1 大学院学生各位
To All Graduate Students

2024 年度

基盤医学特論 開講通知

Information on Special Lecture Tokuron 2024.4-2025.3

日時：令和 6 年 11 月 15 日(金) 16 時 00 分より (90 分)
Time and Date: November 15 (Fri.), 2024 16：00～ (90 minutes)

場所：環境医学研究所 北館セミナー室
Room: N-201 (Seminar Room), North Building, Research Institute of Environmental Medicine (Higashiyama Campus)

言語： 英語
Language: English

Lecture 1

Title: A single PAF1C subunit directs RNA polymerase II from elongation to transcription-coupled DNA repair by stabilizing CSB

Teaching Staff: Associate Professor, Martijn S. Luijsterburg, Department of Human Genetics, Leiden University Medical Center (LUMC)

Abstract: Transcription elongation factors associate with RNA polymerase II (RNAPII) to facilitate its progression along the DNA template. However, transcription stalls at sites of DNA damage, initiating a transcription-coupled repair (TCR) response mediated by the Cockayne Syndrome B (CSB) protein. The mechanisms underlying the switch from elongation to DNA repair remain unclear. Here, we identify that the PAF1 elongation complex (PAF1C) interacts with CSB on arrested RNAPII. All five core PAF1C subunits (PAF1, LEO1, CTR9, CDC73, and SKI8) are required to resume transcription following UV irradiation, with PAF1C operating downstream of DNA repair to restart transcription. Interestingly, we find that PAF1C also has a repair-specific function via its non-essential subunit, LEO1. Loss of LEO1 impairs CSB binding to damaged RNAPII, indicating its role in switching RNAPII from elongation to repair. Together, our findings suggest that LEO1 travels with elongating RNAPII but transitions to a TCR factor at DNA damage sites by stabilizing CSB.

Lecture 2

Title: STK19 facilitates the clearance of lesion-stalled RNA polymerase II during transcription-coupled DNA repair

Teaching Staff: Staff scientist, Diana van den Heuvel, Department of Human Genetics, Leiden University Medical Center (LUMC)

Abstract: Transcription-coupled DNA repair (TCR) removes bulky DNA lesions impeding RNA polymerase II (RNAPII) transcription. Recent studies have outlined the stepwise assembly of TCR factors CSB, CSA, UVSSA, and TFIIH around lesion-stalled RNAPII. However, the mechanism and factors required for the transition to downstream repair steps, including RNAPII removal to provide repair proteins access to the DNA lesion, remain unclear. Here, we identify STK19 as a new TCR factor facilitating this transition. Loss of STK19 does not impact initial TCR complex assembly or RNAPII ubiquitylation but delays lesion-stalled RNAPII clearance, thereby interfering with the downstream repair reaction. Cryo-EM and mutational analysis reveal that STK19 associates with the TCR complex, positioning itself between RNAPII, UVSSA, and CSA. The structural insights and molecular modeling suggest that STK19 positions the ATPase subunits of TFIIH onto DNA in front of RNAPII. Together, these findings provide new insights into the factors and mechanisms required for TCR.

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(事前の申込みは不要です。No Registration Required.)

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