Characterization of the expression pattern of the human L1 protein machinery during embryonal and fetal developmental stages

Research project summary

Since the presence of the intact L1 protein machinery consisting of L1 ORF1p and L1 ORF2p is an essential prerequisite for L1-mediated retrotransposition and genomic expansion of L1, we are systematically analyzing human cell types and tissues for the presence of both L1 proteins. By analyzing fetal testicular tissue applying novel polyclonal antibodies raised against the L1-EN domain of ORF2p as well as polyclonal anti-ORF1p antibodies, our laboratory was able to detect the L1-encoded protein machinery not only in prespermatogonia of fetal testis and in germ cells of adult testis, but also in somatic subsets of testicular cells (Sertoli, Leydig, testicular covering cells) and vascular endothelial cells. We also confirmed the identification of functional L1 proteins by MALDI-TOF (J. Biol. Chem. 279: 27753-63 (2004)). The results we have obtained so far, are consistent with the hypothesis that L1-mediated retrotransposition events that are responsible for the evolutionary genetics of L1 elements or caused genetic disorders must have occurred in the germ line and/or during early stages of the human embryonal development.
It is our goal to identify developmental stages, tissues and cell types of the human embryonal and fetal development, in which the presence of the L1-encoded protein machinery facilitates L1-mediated retrotransposition which can cause or participate in the generation of genetic disorders and/or tumorigenic disease, respectively. Therefore, embryonal and fetal tissues are screened for the presence of L1-encoded proteins applying a variety of methods including immunohistochemical analyses of tissue sections.

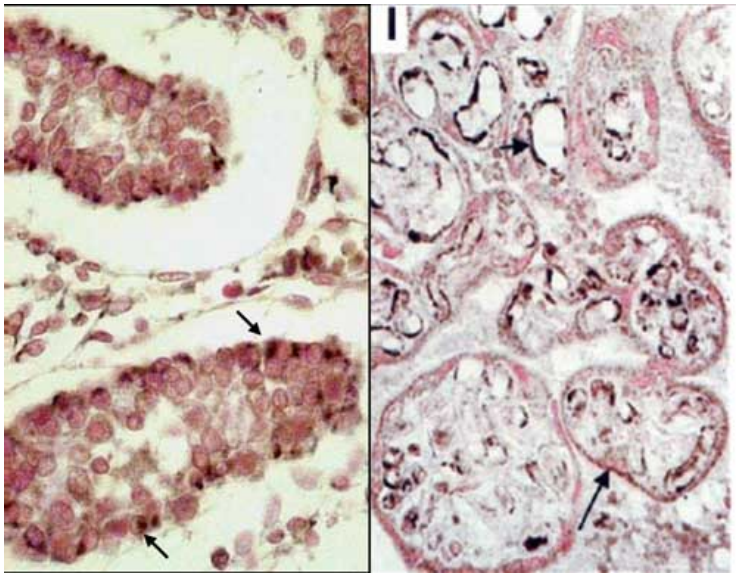

Figure: Immunolocalization of L1-encoded proteins (dark stained) in human fetal germ cells (left) and in syncytiotrophoblasts (long arrows) and vascular endothelial cells of the placenta (right). Source: PEI