Mouse genetic models of placental function: Friday 6th July 09.00

The rapid expansion in transgenic techniques and gene knockouts offers unique opportunities of identifying genes with roles in placental function. The Jackson laboratory "mouse genome informatics phenotypes" database (http://www.informatics.jax.org) holds searchable phenotypic data of over 40.000 mouse mutants, with a significant proportion of these showing abnormal placental morphology. We have recently used this database to screen for genes and gene pathways that are associated with placental developmental defects and sub-optimal fetal growth trajectories. A particular class of genes that are overrepresented are imprinted genes. These genes are unique in the genome of mammals because they retain information about their parental origin and are involved in regulating maternal investment in pregnancy. The fetal trophoblast is a strong site of expression, and mouse imprinting knock-out models frequently show altered placental development and function. During this talk I will give illustrative examples of genetic mutations (imprinted and non-imprinted) that disturb the function of the exchange barrier for nutrient transport, and/or the endocrine layer with potential implications for maternal physiology. I will highlight how the studies of mouse genetic models are providing key novel insights into placental adaptive responses to intrinsic and extrinsic factors, such as physiological stressors and fetal demands for growth. Understanding the basic molecular mechanisms that underlie the adaptive signaling between the mother, the placenta and the fetus will be essential to devise interventional approaches to improve the outcomes of human pregnancy complications. There are strong arguments in favor of mouse modeling in spite of the obvious morphological differences between the human and the mouse placenta.

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