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iPSZÜRICH

A Lecture Series Focused on Induced Pluripotent Stem Cells



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## USE OF AN iPSC-DERIVED HEPATOCYTE PLATFORM TO IDENTIFY TREATMENTS FOR HYPERCHOLESTEROLEMIA

Familial hypercholesterolemia (FH) patients suffer from excessively high levels of Low Density Lipoprotein Cholesterol (LDL-C), which if left untreated results in death from severe cardiovascular disease. FH is caused primarily by mutations in the LDL receptor (LDLR) that prevent the uptake and clearance of LDL-C by the liver. The identification of novel small molecules to treat hoFH, has been hampered by the lack of a drug discovery platform that can recapitulate the deficiencies in liver function and cholesterol metabolism that are present in FH patients. To circumvent this barrier, we generated induced pluripotent stem cells (iPSCs) from a hoFH patient. When the hoFH iPSCs were induced to form hepatocytes, they recapitulated the pathophysiology of FH in culture. We used this platform to screen a proprietary drug library and identified a family of structurally related small molecules that could reproducibly reduce the production of LDL-C in both control and hoFH iPSC-derived hepatocytes.



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