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RESEARCH CENTER IN BIOSCIENCES & HEALTH TECHNOLOGIES

CBiOS Science Sessions - 2013 -

Cell culture as a useful tool in drug discovery: from cancer research to safety assessment

A cultura celular como uma ferramenta útil na descoberta de novos fármacos: aplicações na investigação em oncologia e na avaliação da segurança

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Abstract

Cell culture is a tool of utmost importance in the context of drug discovery, being useful in different steps, from the high throughput screening of a given pharmacological activity, to the pre-clinical safety assessment (cytotoxicity and genotoxicity studies). In our lab, we are interested in understanding the effect of redox regulators in the formation of breast cancer metastases. These studies could contribute to the comprehension of the redox biology of breast cancer and to the development of novel therapeutic strategies. For this purpose, we have implemented different in vitro assays using human breast cell lines, in order to study cell proliferation and viability, cell motility, and cell invasion. The effect of superoxide dismutase mimics and of diterpenic compounds has been studied in these models. We are also interested in the preliminary safety assessment of potential novel ingredients for skin products. In this context, the cytotoxicity profile of several natural products, especially plant extracts, has been characterized in HaCat cells, a widely used human keratinocyte cell line.

Lecturer's resumé

Ana Fernandes graduated in Pharmaceutical Sciences in 2004 and finished her PhD in Pharmacy (specialty of Toxicology) in 2010. She is currently the coordinator of the Laboratory of Pharmacology and Therapeutics of CBiOS and is also an Assistant Professor of Pharmacology and Toxicology at Universidade Lusófona. Her main research interest is the potential therapeutic role of redox-active molecules, especially in the context of breast cancer treatment. She received an international award and a national Honor. She is author/co-author of several communications and publications.

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Ethics and Research

Ética e Investigação

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Abstract

O "Conselho Nacional de Ética para as Ciências da Vida" (CNEV), National Ethics Council for the Life Sciences is an independent body that analyze systematically the ethical problems which arise out of scientific progress in the fields of biology, medicine or general health care and life sciences (<http://www.cnevc.pt/index.php>). Ethic and Moral are two concepts which have an inseparable relationship. With the first we establish what is right and what is wrong and, with the second the way we apply in practice the first. The use of animals, humans included, in experimentation rises permanently discussions on Ethic. Historical reasons lay under the steps towards the establishment of the rules concerning the ethical behaviour, more or less mandatory, when the law is not the entity that defines the borders. The International Guiding Principles for Biomedical Research Involving Animals were developed by the Council for International Organizations of Medical Sciences (CIOMS) 1985 (<http://www.cioms.ch/>) and experimentation involving animals is regulated in Portugal by law, Portaria 1005/92 that regulates the Decreto-lei nº 129/92 and Lei nº 92/95 on Animal Rights. Along the times, up to the 70ths of the 20 century, humans were object of experimentation, more or less without respect for their fundamental rights. Nuremberg Code 1947, The Universal Declaration of Human Rights 1948, The Belmont Report 1979, Declaration of Helsinki 1964 including six revisions and its clarifications, and CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects 2002 have been considered the ground for the sustaining and development of Ethics applied to the research.

Lecturer's resumé

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Modeling and simulation on pharmacokinetics

Modelação e simulação em farmacocinética

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Abstract

Discovery of new drugs is nowadays based on the knowledge and characterization of therapeutic targets and in the use of computational techniques for drug design. This methodology is able to propose thousands of new drug entities, however, the rate of drug approvals has been fairly constant over the last 30 years. Bad pharmacokinetic characteristics, despite the huge evolution in the in vitro testing for ADME, are still one of the major reasons for this attrition. In this presentation, it will be proposed an integral approach for the characterization and interpretation of the potential hits ADME, based on in vitro data and on QSAR models, as well as on the integration of these different models on physiologically based pharmacokinetic models.

Lecturer's resumé

Paulo Paixão holds a BSc. in Biochemistry, a MSc and a PhD in Pharmacokinetics from the Lisbon University. He is an Assistant Professor at the Lusofona University and Visiting Professor at the Lisbon University where he teaches Biopharmaceutics and Pharmacokinetics. He is also an assessor at the Portuguese Medicines Agency (INFARMED), on the evaluation of the pharmacokinetics and bioequivalence in various types of drug applications and on the European Medicines Agency (EMA). He has several publications on peers reviewed international journals, and was granted with the 2012 "Outstanding Manuscript Award in Modeling and Simulation" by the AAPS. His research interests are on the simulation of pharmacokinetic profiles, QSAR and Physiologically based Pharmacokinetic models to early predict the ADME and PK characteristics of new drug entities.

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In vivo models for the study of peripheral microcirculation

Modelação e simulação em farmacocinética

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Abstract

Cutaneous circulation serves as an interesting model for studying the microcirculatory function and dysfunction mechanisms. In this project we've applied three peripheral perfusion-conditioning maneuvers to a group of healthy young individuals (n=8, 24,5 ± 0,8 years old), both gender and evaluated the response profiles. Maneuvers implied the lower limb elevation while seated (A), and during dorsal decubitus (B) and the ankle supra-systolic occlusion by a tourniquet-cuff (C). Non-invasive transcutaneous variables included local blood flow by Laser Doppler Flowmetry (LDF), (tc) pO₂ and pCO₂ partial pressures by gasimetry and Transepidermal Water Loss (TEWL) by evaporimetry. Descriptive and nonparametric statistics were applied and a 95% confidence level adopted. tcpO₂ and tcpCO₂ changed significantly during these maneuvers. A reciprocal evolution profile was registered for LDF and TEWL in A and C which might suggest that under the present experimental conditions local perfusion might influence the epidermal "barrier" function. The proposed models seem to be appropriate to characterize the peripheral microcirculation in vivo, justifying further development studies.

Lecturer's resumé

Henrique Silva obtained his Master Degree in Pharmaceutical Sciences in 2011 from the Universidade de Lisboa (Faculty of Pharmacy). Currently he's a teaching assistant at the Universidade Lusófona, and an invited assistant at Universidade de Lisboa, as part of the Physiology and Pathophysiology staff. He is also (2012-) a PhD student in the Universidad de Alcalá – Universidade Lusófona Health Sciences PhD Program.

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