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Transcription Factor-Driven hiPSC Differentiation Platform for 3D Cardiac Tissue Engineering

Stanford researchers have developed an innovative method for efficiently generating robust lymphatic endothelial cells (iLECs) from human induced pluripotent stem cells (hiPSCs) through transcription factor-based protocols. This technology enables scalable production of lymphatic and cardiac cells in 3D-printed tissue constructs, addressing critical limitations in cell maturity, expansion, and differentiation efficiency encountered by current growth factor-based methods.

The ability to reliably and reproducibly generate iLECs and cardiac cells from hiPSCs is foundational for tissue engineering, disease modeling, and regenerative medicine. Today's differentiation protocols yield immature or unstable cell phenotypes, limiting the scalability and translational impact of engineered tissues for research and therapeutic applications. The inventors' approach uniquely harnesses controlled overexpression of master regulatory transcription factors (SOX18, COUP-TFII, PROX1, ETV2) using inducible, endothelial-specific promoter systems. This strategy bypasses exogenous growth factor requirements, dramatically increasing differentiation efficiency and enabling orthogonal generation of blood and lymphatic vasculature in cardiac organoids. The result is mature, highly expandable iLEC lines and multi-vascularized cardiac tissues with improved cell survival and function.

Stage of Development
Prototype, with associated *in vitro* data acquired

Applications

- Scalable generation of cardiac and lymphatic endothelial cells for biofabrication, precision modeling, and drug screening

- Custom organoid manufacturing and therapeutic tissue engineering
- Commercial cell culture and differentiation kits
- Research reagents for vascular biology, regenerative medicine, immunology, and cardiovascular research

Advantages

- Robust, reproducible cell phenotype surpasses growth factor-based induction methods
- Eliminates need for costly exogenous reagents
- Differentiation workflow is readily compatible with kit-based distribution
- Facilitates co-differentiation protocols for multi-vascularized organoid assembly in 3D bioprinting and advanced tissue engineering

Patents

- Published Application: WO2026165249

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