

HONG KONG RNA CLUB

Seminar



香港城市大學
City University of Hong Kong

27 Apr 2018 (Fri) / 4:30-5:30pm

G5-216, Yeung Kin Man Academic Building (AC1)

City University of Hong Kong

Guest Speaker:

Prof. David Lilley (李大衛)

FRS FRSE FRSC

School of Life Sciences,
University of Dundee



*A structural basis of RNA epigenetics,
and gene regulation by riboswitches*

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A structural basis of RNA epigenetics, and gene regulation by riboswitches

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N⁶-methyladenine is the most widespread modification in mRNA. Using crystallography we show that N⁶-methyladenine disrupts *trans* Hoogsteen-sugar A•G (sheared) basepairs, whereas Watson-Crick pairs are tolerated. A sub-set of human box C/D snoRNA species have target GAC sequences that lead to formation of N⁶-methyladenine at a key sheared A•G basepair, of which half are methylated *in vivo*. Methylation prevents binding of the 15.5 kDa protein and the induced folding of the RNA. Thus the assembly of the box C/D snoRNP could in principle be regulated by RNA methylation at its critical first stage. The human signal recognition particle RNA and many related Alu retrotransposon RNA species are also methylated at N6 of an adenine that forms a sheared basepair with guanine and mediates a key tertiary interaction. N⁶-methylation of adenine may be the basis of a widespread regulatory mechanism in the cell.

Bacterial genes encoding proteins that are involved in guanidine detoxification in bacteria are subject to regulation by riboswitches. Three guanidine riboswitches have been identified. We have solved high resolution crystal structures for the guanidine-II and guanidine-III riboswitches. The former comprises two stem-loops that interact via loop-loop interaction and this creates specific binding pockets for two guanidine molecules. The guanidine-III riboswitch adopts a pseudoknot structure that includes a triple-helix, and a left-handed helical ramp. The riboswitches use the Hoogsteen edge of guanine to hydrogen bond the ligand, together with π -cation interactions.

The SAM riboswitches bind *S*-adenosylmethionine. We have solved the crystal structure of the SAM-V riboswitch, that forms an H-type pseudoknot. The structure explains both the mechanism of translational regulation, and the basis of substrate specificity.

L. Huang, S. Ashraf, J. Wang and D. M. J. Lilley: Control of box C/D snoRNP assembly by N⁶-methylation of adenine *EMBO rep.* **18**, 1631–1645 (2017).

L. Huang, J. Wang and D. M. J. Lilley: The structure of the guanidine-II riboswitch *Cell chem. biol.* **24**, 695–702 (2017).

L. Huang, J. Wang, T.J. Wilson and D. M. J. Lilley: The structure of the guanidine-III riboswitch *Cell chem. biol.* **24**, 1407–1415 (2017).

