Mathematical Modeling of Cytosine Demethylation

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In living cells, some reactions can be conducted by more than one enzyme and sometimes it is difficult to establish which enzyme is responsible. Such is the case with proteins from the TET family, capable of converting 5-methyl-2'-deoxycytidine (5-mdC) in DNA to 5-(hydroxymethyl)-2'-deoxycytidine (5-$hmdC$) and further to 5-formyl-2'-deoxycytidine (5-fdC) and 5-carboxy-2'-deoxycytidine (5-$cadC$). The estimation of the efficiency of particular TETs in particular oxidative reactions and different cell types is important but experimentally difficult. The article [1] proposes an original mathematical model of cytosine methylation and demethylation. Experimental data for five cell lines were used to calibrate the model. Instead of building five different models for each cell line, we assumed that similar cytosine transformation mechanisms govern all the cell lines and that differences in the levels of different forms of cytosine are due to different enzyme levels. In particular, we focused on the role of different forms of the TET enzyme at different stages of cytosine transformation. Using one common data set to estimate model parameters allowed us to examine which of the 343 possible model structures has the best generalization ability. The analysis of the best structures allowed us to answer the question about the probable participation of different forms of the TET enzyme at different stages of cytosine transformation. Some of our conclusions have been confirmed in the available literature, some are new.

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References

[1] K. Kurasz, J. Rzeszowska-Wolny, R. Oliński, M. Foksiński and K. Fujarewicz, *The Role of Different TET Proteins in Cytosine Demethylation Revealed by Mathematical Modeling*, Epigenomes, 8(2): 18, `https://doi.org/10.3390/epigenomes8020018` (2024)

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