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This seminar will be held in the manner of online and offline both.

Offline: Faculty Conference room(RM.119/Bldg. No. S3)
Online: Zoom ID 315 451 8934 (Password: Life2021Fa)

Multiple isogenic GNE-myopathy modeling with mutation specific phenotypes from human pluripotent stem cells by base editors

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2005 - 2006 Post-doctoral Fellow, School of Public Health, Harvard University (PI: Dr. Albert J Fornace)

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Abstract

Despite the great potential of disease modeling using human pluripotent stem cells (hPSCs) derived from patients with mutations, lack of an appropriate isogenic control hinders a precise phenotypic comparison due to the bias arising from the dissimilar genetic backgrounds between the control and diseased hPSCs. Herein, we took advantage of currently available base editors (BEs) to epitomize the isogenic disease model from hPSCs. Using this method, we established multiple isogenic GNE myopathy disease models that harbor point mutations on the *GNE* gene, including four different mutations found in GNE myopathy patients. Four different mutations in the epimerase or kinase domains of *GNE* revealed mutation-specific hyposialylation, which was closely correlated to pathological clinical phenotypes. GNE protein structure modeling based on the mutations, addressed these mutation-specific hyposialylation patterns. Furthermore, treatment with a drug candidate currently under clinical trials showed a mutation-specific drug response in GNE myopathy disease models. These data suggest that derivation of multiple isogenic disease models from hPSCs by using genome editing can enable translationally relevant studies on the pathophysiology of GNE myopathy and drug responses.