Student Talk

Inter-Disciplinary Explorations in Chemistry (I-DEC 2018)

Characterization of Epigenetic Modifications in DNA Duplexes Using Solution-state NMR Spectroscopy

Manjula Jaisal, Dr. Bharathwaj Sathyamoorthy*

Department Chemistry, IISER Bhopal

Bhauri, Bhopal Bypass Road, Bhopal – 462066, Madhya Pradesh, INDIA

(E-mail: manjula16@iiserb.ac.in)

Abstract: Epigenetic modifications add another layer of encoding to DNA. These modifications are hypothesized not to affect the canonical DNA base pairing as they occur primarily on the major groove of the DNA[1]. Commonly occurring such DNA epigenetic modification is methylation on 5th position of cytosine (^{5m}C) that are observed on CpG dinucleotide steps. More recently, oxidized congeners of ^{5m}C, *viz.* 5-hydroxymethyl (^{5hm}C), 5-formyl (^{5f}C) and 5-carboxyl cytosine (^{5ca}C) (Fig 1), are also increasingly being attributed towards such epigenetic roles. These modifications affect the thermodynamic stability and mechanical properties of DNA duplex[1,2,3,5]. Crystallographic studies have pointed towards no perturbation of $^{5m/5hm}$C hemi-modified DNA duplexes, conflicting reports have been emerged recently for triply ^{5f}C modified DNA duplex[3,4]. Computational simulations and single molecule fluorescence experiments provide basis for that the oxidized ^{5m}C modification result in local fluctuations and flexibility[5]. In this study, we use solution state NMR to capture the local dynamics that occur for these modifications and are exploring whether any comparative effect of $^{5m/5hm/5f/5ca}$C modifications exist as such modifications are often observed in "CpG rich" islands. I will be presenting preliminary results that have been acquired thus far that point towards that differences in ring opening rates for these modifications.

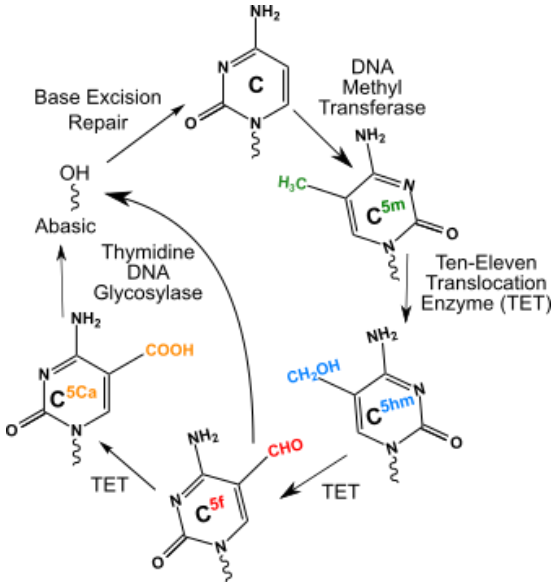

Fig. 1: Methylation and demethylation cycle.

References:

1. Hardwick, J. S.; Lane, A. N.; Brown, T. BioEssays 2018, 40 (3), 1700199
2. Thalhammer A. *et al*., *Chem. Commun*., **2011**, 47, 5325-5327
3. Raiber E. A. *et al., Nat. Struct. Mol. Biol*., **2015**, 22, 44-49
4. Hardwick J. S. *et al., Nat. Struct. Mol. Biol*., **2017**, 24, 544-552
5. (a) Ngo T. T. M. *et al*., *Nat. Commun*., **2016**, 7, 10813 (b) Szulik M. W. *et al*., *Biochemistry*, **2015**, 54, 1294-1305

Student Talk

Inter-Disciplinary Explorations in Chemistry (I-DEC 2018)

Bio-Sketch of Speaker

Ms. Manjula Jaisal
Designation PhD student

Department of Chemistry
Institute Address: Indian Institute of Science Education and Research Bhopal
Contact Number: +91- 9479536625
e-Mail: manjula16@iiserb.ac.in