【Grant-in-Aid for Scientific Research (S)】

Science and Engineering (Chemistry)

Title of Project : Regulation and mechanistic investigation of gene expression by artificial genetic switches

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Research Project Number : 16H06356 Researcher Number : 50183843
Research Area : Chemical Biology
Keyword : Gene Regulation, DNA nanostructure, Functional Py-Im polyamide conjugates

【Purpose and Background of the Research】

This study elucidates a mechanism of the epigenetic gene regulation by our original chemical biology approach.

Principally, for the somatic cell reprogramming and pluripotent stem cell differentiation, we supplement an epigenetic gene activation function to sequence-specific DNA-binding Py-Im polyamide. Successively, we establish a direct imaging technology to visualize key dynamic modifications in nucleosome structures corresponding to gene expression at a single molecule level.

Using these two distinct chemical biology approaches, we push forward the coordinating research like two wheels to elucidate the mechanism of epigenetic gene regulation and to progress the concept of artificial gene switch.

【Research Methods】

In our research, it is important to uncover molecular mechanism and dynamic structural changes associated with gene expression.

1) To develop functional Py-Im polyamide conjugates for inducing cell reprogramming from the human somatic cell through epigenetic gene regulation.
2) To develop functional Py-Im polyamide conjugates for precise epigenetically controlled human iPS cell differentiation.

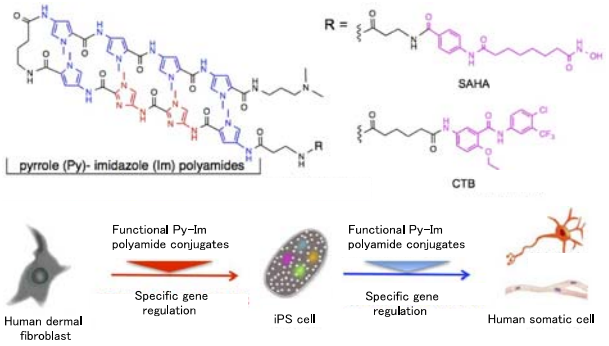

Figure 1. The structure and concept of functional Py-Im polyamide conjugates

3) To regulate gene expression by targeting molecules that alters G-quadruplex or triplex structures.
4) To visualize biological molecular motions and states by direct imaging technology using AFM.
5) To clarify the mechanism related to gene regulation by the analysis of nucleosome adaptations and related functions.

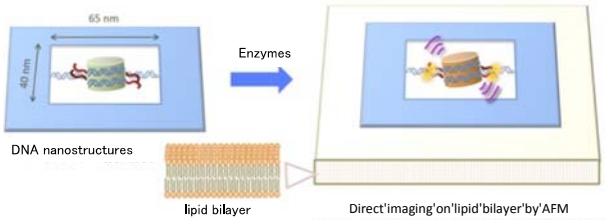

Figure 2. The concept of single molecular analysis of nucleosome using DNA nanostructures

【Expected Research Achievements and Scientific Significance】

Successful development of our coordinated approaches will lead to innovative therapy for refractory congenital gene diseases and cancer. Furthermore, we reveal mechanistic details of epigenetic control of gene expression using *D*NA nanostructure-based direct imaging technique, which in turn will advance this technology.

【Publications Relevant to the Project】

- Suzuki, Y.; Endo, M.; Sugiyama, H. *et al.*, *Nature Commun.*, **2015**, *6*, 8052.
- Suzuki, Y.; Endo, M.; Sugiyama, H. *et al.*, *J. Am. Chem. Soc.* **2014**, *136*, 211-218.
- Pandian, G. N.; Taniguchi, J.; Sugiyama, H. *et al.*, *Sci. Rep.* **2014**, *4*, 3843.
- Han, L.; Pandian, G. N.; Sugiyama, H. *et al.*, *Angew. Chem. Int. Ed.* **2013**, *52*, 13410-13413.

【Term of Project】 FY2016-2020

【Budget Allocation】 133,700 Thousand Yen

【Homepage Address and Other Contact Information】

http://kuchem.kyoto-u.ac.jp/chembio/