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Ajinomoto Innovation Showcase in ISSCR2017

Symposium Title : Genome editing of hPSCs for accurate modeling of human diseases

Date : Friday 16th, June 2017

Time : 11:30-12:30

Visit us at Ballroom West (Level 3)

Chair : Ryuji Morizane, Ph.D., M.D.
Brigham and Women's Hospital Renal Division

Abstract : Human pluripotent stem cells (hPSCs) offer an unprecedented opportunity for giving rise to a wide range of specific differentiated cell types in which we could explore the mechanisms by which particular diseases arise at the cellular level. Recent advances in genome editing technology of hPSCs have allowed for the generation of more accurate human disease models with specific genetic alterations or correction of mutations in the mutant human induced pluripotent stem cell (hiPSC) lines. In this workshop, we will discuss recent technological advances in genome editing, and their use in human biology and disease research.

Speaker 1 : Ryuji Morizane, Ph.D., M.D.
Brigham and Women's Hospital Renal Division

Title Kidney Organoids and Disease Modeling with CRISPR/Cas9

Speaker 2 : Curtis Robert Warren, Ph.D.
Harvard Department of Stem Cell and Regenerative Biology

Title Genome editing: from modeling disease to novel therapeutics

Visit our booth and posters Booth#412

T-2156 : Superior Cloning Efficiency of hPSCs Cultured in a Xeno-free and Defined Culture Medium, StemFit®

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Speaker 1 : Ryuji Morizane, Ph.D., M.D.

Title Kidney Organoids and Disease Modeling with CRISPR/Cas9

Abstract : Significant advances have been made within the past decade that draw upon our knowledge of kidney development to differentiate human pluripotent stem cells (hPSCs) into cells of the kidney lineage.
By recapitulating metanephric kidney development in vitro, we generated nephron progenitor cells (NPCs) with ~90% purity within 9 days of differentiation without additional subpopulation selection during the directed differentiation. hPSC-derived NPCs possess the developmental potential of their in vivo counterparts, forming renal vesicles that self-pattern into nephron structures with characteristics of podocytes, proximal tubules, loops of Henle, and distal tubules. Recent advances in genome editing using CRISPR/Cas9 systems provide the tools to generate specific mutations at desired sites. Genetics is a dominant factor contributing to variation in the differentiation and functional characteristics of differentiated hPSCs. The CRISPR/Cas9 system enables the generation of specific mutations in target genes in normal hPSCs. Kidney organoids differentiated from these cells can then be used to model kidney disease known to be caused by these genetic modifications. The parental hPSC line will be an ideal control for these studies since all genes, except for those targeted for modification, will be the same. These novel technologies contribute to developing novel platforms for studies of human kidney development, modeling of kidney diseases, nephrotoxicity of drugs, and kidney regeneration, and provide a system in vitro for the study of intracellular and kidney compartmental interactions using differentiated human cells in an appropriate nephron context.

Speaker 2 : Curtis Robert Warren, Ph.D.

Title Genome editing: from modeling disease to novel therapeutics

Abstract : Our research is focused on understanding the molecular underpinnings of metabolic diseases such as type 2 diabetes mellitus (T2DM) and coronary artery disease (CAD). Metabolic diseases such as T2DM and CAD are responsible for an increasingly large burden of morbidity and mortality worldwide, afflicting hundreds of millions of people. The development of new and effective treatments for these diseases requires the identification and validation in humans of novel disease mechanisms.
Recent advances in human genetics have begun to explicate the heritable susceptibility to metabolic diseases. We seek to convert novel genetic findings into the knowledge needed to develop therapies for patients. Our approach to linking human genotypes to human phenotypes has three key steps.
The first is to perform human genome editing to introduce disease-associated gene mutations and DNA variants into human pluripotent stem cells (hPSCs). The second is to differentiate and engineer hPSCs into tissue types relevant to disease in order to develop ex vivo models of disease.
The third is to perform functional assays in the genetically modified (and control) differentiated tissues to obtain pathophysiological insights. Once we have identified disease relevant phenotypes we plan to use our human cell-based models of disease to perform genetic and drugs screens to develop novel therapeutics.

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