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DEGREE: Philosophiae Doctor

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AREA OF EXPERTISE: Molecular biology, Biochemistry

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DATE OF DISPUTATION: 10th of March 2017

DISSERTATION TITLE:

"Characterization of Human Lysine-specific Protein Methyltransferases in the METTL21 Subgroup"

Methyltransferases (MTases) are the enzymes that catalyze the transfer of a methyl group from donor to wide variety of substrates. MTases are wide-spread across the different organisms and they play distinct roles in various biological pathways. A recent bioinformatics study indentified 208 MTases encoded by the human genome. It was shown that approximately 30% of these MTases were associated with disorders like cancers and mental disabilities. These MTases belong to several structurally distinct classes such as seven-β-strand and SET-domain.
MTase family 16 (abbreviated MTF16) is a subclass of seven-β-strand consisting ten human members on which we specially focused.

In this study, we have elucidated the functional role of a uncharacterized human member of MTF16 family, METTL21B. We have characterized the METTL21B and demonstrated its orthologs were limited to vertebrates and found that it is localized to cytoplasm and centriole. Further, we have determined that METTL21B specially methylates the eukaryotic elongation factor 1 Alpha (eEF1α), and reported the dynamic nature of this methylation in Balb/c mouse fibroblast exposed to various types of stress and alterations in growth conditions. Also, we found the elevated METTL21B mediated methylation of eEF1α in several cancer derived cells compared to normal rat tissues. In addition, we have tried to elucidate the biological significance of a characterized member of MTF16 family, VCP-KMT. We have also generated *VCPKMT* gene knockout mice and found that VCP-KMT mediated methylation is dispensable for the development and growth of a mouse under unstressed conditions.

Furthermore, we have showed that VCP-KMT is highly specific towards VCP and based on this we have developed the VCP/VCP-KMT pair as a biotechnological tool that can be used as a versatile system to introduce lysine methylation into a desired peptide sequence and to generate combinatorial libraries of methylated peptides.