platelet inhibitor. With the development of ADP

receptor P2Y12 inhibitors the situation has improved but is still far from ideal. Thus, there remains a lively interest in the development of drugs to inhibit receptors that act upstream of thromboxane and ADP release, particularly for protection against thrombosis following unstable plaque rupture. Two important targets are GPVI, the major collagen signaling receptor and GPIb, the major von Willebrand factor receptor but also an important receptor for other ligands including thrombin. Both these receptors are difficult molecules to develop drugs to so that the major emphasis so far has been with small antibodies to establish the efficacity of targeting these receptors. Platelet receptors involved in innate immunity are also of interest in developing drugs to treat sepsis and inflammatory disorders.

Mechanism of action of novel anticoagulants from snake venom. Kini RM National University of Singapore – Biological Sciences, Virginia Common-wealth Universit – Biochemistry, University of South Australia – Pharmacy and Medical Sciences

Anticoagulants prevent the formation of unwanted clots that lead to heart attack and stroke resulting in a large number of deaths in developed countries. Currently available drugs have some drawbacks including their non-specific actions. Therefore novel anticoagulants that target specific steps in the coagulation pathway are being sought. Recently, we have isolated and characterized several anticoagulants from various snake venoms. These anticoagulants belong to three-finger toxin family and exert their effects on the extrinsic pathway of the blood coagulation system. Despite similarity in overall three-dimensional structure, three-finger toxins represent an interesting family of anticoagulants as they are able to recognize various distinct targets in the blood coagulation system. Some of these polypeptides target extrinsic tenase complex, whereas others target prothrombinase complex. Further, they exhibit their anticoagulant function through distinct mechanisms. Here, I will describe the functional characterization of a few of these novel anticoagulants. I will also discuss the mechanism of their anticoagulant function. The structure-function relationships of these anticoagulant polypeptides may help in designing potential leads for the future anticoagulation therapy.

This research is supported by Academic Research Grants from National University of Singapore and Bio-Medical Research Council, Singapore.

Clinical use of antiplatelet agents. Lourenço DM Unifesp – Hematology

Antiplatelet drugs are effective and safe in reducing cardiovascular events in patients with arterial thrombosis, that is coronary thrombosis, and thrombosis of cerebral or peripheral arteries, in which the role of platelets is predominant.

Procedures such as angioplasty and coronary stenting reduce morbidity and mortality from acute coronary syndrome (ACS), but they cause intense platelet activation and blocking platelet function to prevent new thrombosis is required.

This led to the development of new antiplatelet drugs whose efficacy and safety have been analyzed in large clinical studies. Three classes of antiplatelet agents are currently approved for clinical use: irreversible cyclooxygenase (COX-1) inhibitor (Aspirin); adenosine diphosphate (ADP) P2Y12 receptor antagonists (ticlopidine, clopidogrel, prasugrel, ticagrelor); inhibitors of platelet membrane

glycoprotein Iib/IIIa (abciximab, eptifibatide and tirofiban). Aspirin is the oldest and more frequently precribed antiplatelet drug, but some patients show aspirin resistance and it may cause gastric intolerance. Ticlopidine was replaced by clopidogrel due to advantages such as rapid onset of action after a loading dose, although the response to the drug is greatly affected by gene polymorphisms of enzymes involved in its metabolism. Currently, dual antiplatelet therapy with aspirin and clopidogrel is recommended for prevention of events after ACS with angioplasty and coronary stent placement. New drugs have been developed, such as Prasugrel and ticagrelor that show more favorable safety profile and faster onset of action. Drugs that inhibit platelet glycoprotein IIb-IIIa block the final pathway of platelet aggregation, and are used during invasive procedures, but are not used chronically: abiciximab is a chimeric murine and human fragment antibody, tirofiban is a molecule derived from tyrosine and epitifibatide is a hepta-peptide. Drugs that inhibit the PAR-1 (protease activatable receptor 1) present on the platelet surface, are also been tested in clinical trials, and meta-analysis of data obtained so far with Voraxapar and Atoxapar show efficacy in preventing thrombosis but with more bleeding complications. Finally, there is a more recent aproach in preventing thrombosis in ACS patients, that is, the association of low doses of Factor Xa inhibitors to dual antiplatelet therapy. Studies with rivaroxaban and apixaban show good efficacy, but only rivaroxaban was approved for this indication.

INCT-INOFAR A Brazilian network for drug discovery, design & development Barreiro EJ UFRJ

In this presentation we will describe the mission and activities in radical and incremental innovation of drugs and medicines, developed by the National Institute of Science and Technology of Drugs and Medicines (INCT-INOFAR; http://www.inct-inofar.ccs.ufrj.br).

Comparative study of cold allodynia in animal models of neuropathic pain: different ethiologies, distinct pathophy-siologic mechanisms. Jesus CHA, Scarante, FF, Schreiber AK, Cunha JM UFPR – Pharmacology.

Cold allodynia is one of the main signs of polyneuropathy, but little has been explored about the mechanisms involved in abnormal sensitivity to innocuous cold stimuli. Accordingly, in order to ascertain whether different etiologies of neuropathic processes involve the same pathophysiologic mechanisms, the current study aimed to evaluate the development of cold and mechanical allodynia in two models of neuropathic pain in rats: diabetes chemically induced by streptozotocin (STZ, 50 mg/kg; diabetic group; DBT) and chronic constriction injury (CCI) of sciatic nerve, attesting the involvement of TRPM8 and TRPA1 receptors. Control groups were also conducted (normoglycemic, NGL; sham and naïve). Cold allodynia was assessed by acetone test (TRPM8 activation) and cold plate test while mechanical allodynia was evaluated by electronic Von Frey test. Nociceptive response to TRPA1 agonist, mustard oil (MO; 0.1%, 0.5% and 1%; 50µL/paw) or menthol, a TRPM8 agonist (MT 0.1% 0.5% and 1%; 50 µL/paw) was also investigate. Our data showed that 4 weeks after STZ injection, DBT animals performed 37% more flinches after acetone instillation when compared to NGL rats. Animals submitted to CCI had a more exacerbated acetone-induced

flinches since first week post-surgery (112%), persisting until the 4th week (204%). Mechanical response threshold was significantly reduced in DBT animals since the second week, peaking 4 weeks after diabetes injection while the CCI animals exhibited the mechanical threshold reduction since the first week. Considering the nociceptive responses to MO, diabetic animals had a number of flinches 53% lower than the NGL animals, while CCI animals had greater responsiveness (108%) when compared to sham animals. Mentholchallenge (at concentrations of 0.5% or 1%) caused a hyporesponsiveness in the DBT animals when compared to NGL(response 168% and 81% lower, respectively). In CCI rats, MO (at a concentration of 1%) caused a 53% lower response when compared to sham animals. When evaluated in cold plate test, menthol injection caused a sensitization to cold stimulation in sham animals, but not in CCI animals. These results show that TRPM8 and TRPA1 receptors may be sensitized differently depending on the etiology of neuropathic pain, which is especially relevant when one considers that, in clinical practice, this type of pain is treated symptomatic and ineffective, without regard to the pathophysiology involved.Financial Support: CNPq (#477452/2011-6), Fundação Araucária.

Aldehyde Dehydrogenase-2 activation induces analgesia in rodents: **implication for the Human East Asian with ALDH2*2 mutation**. Zambelli VO Butantan – Pain and Signaling.

Pain is an international health problem affecting approximately 1 in every 5 individuals. Opioids are a commonly prescribed drug. However, the opioid drug class leads to secondary health complications including accidental overdose and death and to opioid addiction, another serious health issue. Anti-inflammatory pain medications, such as cyclooxygenase-2 inhibitors, may also cause gastrointestinal bleeding and increased risk of cardiac. Thus, discovering further molecular events regulating pain may provide a means to develop additional therapeutics for pain control. Initial observations suggest that reactive aldehydes, including 4-hydroxynonenal and acetaldehyde, cause pain when directly applied to rodents. However, it is unknown whether altering the enzymatic activity of the mitochondrial aldehyde dehydrogenase-2 (ALDH2), which can catalyze removal of these reactive aldehydes, may alter pain response. Understanding how this enzyme mediates pain is also important, since a common inactivating point mutation in the mitochondrial aldehyde dehydrogenase 2 (ALDH2; Glu^{487} to Lys^{487}), occurs in 0.54 billion Han Chinese. The ALDH2*2 mutation is known for causing a flushing response after consuming alcohol yet also causes a reduced ability to metabolize other reactive aldehydes, including acetaldehyde and 4-hydroxynonenal (4-HNE).

Our colleagues discovered a small molecule that selectively enhances the activity of ALDH2, Alda-1 (*N*-(1,3-benzodioxol-5-ylmethyl)-2,6-dichlorobenzamide). Alda-1 can also correct the structural defect in the mutant ALDH2, ALDH2*2, thus increasing ALDH2*2 activity. This talk will show you the contribution of ALDH2 enzymatic activity to inflammatory-induced hyperalgesia and whether a small molecule ALDH2 activator may be a potential drug to reduce pain. Financial Support: FAPESP 2011/08873-8 and 2012/05035-4, NIH MERIT award AA-11147, NIH K award HL-109212.

The role of inhibiting glycogen synthase kinase-3 in the treatment of painful diseases. Santos ARS UFSC – Neuro-biology of Pain and Inflammation

Glycogen synthase kinase-3 (GSK3)was originally isolated and characterized from skeletal muscle almost 30 years ago. Since its initial characterization as a critical enzyme involved in glycogen biosynthesis, GSK3 has been demonstrated to be a point of convergence for numerous cell-signaling pathways involved in a multitude of physiologicalprocesses.GSK3 is a highly conserved serine/threonine kinase that has highest abundance in the brain during development and is localized primarily in neurons. Although GSK3 has two major isoforms, α and β, identifying an isoform-specific GSK3 inhibitor is challenging since the two isoforms are 98% identical within the ATP pocket of the catalytic domain.The incredible numbers of cellular processes that are directly or indirectly controlled by GSK3 have been shown to be due, in large part, to its ability to post-translationally modify transcription factors via itsability to phosphorylate consensus site specific serine or threonineresidues. Due to the ability of GSK3 to impactnumerous intra-cellular signaling pathways, it is not surprising thatthe dysregulation of GSK3 has been shown to be involved in theregulation of embryonic development, the cell cycle control, cell differentiation, cell motility, microtubule function, apoptosis, cell adhesion, pain and inflammation. Pain is a complex process involving activation of nociceptors, chemical mediators and inflammation, which indicates that something is wrong. Each individual is the best judge of his or her own pain, which can be classified as acute pain or chronic pain. Acute pain might be caused by many events or circumstances, including surgery, broken bones, dental work, burns or cuts, among others. In most cases, acute pain does not last longer than six months, and it disappears when the underlying cause of pain has been treated or has healed. Unrelieved acute pain, however, might lead to chronic pain, which is associated with headache, low back pain, cancer pain, and arthritis pain. Chronic pain persists despite the fact that the injury has been healed. Pain signals remain active in the nervous system for weeks, months, or years. Physical effects include tense muscles, limited mobility, a lack of energy, and changes in appetite. Emotional effects include depression, anger, anxiety, and fear of re-injury. Such a fear might hinder a person's ability to return to normal work or leisure activities. Our research group has demonstrated thatGSK3 inhibitor AR-A014418 has antinociceptive effects in acute (i.e., postoperative, acetic acid, glutamate and formalin tests) and chronic (i.e., complex regional pain syndrome type-I and partial ligation of the sciatic nerve) models of pain in mice. Thus, these results emphasize the importance of the GSK3 inhibitor as a potential therapeutic to treat different clinical pain states. Financial Support: CNPq, CAPES, FAPESC, and UFSC.

Chemotherapy-induced peripheral neu-ropathy – Role of DNA damage and repair. Duarte DB FCS-UnB

Chemotherapy-induced peripheral neuro-pathy is one of the major side effects observed in patients using different classes of antineoplastic drugs, and to date there is still no effective treatment to counteract this toxicity. Patients usually report sensory symptoms such as numbness and tingling in extremities and acute or chronic pain that can be severe enough

to limit the chemotherapy treatment. Moreover, as cancer survival continues to improve, we learn that neurotoxicity may or may not resolve after therapy is discontinued and that the quality of life of the patients and their families is often impaired. Thus, understanding how these anticancer drugs induce peripheral neuropathy is crucial to the development of new strategies to prevent and treat such adverse effects. We choose to focus on cancer therapies that produce neurotoxicity as a result of DNA damage in neurons. There are several studies suggesting that drugs that produce DNA damage and/or oxidative stress in neurons also induce neurotoxicity. Furthermore, DNA repair mechanisms are important to maintain neuronal function during the life time of such cells, despite the fact that these are post-mitotic cells. Base excision repair, nucleotide excision repair, mismatch repair, direct damage repair and non-homologous end joining are all present in the nervous system. Also, modifying DNA repair mechanisms in neurons alters neurotoxicity induced by cisplatin, for example. Indeed, sensory neurons with the cell bodies in the dorsal root ganglia are the primary target of platinum compounds. Alterations in the expression and activity of the APE1, a DNA base excision repair of oxidative DNA damage, decrease the cisplatin-induced toxicity in isolated rat sensory neurons. Taken together, these results provide strong evidence that enhancing DNA repair mechanisms in neurons could represent a novel approach to address the neurotoxicity induced by anticancer drugs that produce DNA damage. Financial Support: NIH (NS048565).

CPQBA-Unicamp: **25 years of research and development of natural products**. de Carvalho JE CPQBA-Unicamp – Farmacologia e Toxicologia.

The Chemical, Biological and Agricultural Pluridisciplinary Research Center (CPQBA) at Campinas State University (UNICAMP) is composed bythe Divisions of Agrotechnology, Phytochemistry, Organic and Pharmaceutical Chemistry, Pharmacology and Toxicology, Microbiology, Residues and Microbial Resources. Due to its multidisciplinary characteristics, many research projects are held together by various Divisions, in an integrated way. The first integrated project was the domestication of *Artemisia annua*, cultivation, extraction and large scale production of the antimalarial artemisinin and its derivative substances. CPQBA currently is capable of producing all the necessary artemisinin for the treatment of severe malaria cases in Brazil. The first collaborative projects of the Pharmacology Division havebeen directed to the study of the antiulcer activity of whey proteins as well as extracts and products obtained from plant species, such as *Rosmarinusofficinalis*, *Artemisia annua*, *Mikaniaglomerata*, *Arrabidaeachica* and *Pterodonpubescens*, resulting in several thesis and patents. The healing effects of *A. chica*crude extract will be clinically evaluated in patients suffering from oral mucositis induced by chemotherapy and radiotherapy after the non-clinical safety studies are performed. In cancer research, every year, the Pharmacology and Toxicology Division performs screening tests evaluating hundreds of plant extracts, active principles and products obtained by synthesis, in collaboration with both national and international research centers. The test substances with best *in vitro* anticancer activity have their pharmacological

activity confirmed with the help of laboratory animal cancer models, as well as studies of cell death mechanisms. The active principles responsible for the anticancer, antinociceptive and anti-inflammatory activities of *P. pubescens* have also been identified. The relationships between anticancer and anti-inflammatory activity of *styryl lactones* and their derivatives have been studied in a project in co-operation with the Chemistry Institute of UNICAMP. *Fapesp and CNPq support*.

Author Index

A

B

C

D

E

F

G

H

I

J

K

L

M

N

O

P

Q

R

S

T

Zapata-Sudo G 01.016, 05.008, 06.002, 07.001
Zarpelon AC 05.009, 05.010
Zelanis A 09.049
Zilli TLS 02.009
Zjawiony JK 02.024