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Department for BioMedical Research

Prize for Best DBMR Publication 2024

The prize is awarded in recognition of an outstanding publication published during the 2024 calendar year led by an investigator from the DBMR.

Best DBMR Publication 2024

At the DBMR Day of BioMedical Research 2025 on July 2 2025, it was announced that the winner of the Best DBMR Publication 2024 was:

Dr. Noëlle Dommann

Department for BioMedical Research
Systems Biomedicine of Cellular Development and Signaling in Health and Disease

For the paper *In vivo DNA replication dynamics unveil aging-dependent replication stress, Cell* 187,6220–623 (2024). DOI: 10.1016/j.cell.2024.08.034

The accumulation of mutations in DNA is often used to explain the aging process, but it remains one of many hypotheses. In our study, we reveal a fundamental aging-dependent replication stress mechanism that explains why some organs age faster than others. By analyzing DNA replication initiation dynamics in regenerating livers of young and old mice, we found that although replication origins remain conserved with age, their firing becomes inefficient, triggering a replication stress response.

Our findings highlight that hidden damage in non-coding DNA, which accumulates over time in slowly proliferating liver tissue, remains undetected until cells attempt to divide.

Unlike in rapidly regenerating tissues, such as the skin and intestine, where frequent replication helps repair damage, the liver experiences prolonged exposure to these cryptic DNA lesions, ultimately impairing cell division in aged animals.

Using ATR checkpoint kinase inhibitors, we were able to restore origin firing efficiency in aged livers. However, this rescue came at a cost: increased inflammatory responses, without significantly enhancing liver cell proliferation. These findings suggest that aging-dependent replication stress, rather than DNA sequence damage alone, plays a crucial role in organ aging and that targeting ATR could be a double-edged sword in regenerative medicine.

This discovery challenges existing models of aging and opens new research avenues for therapeutic strategies. By linking genomic stability, cellular replication stress, and inflammation, our work offers a novel framework for understanding aging at an organ-specific level. Future studies may explore targeted DNA repair to slow down aging in slow-proliferating tissues.

The DBMR congratulates Dr. Dommann for the award and all co-authors for the excellent publication!