DANDRITE
Danish Research Institute of Translational Neuroscience
Nordic EMBL Partnership for Molecular Medicine

Virtual DANDRITE Topical Seminar

Tuesday 24 January 2023
From 10:00 – 11:00 (CET)

Online via zoom
Please write an email to Astrid Munk (asmu@dandrite.au.dk) to obtain link.

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Vice President, Tevard Biosciences
Angel Investor, HyperGuap Group

AAV Gene Therapy in vivo Evolution Using Machine Learning

Parvoviruses are a diverse family of small, non-enveloped DNA viruses such as Adeno-associated virus (AAV). Parvoviruses exhibit broad host specificity (tropism) and have motivated efforts to develop parvoviruses as gene delivery vectors for human gene therapy applications. On-going preclinical and clinical data consistently demonstrates the great potential of these vectors, the in vivo performance of AAV also illustrate the importance of enhancing and restricting transgene expression in desired cell types. Here, we provide an example of the state-of-the-art computational and molecular approaches to create new AAV variants with higher specificity and efficiency of gene transfer for human CNS diseases such as Spinal Muscular Atrophy (SMA). By comparing traditional and novel computation directed evolution approaches, including high-throughput screening of AAV capsid libraries and Machine Learning DNA designs, we highlight one of the latest gene therapy pipeline progress using machine learning designs to optimize SMA gene therapy, which facilitated and accelerated the identification of next-generation, safer and more effective gene therapy compared with Novartis' gene therapy Zolgensma. We demonstrated our next-generation SMA therapy is able to extend the median survival date of the SMNΔ7 mouse model by 5 times longer than previous Novartis' Zolgensma, with only half the AAV dosage. Most importantly, lower dosage immediately provides clinical benefits, such as undetectable DRG tox, and undetectable heart tox, much lower CMC production cost etc. With the exciting progress, we are applying computational designs to facilitate AAV gene therapy in vivo evolution and its application in other disease areas.

Host: Group Leader Keisuke Yonehara, DANDRITE