Krajowa Konferencja Zastosowań Matematyki w Biologii i Medycynie

Jugowice, 11th–15th September 2017

MODELING CYTOSINE METHYLATION AND DEMETHYLATION

Karolina Kurasz[1], Dorota Hudy[1], Magdalena Skonieczna[1], Ewelina Zarakowska[2], Krzysztof Fujarewicz[1], Joanna Rzeszowska-Wolny[1]

[1]Silesian University of Technology
Akademicka 16, 44-100 Gliwice, Poland
[2]Department of Clinical Biochemistry, Faculty of Pharmacy,
Collegium Medicum in Bydgoszcz,
Nicolaus Copernicus University in Toruń,
Karlowicza 24, 85-092 Bydgoszcz, Poland
[1]karolina.kurasz@polsl.pl

ABSTRACT

Recent discovery of the TET family proteins, capable of converting 5-methylcytosine (5-mC) to 5-hydroxymethylcytosine (5-hmC), has allowed the description of the pathway of demethylation of DNA. The aim of this study is to propose a mathematical model of methylation and demethylation of cytosine forms and parameter estimation of the model based on biological experiments. Selection of the model structures aims to clarify which TET proteins are involved in further oxidation steps that modify 5-hydroxymethylcytosine first to 5-formylcythosine (5-fC) and then to 5-carboxylcythosine (5-caC).

ACKNOWLEDGMENTS

This work was funded by the Silesian University of Technology under grant BKM/506/RAU1/2016/11 (KK) and by Polish National Science Centre under grant DEC-2012/04/A/ST7/00353 (KF).

REFERENCES

[1] Jones P.A. *Functions of DNA methylation: Islands, start sites, gene bodies and beyond*. Nat. Rev. Genet. 2012;13:484–492.
[2] Ito S., Shen L., Dai Q., Wu S.C., Collins L.B., Swenberg J.A., He C., Zhang Y. *Tet proteins can convert 5-methylcytosine to 5-formylcytosine and 5-carboxylcytosine*. Science. 2011;333:1300–1303. doi: 10.1126/science.1210597.
[3] Cortellino S. et al.; *Thymine DNA Glycosylase is Essential for Active DNA Demethylation by Linked Deamination - Base Excision Repair*; Cell 2011; 146(1):67-79.
[4] Klungland A., Robertson A.B., *Oxidized C5-methyl cytosine bases in DNA: 5-hydroxymethylcytosine; 5-formylcytosine; and 5-carboxycytosine*, Free Radic. Biol. Med. 2017; 107: 62-68.
[5] Modrzejewska M., Gawronski M., Skonieczna M., Zarakowska E., Starczak M., Foksinski M., Rzeszowska-Wolny J, Gackowski D., Olinski R., *Vitamin C enhances substantially formation of 5-hydroxymethyluracil in cellular DNA*, Free Radic. Biol. Med. 2016; 101: 378-383.
[6] Lawson, C.L. and R.J. Hanson, *Solving Least Squares Problems*, Prentice-Hall, 1974, Chapter 23, p. 161.
[7] Krokan H.E., Drablos F., Slupphaug G., *Uracil in DNA – occurrence, consequences and repair*, Oncogene 2002; 21(58):8935-8948.
[8] Branco MR, Ficz G, Reik W: *Uncovering the role of 5-hydroxymethylcytosine in the epigenome*. Nat Rev Genet 2012;13: 7-13
[9] S Glowacki, Janusz Błasiak.: *Rola 5-hydroxymatylocytozyny i białek Tet w epigenetycznej regulacji ekspresji genów.* Postępy Biochemii 2013;49: 0032-5422: 64-69

[10] Kramer M., Serpa C., Szurko A., Widel M., Sochanik A., Snietura M., Kus P., Nunes R.M, Arnaut L.G., Ratuszna A.: *Spectroscopic properties and photodynamic effects of new lipophilic porphyrin derivatives: efficacy, localization and cell death pathways*. J. Photochem. Photobiol. B; 2006; 84: 1-14