Immunology, lymphocyte development
Functional characterization and physiological significance of SETD3-mediated methylation in immune responses
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Co-supervisor/ Collaborator(s) (if any):

Project Description

a) Background:

We identified SETD3 as one of the lysine methyltransferases with predominate cytoplasmic localization in immune cells. Our preliminary data revealed that the sub-cellular localization of SETD3 is likely to be cell type specific and SETD3 is able to methylate several non-histone substrates in the cytosol. Moreover, the SETD3 expression level was rapidly upregulated in various immune cells upon mitogenic stimulation.

b) Proposed work:

To further characterize SETD3 protein and determine whether SETD3 plays a functional role in immune responses, we propose four complementary Specific Aims, which will make use of biochemical and proteomic approaches, *in vitro* culture systems and *in vivo* conditional knockout mouse models.

Specific Aim 1: To further characterize SETD3 methyltransferase activity and its substrates
Specific Aim 2: To determine functional implications of SETD3-mediated non-histone protein methylation
Specific Aim 3: To determine the role of SETD3 in the activation and effector function of innate immune cells
Specific Aim 4: To determine whether SETD3 is critical for lymphocyte development and function.
Should we complete the proposed aims, our research outcomes will not only extend our understanding of the regulatory networks underlying the lysine methylome, but also aid to explore the prospect of lysine methylation as a novel drug target in the treatment of various human diseases.

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