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).

Conslusion: 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

Luís Lima[1,2], José A Ferreira[1], Rui Medeiros[3], Lúcio Santos[1]

[1]Experimental Pathology and Therapeutics Group, Portuguese Institute of Oncology - Porto
[2]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
[3]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-

197G/A (rs2275913), IL17RA-809A/G (rs4819554), IL18R1 rs3771171 T/C, intercellular adhesion molecule 1 (ICAM-1) K469E (rs5498), Fas ligand (FASL)-844T/C (rs763110) and TNF-related apoptosis-inducing ligand receptor 1 (TRAILR1)-397T/G (rs79037040)] in association with clinicopathological variables, that permits to categorize patients into risk groups. According to our model, patients within the Low Risk groups have a 90% chance of successful treatment, whereas patients in the High Risk groups present 75% chance of recurrence after BCG treatment.

Conclusion: This study has allowed the establishment of a genetic risk score that could stratify patients according to the risk of recurrence after BCG immunotherapy. This score may be a helpful tool to identify patients with poor prognosis and to improve clinical decision.