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(Form 2)

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Report

We are once again grateful to IMSUT for supporting our collaborative research with Drs. Atsuya Nishiyama and Makoto Nakanishi.

Thanks to this generous support, I had the opportunity to visit IMSUT in February 2025. During the visit, I gave a formal seminar and engaged in in-depth discussions with Dr. Nishiyama and members of his group. These exchanges significantly advanced our joint investigation into the molecular coordination between DNA replication and epigenome maintenance, with a particular focus on the regulatory functions of UHRF1.

Our current work has led to the identification of a novel role for UHRF1 in the ubiquitylation of PCNA, a key sliding clamp protein involved in DNA replication. Together with Dr. Nishiyama's team, we are working to elucidate the molecular basis of this activity. Specifically, we are focusing on two putative PCNA-interaction motifs in UHRF1—the PIP-box and the APIM motif—and have generated corresponding mutant constructs. These are being analyzed in parallel using two complementary systems: Xenopus egg extracts provided by Dr. Nishiyama's laboratory, and UHRF1-AID degron cell lines established in our lab.

This collaboration is enabling us to explore how UHRF1 contributes to replication-coupled chromatin regulation through PCNA ubiquitylation. The combined biochemical and cellular approaches promise to yield important mechanistic insights.

We thank IMSUT and Professor Nakanishi again for their generous and ongoing support, which continues to f acilitate impactful collaborative research.