# BIOMARKERS OF TREATMENT NAIVE PSYCHOSIS

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ABOUT THE PROJECT

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The investiqation of individuais during their first-episode psychosis (FEP) before the proqression of the disorder and particularly before treatment with antipsychotic medications is helpful for understanding the complexity of schizophrenia. Several studies suggested that gene expressron in blood could serve as a diagnosis tool for brain-related diseases. Considering that schizophrenia is a chronic condiction that requires a lifelong treatment, disease progression and use of antipsychotic medication can confound results on gene expression and DNA methylation. Our main aim of this study is to identify genetic markers using genomic, transcriptomic and methylomic approaches in a longitudinal cohort of FEP. The patients will be assessed in the baseline, all antipsychotic naive, (anFEP, N=80), and after eight weeks (FEP-8w, N=80) and one year (FEP-1Y, N=30) of antipsychotic treatment. Until this moment, we collected and isolated the mRNA and the DNA of more than 75 anFEP, 75 FEP-8w and 20 FEP-1Y. The remaining patients will be collected during the first semester of this Project. The DNA Genotyping array will be performed in Brazil using the PsychChip array with a GWAS core backbone and specific content from the Psychiatric Genomics Consortium, under the hypothesis that gene expression and methylation differences for FEP individuals and for treatment response are determined by genetic variance. Transcriptomic and methylomic approaches will be performed in UK. For the whole gene expression arrays we are going to use the "HumanHT -12 v4 Expresston BeadChip". witch provides genome-wide transcriptional coverage of well-characterized genes (approx. 25,000 genes). Concerning DNA methylation analysis, we will generate data using the lnfinium Human Methylation 450 BeadChip, which interrogates more than 485,000 methylation sites per sample. With these data, we expect to find potential blood biomarkers for disease and for treatment response (anFEP x FEP-8w and FEP-1 Y). Moreover, we will hold an advanced course in bioinformatics focusing on gene expression and methylation analysis at UNIFESP lasting a week. This will be available to 30 PhD students of São Paulo State with no charge. The analysis course will be leaded by Dr. Breen's team. This Project is a great opportunity for both sides. Dr. Breen will contribute with this expertise in bioinformatics and will analyze the "big data" generated by transcriptome and methylome analysis. Moreover, his team will teach for a grad students about this analysis. Thus, we would be able to perform it by ourselves. On the other hand, the Brazilian group will contribute with a unique anFEP cohort including a multimodal assessment, besides expertise and background in genomic and epigenomic techniques. Both sites will contribute equally to the Project performance, helping to find out genetic markers to schizophrenia.