

**Results and Discussion:** A mixture of quercetin and biapigenin was isolated from *H. perforatum* and successfully encapsulated on PCL nanoparticles. The better proportion of PCL: HP of those studied, was of 1:0.1, with association efficiency of 99.7% and loading capacity of 5.3%. On the release profile, biphasic release was verified, including an initial burst followed by a slow release. Antioxidant activity assays revealed that encapsulation didn't alter HP functional properties. All cell lines responded differently to HP and its nanoparticles. Effects of HP and its nanoparticles against t-BOOH-induced lipid peroxidation were coherent with MTT results. Regarding permeability assay, HP PCL-loaded nanoparticles revealed to be more permeable than HP.

**Conclusion:** This is the first report of effective encapsulation of HP into PCL nanoparticles and also revealed its potential for brain delivery. More studies are however needed in order to extrapolate to in vivo situations.

**Acknowledgments:** This work was supported by FCT, projects PTDC/AGR-ALI/105169/2008, PEst-OE/AGR/UI4033/2014. Ana Isabel Oliveira is supported by ESTSP-IPP (Programa de Formação Avançada de Docentes).

### ***Role of pharmacogenomics in predicting antidepressant response and individualizing therapy***

Marlene Santos<sup>1,2,3</sup> Serafim Carvalho<sup>4,5</sup>, Luís Lima<sup>6,2</sup>, Jorge Mota-Pereira<sup>7</sup>, Paulo Pimentel<sup>8</sup>, Dulce Maia<sup>8</sup>, Diana Correia<sup>4</sup>, Sofia Gomes<sup>4</sup>, Agostinho Cruz<sup>2</sup>, Rui Medeiros<sup>1,9,10,11</sup>

<sup>1</sup>Molecular Oncology Group, IPO-Porto Research Center (CIPOP), Portuguese Institute of Oncology, Porto, Portugal

<sup>2</sup>Center for Research and Information in Pharmacy-NIIF, Research Centre on Health and Environment-CISA, School of Allied Health Technologies, Polytechnic Institute of Porto, Vila Nova de Gaia, Portugal

<sup>3</sup>Faculty of Medicine, University of Porto, Porto, Portugal

<sup>4</sup>Hospital de Magalhães Lemos, Porto, Portugal

<sup>5</sup>Instituto Superior de Ciências da Saúde, Norte, Portugal

<sup>6</sup>Experimental Pathology and Therapeutics Group, Portuguese Institute of Oncology, Porto, Portugal

<sup>7</sup>Clínica Médico-Psiquiátrica da Ordem, Porto, Portugal

<sup>8</sup>Trás-os-Montes e Alto Douro Hospital Centre, Vila Real, Portugal

<sup>9</sup>Department of Pathology and Molecular Immunology, ICBAS, Abel Salazar Biomedical Sciences Institute, University of Porto, Porto, Portugal

<sup>10</sup>Health Faculty of University Fernando Pessoa, CEBIMED, Porto, Portugal

<sup>11</sup>Research Department, Portuguese League Against Cancer (Norte), Porto, Portugal

**Introduction:** Major Depressive Disorder (MDD) is a highly prevalent chronic psychiatric condition with significant morbidity. Despite several antidepressants drugs (AD) available, a wide fraction of patients fail to respond, present relapse or display treatment resistant depression (TRD). Pharmacogenomics could help identify patients at risk of relapse or TRD and possibly have a direct impact on personalizing therapy. Additionally, recent studies suggested that immune activation and cytokines may be involved in depression, and its normalization occurs after antidepressant treatment. The proinflammatory cytokines interleukin-18 (IL-18) and IL-6 are less reported in depression, but considered to be relevant since they have been found to be increased in patients with depression.

Objectives: Since IL6 and IL18 polymorphisms have never been studied in antidepressant treatment phenotypes, we evaluated their role in AD treatment phenotypes, specifically remission, relapse and TRD.

Materials and Methods: We genotyped the referred polymorphisms using Sequenom MassARRAY technology in a subset of 80 MDD patients followed at Hospital Magalhães Lemos, within a period of 27 months, treated with AD according with Texas Medical Algorithm.

Results and Discussion: We found that patients carrying IL6-174GG genotype are more prone to develop TRD as well (OR=4.125; 95%CI: [1.151-14.786]; p=0.038). Regarding IL-18 polymorphisms we observed that patients carrying IL18-607CA/AA genotypes are more prone to relapse after AD treatment (OR=4.145; 95%CI: [1.038-16.555]; p=0.043) and present a lower time to relapse than patients carrying CC genotype (69vs115 weeks, p=0.019, Log-rank test). We also observed that patients carrying IL18-137GC/CC genotypes have a higher risk of relapse (OR=3.988; 95%CI: [1.176-13.516]; p=0.022) and display relapse earlier than the ones carrying GG genotype (64vs112 weeks, p=0.006, Log-rank test).

Conclusion: The referred polymorphisms influence antidepressant treatment phenotypes in our subset of MDD patients. They should to be integrated with others to develop a profile to detected patients at risk of relapse or TRD.

***A step towards personalized medicine: establishment of a pharmacogenomics profile of response to BCG intravesical immunotherapy in bladder cancer***

Luis Lima<sup>1,2</sup>, José A Ferreira<sup>1</sup>, Rui Medeiros<sup>3</sup>, Lúcio Santos<sup>1</sup>

<sup>1</sup>Experimental Pathology and Therapeutics Group, Portuguese Institute of Oncology - Porto

<sup>2</sup>Center for Research and Information in Pharmacy-NIIF, Research Centre on Health and Environment-CISA, School of Allied Health Technologies, Polytechnic Institute of Porto, Vila Nova de Gaia, Portugal

<sup>3</sup>Molecular Oncology Group, Portuguese Institute of Oncology - Porto

Introduction: The most effective adjuvant therapy of non-muscle invasive bladder cancer (NMIBC) during the last 35 years has been the intravesical instillation with Bacillus Calmette-Guerin (BCG). However, despite its efficacy, approximately 30% of the patients present treatment failure and tumor may progress.

Objective: The goal of this work was to evaluate the predictive value of genetic polymorphisms in the context of BCG immunotherapy outcome and create a predictive profile that may allow the early identification of patients at risk of treatment failure.

Material and Methods: In a dataset of 204 NMIBC patients treated with BCG, we evaluate 42 genetic polymorphism in 38 genes involved in the BCG mechanism of action, using Sequenom MassARRAY technology. Stepwise multivariate Cox Regression analysis was used to create a profile that could predict treatment response.

Results and Discussion: We propose the first predictive profile of BCG immunotherapy outcome and a risk score based on polymorphisms in immune system molecules [single nucleotide polymorphisms in tumour necrosis factor (TNFA)-1031T/C (rs1799964), interleukin 2 receptor (IL2RA) rs2104286 T/C, IL17A-