セミナーのご案内

日　程：　平成２５年１０月２５日（金）　15：30 –17：00

会　場：　J232講義室（すずかけ台キャンパス）

講　師：　Prof. Rodney Rothstein

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Chromosome mobility during double-strand break repair

Using high-resolution 4D tracking, pioneered by the Sedat lab in the mid-90's (Marshall *et al.* 1997), we showed that chromosomal loci in diploid budding yeast cells show an increase in chromosome mobility after DNA damage (Miné-Hattab & Rothstein, 2012). In our initial analysis, we concluded that the broken chromosome explores a more than 10 times larger nuclear volume compared with that seen in the absence of DSBs. In addition, we found that the increased mobility is general, as the dynamics of the unbroken chromosomes also increases depending on the number of DSBs. We also observed the pairing of the homologous chromosomes in real time, and once started, it takes approximately 20 minutes before the loci separate again. This separation is associated with the disassembly of the repair center. We have measured the mobility of the repair complex and find that it explores less space than even the undamaged loci. Recently, we have begun to combine ultra fast *in vivo* imaging with analytical tools applicable for diffusion-controlled reaction processes. Our new studies provide additional insight into the nature of DNA motion in the context of DNA repair. We have established a link between the increased mobility of DNA and how DNA explores the nuclear space. For example, after DNA damage, we find that a locus explores the nuclear space more efficiently allowing it to reach further potential targets, suggesting that the increase in chromosomal mobility likely facilitates the search for homology (Miné-Hattab & Rothstein, 2013).

The studies described above were performed in diploid S phase cells. We find that undamaged chromosomal loci in diploid G1 cells sample space similarly to that seen in S phase. Interestingly, after DNA damage, the chromosomes in G1 phase repeatedly resample the same space, but at an increased rate allowing the locus to explore a slightly larger nuclear volume. This exploration likely depends upon resection and checkpoint activation since caffeine treatment abrogates the increased movement. Importantly, the nature of the exploration in G1 phase differs from that observed in S phase cells. We suspect that the difference is related to the function of the recombination machinery. Experiments are in progress to test this notion.

References:

Marshall, W. F. et al. Interphase chromosomes undergo constrained diffusional motion in living cells. Curr. Biol. ***7***: 930-939 (1997).

Miné-Hattab, J. and Rothstein, R. Increased chromosome mobility facilitates homology search during recombination. Nature Cell Biol., ***14***: 510–517 (2012).

Miné-Hattab, J. and Rothstein, R. DNA in motion during double-strand break repair. Trends in Cell Biol., *in press*, (2013).

Prof. Rothsteinは酵母分子遺伝学のパイオニア的研究者で、現在もフロントランナーとして活躍されております。
今回の来日を機に、最新の研究成果をお話ししていただくことになりました。皆様、是非ご参加ください。

＜問合せ先＞　生体システム専攻　岩崎研究室（内線：5105）