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HOW HORMONES INFLUENCE GENE EXPRESSION: IMPLICATIONS TO THE PATHOPHYSIOLOGY OF SCHIZOPHRENIA

H. Brentani¹, D. Carraro¹, L. D. Mota¹, M. Maschietto¹, H. B. Mello¹, C. H. Torres¹, C. S. Gama², A. B. Goodman³, P. Belmonte-de-Abreu², **J. A. Palha**⁴

¹Laboratório de Genômica e Biologia Molecular, Hospital A. C. Camargo, São Paulo, ²Department of Psychiatry, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, Brazil, ³The Massachusetts Mental Health Center Academic Division of Public Psychiatry, Harvard Medical School, Boston, USA, ⁴Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal

Schizophrenia is a complex genetic disorder. The lack of concordance on disease manifestation in monozygotic twins provides clear evidence that environmental factors are key determinants in disease aetiology. In accordance, various environmental modulators such as hormones and vitamins may well contribute to the altered expression pattern of several genes identified in post-mortem brain tissue of patients. We constructed a microarray platform containing 1,808 human genes, where 142 belong to vitamin A, thyroid hormone and estrogens' metabolic pathways, to specifically address whether these could contribute to a molecular signature of schizophrenia in peripheral lymphocytes. We found that the genes encoding for PLP1, UGT1A6, NTRK1, THRAP1, ESR2, TRIP13, MAPK8, TGFB2, IGFBP4 are differentially expressed in lymphocytes of patients under treatment with clozapine, risperdal or haloperidol. Some of these genes have been previously reported by others to be altered in brain regions of schizophrenic patients, and all are implicated in pathways suggested to be involved in the disease. These observations further support that:

1. studies in peripheral blood lymphocytes may contribute to reveal candidate genes in schizophrenia;
2. transcription modulation of several genes may occur through the mediation of vitamin and hormones, therefore linking genes and environment in schizophrenia.

In order to understand the involvement of these genes in schizophrenia, future studies should investigate whether some of the observed changes are replicated in animal models of the disease, and how antipsychotic treatment interferes with their expression.