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Towards personalized healthcare engineering: A new paradigm in blood disorder treatment

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Personalized medicine is a medical model that proposes the customization of healthcare with decisions and practices being tailored to the individual patient by use of patient-specific information (initially genetics information) and/or the application of patient-specific cell-based therapies. The BioBlood project aims to deliver personalized healthcare through a "step change" in the clinical field of hemato-oncology. BioBlood represents an engineered bio-inspired integrated experimental/modeling platform for normal and abnormal hematopoiesis that receives disease & patient input (patient primary cells & patient/disease-specific data) and will produce cellular (red blood cell product) and drug (optimal drug treatment) therapies as its output. Herein, we will present the experimental platform, which is a novel three-dimensional hollow fibre bioreactor capable of culturing normal and abnormal hematopoietic cells in the absence of exogenous growth factors by mimicking the structure and function of the bone marrow, alongside a population balance model (PBM) that is able to capture cellular heterogenity and in particular leukemia heterogenity. The PBM, which is able to extract patient and disease-specific information are linked to a pharmacokinetic/pharmacodynamic (PD/PD) model, which is the used to optimize chemotherapy treatment in a personalized manner.

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Human amniocytes are receptive to chemical induced reprogramming to pluripotency

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Restoring the pluripotent state of somatic cells using chemical compounds alone would be a major step forward in developing clinical grade pluripotent stem cells but this has not yet been reported in human cells. We previously demonstrated that human amniocytes cultivated with valproic acid (VPA_AFS cells) formed well differentiated teratomas containing derivates of the three germ layers when transplanted into immunodeficient mice, indicating they acquired functional pluripotency. However, VPA_AFS cells remained distinct from hESCs, questioning the relationship between modulation of cell fate potency and molecular regulation of the pluripotency network. Here, we used single cell analysis and functional assays to analyze the features of the molecular state of VPA_AFS cells and understand how they relate to hESCs. We reveal that VPA treatment resulted in a homogenous population of self renewing non-transformed cells and induced transcriptional and phenotypical changes that fulfill hallmarks of pluripotency i.e., a short G1 phase, a dependence on glycolytic metabolism, expression of epigenetic modifications on histones 3 and 4 and reactivation of endogenous OCT4 and downstream targets (including Tra-1-60, REX1, DNMT3B, NANOG and SOX2), which were expressed in all VPA_AFS cells but at a lower level than that observed in hESCs. Our data identify for the first time the pluripotent transcriptional signature and metabolic status of human chemically induced pluripotent stem cells.

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