

Using polygenic risk scores to dissect the heterogeneity of Autism Spectrum Disorder

PhD project proposal

Common chronic conditions, like cardiovascular or neuropsychiatric diseases, are thought to be multifactorial, with a complex polygenic architecture compounded by environmental factors contributing to disease risk. For many such diseases, understanding the genetic risk component remains a challenge, mainly because it is difficult to identify the many common genetic variants conferring small increments in disease risk, which each explain only a very small proportion of genetic risk variance. Polygenic risk scores (PRS) are increasingly seen as a promising tool in both research and clinical settings. By combining the effects of a large number of genetic variants, PRS offer a quantitative assessment of the component of disease risk associated with common genetic variation. One of the applications of these techniques is to characterize complex disorders, where the genetic determinants stem from both common and rare variants, as well as their interactions. This is particularly the case for Autism Spectrum Disorder (ASD). ASD is a heterogeneous neurodevelopmental disorder, complex from both the phenotypic and genetic points of view. While ASD has an important genetic component, genetic factors are present in both common and rare genetic variation, posing a challenge for the identification of biomarkers and potential therapeutic targets. This proposal aims to address this challenge by developing innovative data analysis approaches making use of PRS to analyze clinical and genetic data from large Whole-genome Sequencing cohorts of ASD patients. Validation of outcomes is possible in a cohort of patients from Portugal, with extensive clinical characterization, leading to novel etiological diagnosis that truly integrates the multigenic component of ASD genetic risk. Work will be developed at Instituto Nacional de Saúde Doutor Ricardo Jorge, in a multidisciplinary research group including biologists, psychologists and bioinformaticians.

If you are interested in pursuing a PhD in this area and would like to submit a proposal for funding to the ongoing FCT PhD fellowship call, please send your CV to: Hugo Martiniano (hugo.martiniano@insa.min-saude.pt).