EPIBLAST - Enhanced Platform for the Identification of molecules Boosting or Limiting Amniotic cavity and primitive STreak formation

Drug teratogenicity, namely the potential of a drug to cause birth defects, is a major concern for anyone becoming pregnant. The infamous Thalidomide case in the 1960s raised public awareness of this issue. Notably, only about 30% of embryos successfully implant during early development, but the reasons for this low rate remain unclear. Nobody knows if this is due to the teratogenic effects of common drugs, or a lack of essential nutrients needed for development, similar to how folate is used to support proper nervous system development. There is a significant gap in our understanding of drug teratogenicity because pregnant women are excluded from clinical trials, and preclinical animal studies have limitations due to ethical concerns and differences between species. This gap leaves the effects of many drugs on early human development uncertain. As a result, many potentially beneficial medications are often discontinued during pregnancy, despite the lack of strong scientific evidence to justify such decisions. The goal of this Proof of Concept is to develop a fully automated 3D in vitro model that replicates the first 14 days of human development. Using human pluripotent stem cells, during the ERC Starting grant, we have created a chemically defined and efficient 3D model that accurately mimics peri- and post-implantation stages, including the formation of the epiblast epithelium, primitive streak, and amniotic cavity. We now aim to validate and automate this model for rapid, high-throughput assessment of drug teratogenicity. By accurately simulating human development, enabling high-throughput screening, and reducing reliance on animal testing, our model addresses critical gaps in current testing methods. This innovative approach could lead to the identification of supplements that improve pregnancy success rates and ensure safer medication use during pregnancy, ultimately benefiting patients, healthcare providers, and regulatory agencies

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