Ex-vivo large-scale production of platelets from human pluripotent stem cells for human transfusion and drug screen

Raslova H.

INSERM U1170, Normal and pathological hematopoiesis Gustave Roussy Institut, Paris

Due to the ageing population and ever more aggressive chemotherapies, platelet demand is increasing by 10% every year, while the supply of platelets is entirely dependent on allogenic donations. In Europe, the demand of platelets averages 5 units per 1,000 population per annum, i.e. 2.5 million units per year, costing over €375 million. Lastly, there is a clear need for reproducible solutions to assist patients with acute haemorrhage resulting from trauma, surgery and emergency treatment in conflict zones.

The limited supply of human platelets and the rapidly growing demand for medical research and clinical applications require a development of new modes to generate functional platelets *ex-vivo* to address these clinical needs as well as for insight into fundamental studies of mechanisms of physiologic and pathologic platelet production.

The primary goal of SilkFUSIONconsortium is to engineer groundbreaking 3D nanotechnologies for large-scale production of blood platelets for human transfusion from human pluripotent stem cells (hPSCs). Our hypothesis is that plt production ex-vivo can be optimized by providing platelet precursors, megakaryocytes (Mks), with the correct physical and biochemical environment. To prove this, we develop a unique technological platform by engineering non-thrombogenic silk-fibroin biomaterial with proteins that were proven to promote a gain in platelet production of at least one order of magnitude, through the creation of a three-dimensional ex-vivo bone marrow model that will enhance platelet release from hPSCs derived-Mks.

Our platform includes (i) novel applications to study pathogenetic mechanisms in patients with inherited platelet production disorders using genetically modified hPSCs; (ii) screening technology for predicting therapeutic efficacy of drugs for thrombocytopenic patients. The development of this technology will exploit an extremely innovative approach using silk-fibroin as a bio-ink for 3D printing a ""live chip"" containing viable Mks for reproducible drug testing.