Title	A Novel Method to Investigate the Influence of H3K9-methylated Heterochromatin on Genetic Mutations [an abstract of dissertation and a summary of dissertation review]
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Degree Grantor	北海道大学
Degree Name	博士(総合化学)
Dissertation Number	甲第16137号
Issue Date	2024-09-25
Doc URL	https://hdl.handle.net/2115/93464
Rights(URL)	https://creativecommons.org/licenses/by/4.0/
Type	doctoral thesis
File Information	Ola_Mahmoud_abstract.pdf, 論文内容の要旨

学位論文内容の要旨

博士の専攻分野の名称　博士（理学）　氏　名　Ola Mahmoud Ibrahim Abdalla

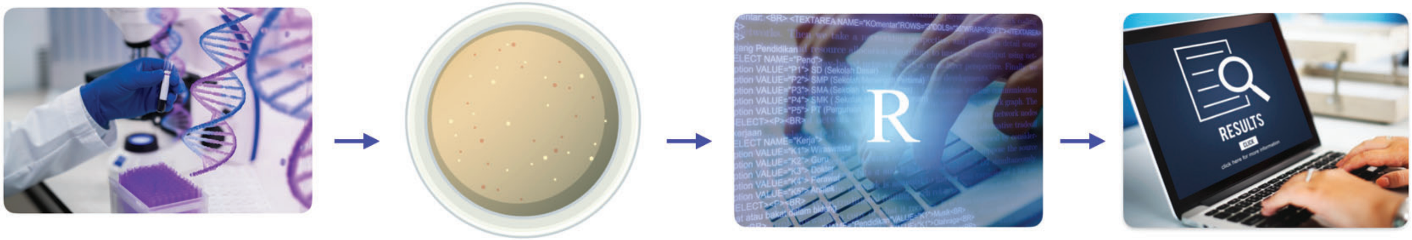
学位論文題名

A Novel Method to Investigate the Influence of H3K9-methylated Heterochromatin on Genetic Mutations

(遺伝子変異に対するH3K9メチル化ヘテロクロマチンの影響を調査する新しい方法)

Genetic variation, driven by mutations, plays a crucial role in the evolution of species and the development of cancer. The mutation rate varies across the genome and can be influenced by chromatin organization and other factors. However, the relationship between chromatin organization and mutation rates has yet to be fully understood. One modification that affects chromatin organization is the methylation of histone H3 at lysine 9. This modification creates heterochromatin, which represses transcription in euchromatin and maintains genome stability, which is essential for the organism's survival. This research has two significant objectives. Firstly, it aims to investigate the impact of H3K9 methylation alone on mutation rates in fission yeast without considering other histone markers. This groundbreaking research method uses fluctuation assays and tetracycline-activated genes to estimate mutation rates accurately and precisely on a single gene under two different conditions in a single experiment using only one isogenic clone. Secondly, this research seeks to

solve the problem of statistically calculating mutation events and their 95% confidence intervals using the most accurate method, "Ma–Sandri–Sarkar Maximum Likelihood " (Figure. 1). The results suggest that the H3K9me markers can increase the phenotypic mutation rate of a single gene. Moreover, this study presents an R-code that uses the non-recursive version of the MSS likelihood to statistically analyze the genetic data efficiently and avoid software-related issues. The significance of the research goes beyond the results themselves. The genetic assay and R-code utilized in this study have the potential to be used as powerful tools by future scientists to investigate the organization of chromatin and its influence on mutation rates. This could lead to significant breakthroughs in genetic mutation research, cancer, and evolutionary biology while paving the way for life-saving treatments.



Conducting Fluctuation assays experiments at the Laboratory

Counting the number of mutant *r* or colonies on selective media after the experiments

Using this study's R-code to statistically analyze the number of mutants *r* by R software

Getting the results with 95% confidence Intervals within few minutes

Figure 1. The Second Research Purpose. It is vital to provide an easy and user-friendly statistical analysis method for upcoming scientific researchers to analyze fluctuation assay results.