【Abstract of 2011 Grant - in - Aid for Scientific Research on Innovative Areas (Research in a proposed research area)】

Biological Science

Title of Project : Crosstalk of transcriptional control and energy pathways by hub metabolites

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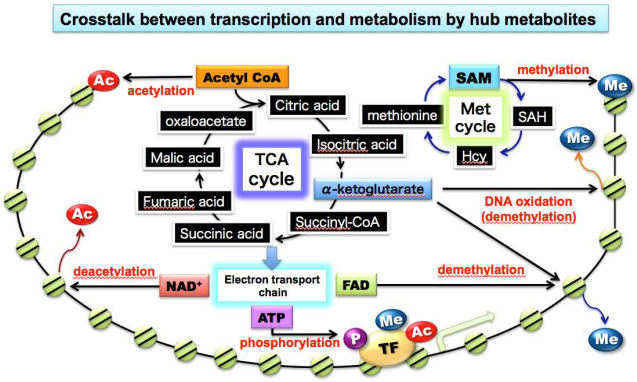
【Purpose of the Research Project】

Gene expression is controlled by transcriptional environments that are formed by the genomic information encoded by DNA; DNA methylation; epigenomic information regulated by chromatin modifications such as phosphorylation, acetylation, and methylation of histones; and the effect of transcription factors. These transcriptional environments are deeply involved in a variety of cell functions such as the establishment of cell specific identity, cell proliferation, and differentiation coupled with signal pathways and intranuclear complexes. On the other hand, cell metabolism is dynamically regulated by cell proliferation conditions and differentiation steps; thus, it enables the maintenance of homeostasis and the transition into a new steady state. In this case, some metabolites (hub metabolites; ATP, SAM, and so on) such as those generated by glycolysis, the TCA cycle, and the methionine cycle, are utilized in the formation of transcriptional environments.

Therefore, we aim to understand the effect of transcriptional environments on metabolism or the effect of metabolic changes induced by the stimulation of cells as well as internal and external stimulation of individuals on the construction of transcriptional environments.



【Content of the Research Project】

Research in transcription and metabolism has greatly progressed independently; however, a research field that encompasses transcription and metabolism fields and links them to a vital function has not been established. Complex network and transcription-metabolism systems relating to the expression of target genes are investigated by focusing on mechanisms such as “writing” by modification transferase, “reading” of modifications by adaptor factors, “erasing” by demodification enzymes, and “rewriting” by chromatin repair, in order to understand the crosstalk control between the formation of transcriptional environments and energy metabolism.

【Expected Research Achievements and Scientific Significance】

It has been shown the analyses of genomic predisposition (genetic alteration) contribute greatly to resolving of the pathogenic mechanism of diseases depending on gene mutations. Recently, a new concept has been proposed wherein a change in the transcriptional environment, not accompanied by DNA mutation, widely associates with the onset of diseases involved in nutrition and energy metabolism as well as functions as an epigenomic predisposition (epimutation). Thus, focusing on the crosstalk between transcriptional environments and energy metabolism may elucidate a new molecular mechanism in the maintenance of homeostasis, stress response, and signaling. Furthermore, it will contribute to the understanding of the cause of diseases such as metabolic diseases and cancer and validation of therapeutic targets.

【Key Words】

Hub metabolites: Functional small molecules produced from a variety of metabolic pathways.
Epigenome: The state of chromatin modification in specified cells.

【Term of Project】

FY2011-2015

【Budget Allocation】

1,146,200 Thousand Yen

【Homepage Address and Other Contact Information】

http://tmsystem.tara.tsukuba.ac.jp/