THE CHINESE UNIVERSITY OF HONG KONG
FACULTY OF MEDICINE
SCHOOL OF BIOMEDICAL SCIENCES

SBS PI Seminar Series 2022-2023

Prof. FENG Bo

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will present a seminar entitled

"AAV-delivered CRISPR Strategies for Gene and Cell Therapy"

Abstract: AAV-delivered CRISPR/Cas9 has shown promising potentials to efficiently insert therapeutic gene sequences in somatic tissues to treat human diseases. We have performed AAV-CRISPR mediated gene knock-in via homology-dependent and independent strategies, under both *in vivo* and *ex vivo* conditions using mouse models. By targeting at *mAlb* 3'UTR, we demonstrated that single dose of AAVs enabled long-term integration and expression of *hF9* transgene in both adult and neonatal hemophilia B mice (*mF9 -/-*), resulting in high levels of circulating hFIX and hemostasis restoration during entire 48-week observation period. Furthermore, we explored liver-specific gene knock-in of hyperactive $hF9^{R338L}$ variant and achieved hemostasis correction with a significantly lower AAV dose. The plasma antibodies against Cas9 and AAV in the neonatal mice receiving low-dose AAV-CRISPR were negligible. Besides *in vivo* targeting, we also explored the potential of *ex vivo* gene editing by targeting the *TRAC* locus in human T cells, and demonstrated simultaneous knock-in of anti-CD19 chimeric antigen receptor (CAR) and knockout of TCR to generate TCR-negative CD19CAR-T cells, which has potentials for allogenic CAR-T therapy to treat patients with acute lymphocytic leukemia. Collectively, our research lent support to the development of AAV-CRISPR mediated gene knock-in strategies for both *in vivo* and *ex vivo* applications for treating human diseases.

22 September 2022, Thursday, 4:00 – 5:00 pm

On-site & via Zoom
G02, Lo Kwee-Seong Integrated Biomedical Sciences Building, Area 39, CUHK
Registration link:
https://cuhk.zoom.us/j/99312556068?pwd=b2tVNWxWdGxiRTNQYXRtYWdJYWZsQT09
Deadline: 12:00 noon, 21 September 2022 (Wed)