Oxygen Sensing and Placental Cell Differentiation

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Mammalian embryogenesis relies on a functional placenta, a transient organ responsible for implantation, communication, nutrient, waste product, and oxygen (O_2) exchange between mother and fetus. Placenta formation occurs with physiologically low O_2 concentration (2%) and a postulated oxygen gradient. Successful placentation depends on constant feedback mechanisms between embryonic cells and their maternal microenvironment to drive cell fate choices, changes in cellular and organ architecture, and maternal tissue remodeling. We use human placenta organoids as an *in vitro* system to model the three major placental cell types, one of which, the extravillous trophoblast, is highly invasive and differentiates from trophoblast stem cells (TSC). We find that culutring organoids at 2% O_2 leads to a more immature state of differentiation when compared to the standard culture at 21% oxygen. This indicates an importance of the right temporal control of oxygen levels. Moreover, knock-out of hypoxia inducible factor (HIF) pathway member HIF1α, a protein for cells to sense environmental O_2, impairs the TSCs ability to differentiate into extravillous trophoblasts. These findings point to the involvment of the HIF pathway in trophoblast differentiation. In the future, we will analyze downstream targets of the HIF pathway members using molecular and morphodynamic analysis, to shed light on external microenvironmental and intracellular signal integration. I expect to describe the role of O_2 as a morphogen in shaping placenta development and we will gain an insight into the molecular and cellular mechanisms that govern cell-cell and cell-environment crosstalk during placenta development.