Endogenous retroviruses in schizophrenia and other psychoses

Håkan Karlsson, Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden.

The etiology and pathogenesis of schizophrenia and related psychoses remain to be established. During a search for transcripts of retroviral origin in cerebrospinal fluids of first-episode patients, RNA related to the W family of human endogenous retroviruses (HERV) were identified. HERV-W sequences were subsequently also differentially observed in plasma and blood cells of such patients. HERV along with other repetitive elements are normally transcriptionally repressed by extensive DNA methylation and histone modifications, at least in adult tissues. Recent analyses of next generation sequencing data indicate that several HERV loci indeed appear to be transcribed in different regions of the human brain and support previous PCR-based observations of elevated levels of HERV-W transcripts in schizophrenia and bipolar disorder. While the reasons for increased HERV-W expression in these patients remain to be identified, recent experimental studies suggest that infections and other environmental factors can de-repress HERV loci by altering DNA methylation or repressive histone modifications. The potential roles of HERV as marker or mediator of environmental and genetic risk factors in psychoses (and other human diseases) need to be established.