Congratulations to IMCB's latest PhD graduate – Hiu Yan LAM

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Supervisors: Professor Vinay Tergaonkar (Institute of Molecular and Cell Biology, A*STAR), Main Supervisor

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Thesis Title: Understanding The Roles of Elks in Mast Cell Functions

Abstract:

The protein ELKS1 (named for its richness in glutamate, leucine, lysine, and serine) mediates regulated exocytosis in neurons and pancreatic β cells, and is also known to be involved in NF-κB signalling in cancer lines *in vitro*. However, how these two potential roles come together in the physiological setting remains unknown. Innate immune mast cell (MC) activation results in rapid degranulation (regulated exocytosis), followed by a late-phase NF-κB-mediated cytokine response, making them the ideal system for dissecting the *in vivo* roles of ELKS1. During my PhD studies, I generated mice lacking ELKS1 in connective tissue MCs (*Elks1f/f Mcpt5-Cre*) and found that, while ELKS1 was dispensable for NF-κB-mediated cytokine production, it was essential for MC degranulation both *in vivo* and *in vitro*. At the molecular level, impaired degranulation was caused by reduced expression of Syntaxin 4 (STX4) and Syntaxin Binding Protein 2 (Stxpb2), resulting from a lack of ELKS1-mediated stabilization of lysine-specific demethylase 2B (Kdm2b). These results reveal that ELKS1 is not involved in NF-κB signalling in MCs, but mediates MC degranulation through a novel mechanism involving transcriptional regulation of key exocytosis proteins.

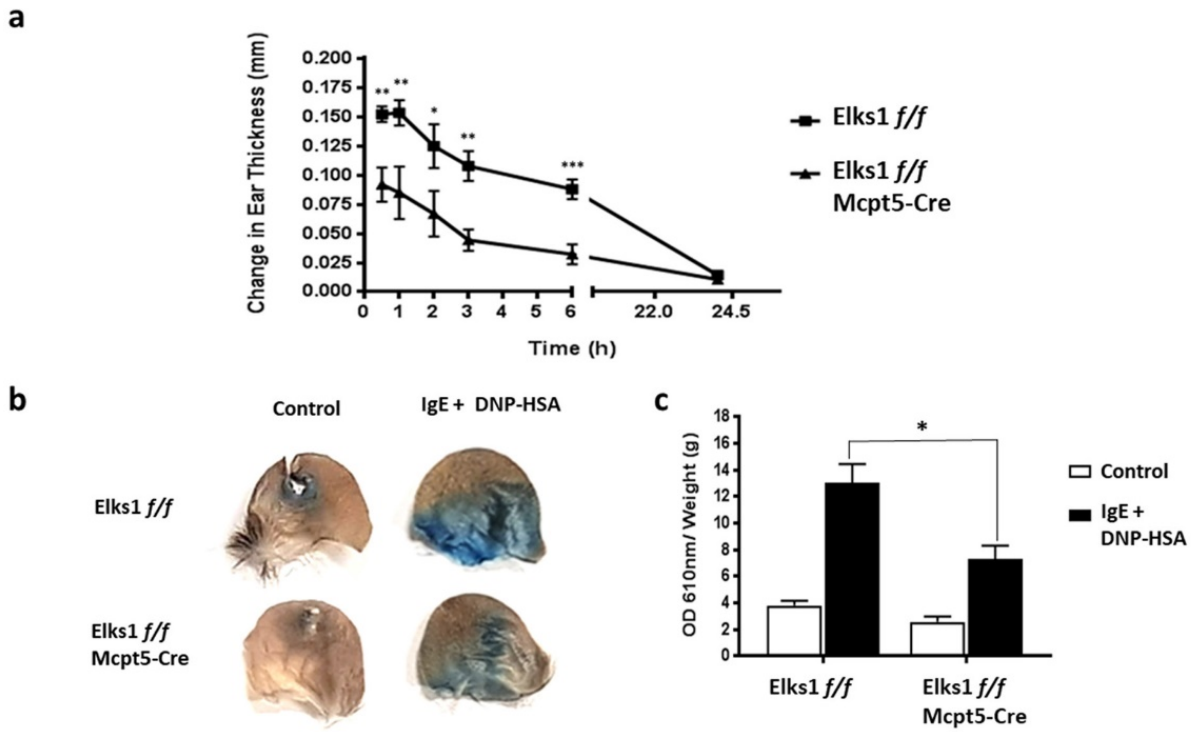

Figure Legend:

a) *Elks1*$^{f/f}$ and *Elks1*$^{f/f}$ *Mcpt5*-Cre mice were injected intradermally with anti-DNP IgE (SPE-7, 100ng) in the right ear pinna, and an equal volume of HEME-Pipes vehicle in the left ear pinna. 16 hours later, DNP-HSA (200µg in 100 µL) was injected intravenously and the increase in ear thickness was recorded at intervals between 0 and 24 hours later. (n=6, *, p<0.05; **, p<0.01; ***, p<0.001)

b) Evans blue dye extravasation from ear of *Elks1*$^{f/f}$ and *Elks1*$^{f/f}$ *Mcpt5*-Cre mice 30minutes after intravenous DNP-HSA (containing 1% Evans blue) administration intravenously. Picture showing ear pinnae of *Elks1*$^{f/f}$ and *Elks1*$^{f/f}$ *Mcpt5*-Cre mice.

c) Evans blue dye extravasation from panel **b** was quantified by O.D. 610nm /weight. (n=3, *p<0.05)

List of publications

1. Lam, H. Y. et al. (2020) 'ELKS1 controls mast cell degranulation by regulating the transcription of Stxbp2 and Syntaxin 4 via Kdm2b stabilization', Science advances. NLM (Medline), 6(31), p. eabb2497. doi: 10.1126/sciadv.abb2497.

2. Lam, H. Y., Tergaonkar, V. and Ahn, K. S. (2020) 'Mechanisms of allergen-specific immunotherapy for allergic rhinitis and food allergies', Bioscience reports. NLM (Medline), 40(4). doi: 10.1042/BSR20200256.