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Generation of a bi-potent hemangiogenic progenitor from human pluripotent stem cells

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Abstract

The close temporal-spatial relationship between hematopoietic and endothelial cells during early embryonic development has led to the hypothesis of a common ancestor, the hemangioblast. Here human pluripotent stem cells (hPSCs) endothelial and hematopoietic differentiation via a bi-potent progenitor and an in vitro equivalent of the hemangioblast were explored. hPSCs were differentiated into hemangiogenic mesoderm through embryoid body (EB) formation under serum-free culture conditions. After three, five days of differentiation, a population positive for CD309 (VEGFR-2), CD144 (VE-Cadherin), CD143 (ACE) and CD34 was isolated based on the expression of CD144 and cultured either under endothelial or hematopoietic conditions. A homogeneous population of functional CD144+CD31+ (PECAM-1) CD34+ and vWF+ endothelial cells was obtained after 4 days of endothelial differentiation. These cells up regulated ICAM upon adding TNF-α, endocytosed acetylated-LDL, expressed eNOS and formed tubular networks when cultured on a matrix gel layer. Additionally, passaging and cryopreservation were possible without modifying their phenotypic and functional characteristics. Furthermore, CD144+ EB sorted cells generated blast colonies (BCs) after 4 to 6 days grown in methylcellulose supplied with growth factors. BCs expressed hematopoietic markers such as CD43, CD45 and CD41 and gave rise to in vitro hematopoietic cells under colony forming cell (CFC) assay conditions. Interestingly, we observed an intermediate population at day 4-6 of BC formation expressing both CD144+ and CD45+ suggesting the hemangioblast-like progenitor may undergo an endothelial-hematopoietic transition. These results suggest the existence of an early, isolable and cryo-preservable hemangioblast like-progenitor derived from hPSCs. Currently, in vivo experiences are carried out to determine the therapeutic potential of the derivate endothelial and hematopoietic cells.

Biography

Alejandra Vargas Valderrama is currently a 4th year PhD student from the University Paris Sud at the laboratory INSERM U1197 leaded by Dr Georges Uzan. Her main research project, supervised by Dr Mitjavila Garcia and Dr Guenou, focuses on the differentiation of hPSC into endothelial cells via a hemangioblast. Thanks to her PhD project, she participated in the iLite (innovations in Liver tissue engineering) project aiming to create an external bio-artificial liver. Her main research areas of interests are related to endothelial development and tissue engineering for the production of external vascularized tissues.

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