

IMSUT International Joint Usage/Research Center
International Project-completion Report (FY2022 ver.)

Date of submission: **Month / Date / Year**

| | |
|---|--|
| Principal Investigator | Position, Institution: Professor, Ajou University School of Medicine |
| | Name: Hyeseong Cho |
| IMSUT Host Researcher | Division: Cancer Cell Biology |
| | Name: Makoto Nakanishi |
| Project Title | Elucidation of mechanisms underlying eukaryotic DNA repair and transcription |
| Duration | From 04/01/2022 to 03/31/2023 *Please enter the entire research period. |
| Project Members *Please enter all of your project members, including IMSUT members. | |
| Name | Position, Institution |
| Hyeseong Cho | Professor, Ajou University School of Medicine |
| Chang-Woo Lee | Professor, Sungkyunkwan University School of Medicine |
| Ho Chul Kang | Assistant Professor, Ajou University School of Medicine |
| Youngsoo Lee | Assistant Professor, Ajou University School of Medicine |
| Makoto Nakanishi | Professor, IMSUT, University of Tokyo |
| Toru Hirota | Head, Cancer Institute of the Japanese Foundation for Cancer Research |
| Project-completion Report on achievements/progress through the entire project period | |

DNA lesions impact on local transcription and the damage-induced transcriptional repression facilitates efficient DNA repair. However, how chromatin dynamics cooperates with these two events remained largely unknown. We here show that histone H2A acetylation at K118 is enriched in transcriptionally active regions. Under DNA damage, the RSF1 chromatin remodeling factor recruits HDAC1 to DSB sites. The RSF1-HDAC1 complex induces the deacetylation of H2A(X)-K118 and its deacetylation is indispensable for the ubiquitination of histone H2A at K119. Accordingly, the acetylation mimetic H2A-K118Q suppressed the H2A-K119ub level, perturbing the transcriptional repression at DNA lesions. Intriguingly, deacetylation of H2AX at K118 also licenses the propagation of γ H2AX and recruitment of MDC1. Consequently, the H2AX-K118Q limits DNA repair. Together, the RSF1-HDAC1 complex controls the traffic of the DNA damage response and transcription simultaneously in transcriptionally active chromatin. The interplay between chromatin remodelers and histone modifiers highlights the importance of chromatin versatility in the maintenance of genome integrity.

Research Results from the Project during FY2022

<Publications>

None

<Patent Applications>

None

Days of visits to IMSUT during FY2022

*Please include visits without travel allowances.

*If the project members could not visit IMSUT due to the pandemic of COVID-19 during FY2022, please present how many days in total your project has held online meetings, discussions via e-mail or communication tools such as Slack, etc. among your project members since April 1st, 2022.

*For the "Sex" and "Age" sections, the information shall be used only for statistical purposes.

*Please select the age range based on the age at the end of FY2022.

| Name | Position, Institution | Sex | Age | Visits to IMSUT (Days) |
|--------------|----------------------------|-------------|-------------|------------------------|
| Hyeseong Cho | Professor, Ajou University | Female | 40 or older | 5 times via Zoom |
| | | Pull-down ▼ | Pull-down ▼ | |
| | | Pull-down ▼ | Pull-down ▼ | |
| | | Pull-down ▼ | Pull-down ▼ | |
| Name | Position, Institution | Sex | Age | Online Meetings (Days) |

| | | | | |
|-------------|------------------------------|-------------|-------------|---|
| | | Pull-down ▼ | Pull-down ▼ | |
| | | Pull-down ▼ | Pull-down ▼ | |
| | | Pull-down ▼ | Pull-down ▼ | |
| | | Pull-down ▼ | Pull-down ▼ | |
| Name | Position, Institution | Sex | Age | Discussions via E-mail, Slack, etc. (Days) |
| | | Pull-down ▼ | Pull-down ▼ | |
| | | Pull-down ▼ | Pull-down ▼ | |
| | | Pull-down ▼ | Pull-down ▼ | |
| | | Pull-down ▼ | Pull-down ▼ | |

Usage of Facilities/Equipment during FY2022

*Please enter '0' or 'N/A' if you have not used any facilities.

*For this fiscal year only, if the project members could not visit IMSUT due to the pandemic of COVID-19, please include the uses by IMSUT faculty members to conduct this joint research project.

| Name of Facility | Equipment | Number of Use (Times) | Usage time (Hours) |
|---------------------------------------|--|-----------------------|--------------------|
| FACS Core Laboratory | e.g.) FACS Aria (BD) | 0 | 0 |
| Medical Proteomics Laboratory | e.g.) Orbitrap QSTAR Elite | 0 | 0 |
| Imaging Core Laboratory | e.g.) Zeiss Multiphoton Microscopy (LSM710NLO) | 0 | 0 |
| Gene Manipulated Mouse Section | Creation and cryopreservation embryo of Knockout mouse | 0 | 0 |
| Human Genome Center | Supercomputer | 0 | 0 |
| Amami Laboratory of Injurious Animals | Experimental lab | 0 | 0 |
| Other | | 0 | 0 |

Usage of Scientific Resources *Please enter '0' or 'N/A' if you have not used any.

| Name of Scientific Resource | Number of Samples/Lines |
|-----------------------------|-------------------------|
| Serum (BioBank Japan) | 0 |
| DNA (BioBank Japan) | 0 |

| | |
|---|----------------------------------|
| Knockout mouse | 1 |
| Pathogenic bacteria | 0 |
| Other | 0 |
| Usage of Database *Please enter '0' or 'N/A' if you have not used any. | |
| Name of Database | Number of Use (Times) |
| | |
| | |