

Target search process of a tumor suppressor p53 revealed by single-molecule fluorescence microscopy

Kiyoto Kamagata

(Institute for Multidisciplinary Research for Advanced Materials, Tohoku University)

e-mail: kamagata@tagen.tohoku.ac.jp

Transcription factors can search and bind specific target sites of DNA, which is the initial stage of transcriptional regulation of target genes. These proteins are considered to have an efficient mechanism that can search the target sites among a huge DNA with 10^9 bps within a physiological time. However, the detailed mechanism based on the dynamics of these proteins on DNA remains unclear. To solve the target search problem of DNA binding proteins, we considered to apply our background in single-molecule measurements [1]. In this study, we investigated the target search dynamics of tumor suppressor protein p53, which is a human transcription factor that controls cell cycle arrest, apoptosis and DNA repair, by using the single-molecule measurement. To examine how dynamics p53 shows in moving along

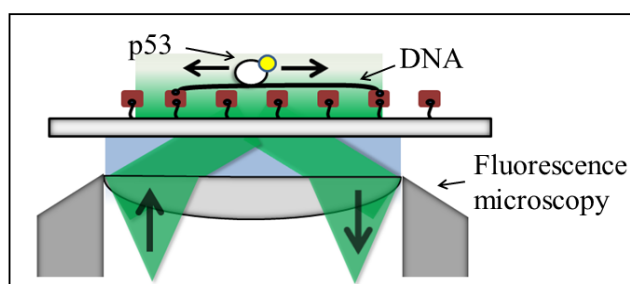


Fig. 1 Single-molecule fluorescence microscopy for detecting 1D sliding motion of p53 along DNA

DNA and reading the sequence, we observed the diffusive movement of p53 labeled with a fluorescent dye along the extended DNA on coverslip by a home-build fluorescence microscopy (Fig. 1). We found that p53 possesses multiple sliding modes and hopping dynamics. Mutations which activate and inactivate the function of p53 modify the sliding dynamics, which might partly alter the activity of p53. Furthermore, we examine how efficiently p53 can recognize the target site and whether p53 can transfer from a segment of DNA to the other segment without dissociating from DNA. These results will be presented.

References

- 1) *Proc. Natl. Acad. Sci. USA*, **104**, 10453-10458 (2007), *J. Am. Chem. Soc.*, **134**, 11525-11532, (2012), *Sci. Rep.*, **3**, 2151, (2013).