Bioengineering Functional Kidney Tissue from Human Pluripotent Stem Cells: A Promising New Treatment for Kidney Disease

Maxim, Demetri

Chronic kidney disease (CKD) is a significant global health problem that affects 10% of the world's population and costs over $200 billion to treat every year. A new treatment for CKD is desperately needed, and the goal of this study is to develop a new treatment using a regenerative medicine approach with patient-derived human pluripotent stem cells (hPSCs). Previously, I developed a protocol for differentiating hPSCs into mature kidney cells with 20% efficiency, and in this study, I report a new protocol that generates mature kidney cells with 70-90% efficiency and allows them to be used therapeutically. This new protocol was developed through a computational approach. Mathematical models of the important signaling pathways involved in stem cell differentiation were constructed. Simulations of the models were run to identify the components of each pathway that should be targeted to maximize pathway activation. All of the predicted pathway targets were subsequently validated biologically using known inhibitors of the pathway components. The final protocol produced cells of the glomeruli, proximal tubules, loops of Henle, distal tubules, and collecting ducts that organized into complete, continuous nephrons when seeded into scaffolds made of 3-D printed polylactic acid (PLA) plastic. These hPSC-derived kidney cells demonstrated functional and regenerative capabilities in vivo when transplanted into NOD-SCID mice, and could perform other major kidney functions including vitamin D activation, blood pressure regulation, and red blood cell health maintenance. These data establish a highly efficient method of creating functional kidney tissue from patient-derived hPSCs, which could someday offer a new treatment for the millions of patients suffering from CKD worldwide.

Awards Won:

First Award of $5,000

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