

### **39. THE MAKING OF AN EMBRYO: SHORT-TERM GOALS AND LONG-TERM IMPLICATIONS**

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At first sight, the construction of the preimplantation embryo in eutherian mammals seems such a simple process: the generation of a hollow ball of cells comprising an outer trophectoderm epithelium (TE) layer and enclosing an inner cell mass (ICM) with placental and fetal fates, respectively. However, the fascination is in the detail and the subtle mechanisms utilising cell-cell interactions, differentiative cell divisions and an inherent gene expression programme to guide the formation, segregation and relative size of these two critical cell populations. The mouse embryo has become an ideal model for understanding how an epithelium forms in a step-wise manner in a 'real' tissue *in situ* engaging temporally controlled gene activity. We have focused on the mechanisms coordinating biogenesis of intercellular adhesion and multi-protein membrane junction complexes in the TE and these will be discussed. With the advent of reproductive biotechnologies, it has become apparent that these short-term goals of lineage formation and diversification prior to implantation may have more lasting consequences. The mammalian early embryo is sensitive to its environment, which may influence both early morphogenesis but most significantly later fetal and postnatal growth and physiology. Thus, in two models we have developed in rodents, (i) maternal low protein diet fed exclusively during the preimplantation period and (ii) in vitro culture followed by embryo transfer, both have been shown to alter postnatal growth, systolic blood pressure and organ allometry in a gender-specific manner. Such potential 'programming' during early development has clear healthcare implications. To unravel mechanisms of dietary influence upon embryos, analysis of maternal serum, uterus or uterine fluid composition indicates potential roles for amino acid and growth factor environments in the mediation of programming. Analysis of embryo responses to adverse conditions indicate subtle changes occur in lineage allocation and gene expression potential, in particular associated with imprinted genes. The legacy of such early changes is under current investigation. For example, in one direction, we find that post-implantation nutritional support provided by the rodent visceral yolk sac becomes compromised. Thus, we consider that embryonic programming involves a combination of interacting processes operating at metabolic, genetic, cellular and physiological levels. The fascination with simple embryos continues!