A Multi-Omic “Digital Embryo” Framework to Model Early Human Preimplantation Development In Silico

Shen, Matthew (School: Saint Theresa of Lisieux Catholic High School)

Nearly 50% of human IVF embryos arrest before reaching the blastocyst stage, yet the molecular mechanisms causing this failure remain poorly understood. Current literature examines omics in isolation, missing the cross-omic interactions governing early development. The Digital Embryo is the first multi-omic framework integrating 6 omics—transcriptomics, proteomics, metabolomics, secretomics, genomics, and epigenomics—into a shared molecular state system spanning 1963 cells across 9 independent datasets. Each omic layer is processed before embedding into a 94-dim feature matrix, with scVI anchoring the transcriptomic backbone. An XGBoost classifier trained on the matrix predicts embryo arrest. On unseen datasets, it achieves 0.870 AUC versus 0.754 for the transcriptomics-only control classifier—a +0.116 AUC gain from multi-omic integration. The Digital Embryo also reveals novel cross-omic signatures that show arrest reflects coordinated failure across molecular layers, a pattern that single-omic studies structurally cannot explain: i) arrested embryos exhibit simultaneous promoter hypermethylation and transcriptional downregulation of DNA damage response genes; ii) protein fold changes corroborate transcriptomic arrest signatures (17/17 concordance, $p<0.00001$). The Digital Embryo introduces a perturbation engine that simulates modifications to an embryo's omic profile, culture conditions, and environmental exposures, and re-predicts its arrest risk. Validated against 85 compounds, 37/40 of the strongest predicted effects on arrest matched known in vitro results. The Digital Embryo further generated 35 candidate treatment combinations against arrest, demonstrating the capacity for computational treatment discovery and personalized, multi-omic-guided reproductive medicine.

Awards Won:

Second Award of $2,400

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The Consortium for Mathematics and its Applications: Honorable Mention In-Kind