



Weill Cornell Medicine

Single-Cell Platform for Mapping DNA Damage in Disease and Aging

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Single-Cell Platform for Mapping DNA Damage in Disease and Aging

Background & Unmet Need

- DNA damage is a critical factor in cellular aging and disease, but current technologies can only measure damage across bulk cell populations
- Single-cell approaches have revolutionized our understanding of cell-specific molecular programs but mapping DNA damage at single-cell level has remained challenging
- The stochastic nature of DNA damage formation complicates investigation of its relationship with other cellular functions
- **Unmet Need:** Methods that can simultaneously map DNA damage and gene expression at single-cell resolution to understand how DNA damage impacts cellular function

Technology Overview

- **The Technology:** A high-throughput method, termed Paired-Damage-seq, that enables simultaneous mapping of oxidative & ssDNA damage with transcriptomes at single-cell resolution
- The "labeling-by-repair" approach uses DNA repair proteins to remove existing DNA damage sites, followed by incorporation of biotin-modified dUTPs at the damaged sites
- The method combines Paired-Tag RNA sequencing with split-pool barcoding to enable high-throughput analysis of hundreds of thousands to million of cells
- **PoC Data:** Validated in HeLa cells with strong agreement to existing bulk methods, showing 87% correspondence with RNA-seq and 72% similarity to CLAPS-seq DNA damage profiles
- Successfully applied to mouse brain tissue demonstrating cell-type specific damage patterns
- Demonstrated connection between DNA damage accumulation and epigenetic information loss

Inventors:

Chenxu Zhu
Dongsheng Bai

Patents:

[PCT Application Filed](#)

Publications:

[Bai et al. Nat Methods.](#)
2025.

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Technology Applications

- Screen chemical compounds to identify promising drug candidates
- Identify and validate therapeutic targets to develop cell-specific treatments based on DNA damage patterns
- Facilitate biomarker discovery for diseases associated with DNA damage and repair deficiencies

Technology Advantages

- Simultaneously measures DNA damage and gene expression at single-cell resolution
- High-throughput capability at single-cell resolution
- Seamless integration with existing sequencing workflows and screening platforms

Supporting Data / Figures

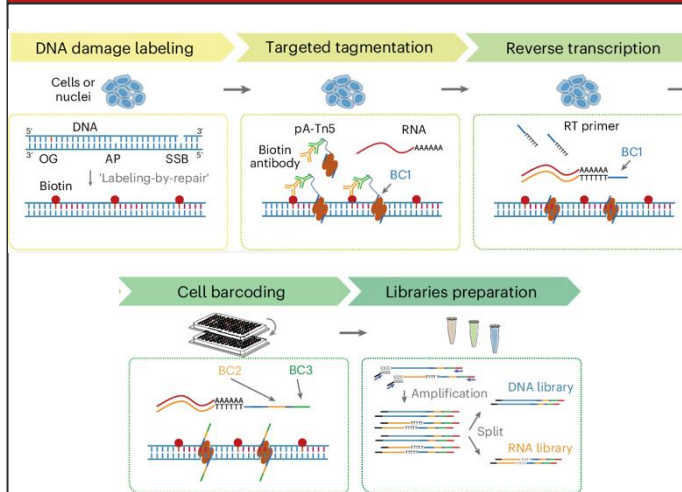


Figure 1: Schematic of the Paired-Damage-seq workflow with the 'Labeling-by-repair' strategy to label damage sites. OG, 8-oxoguanine; AP, apyrimidinic site; RT, reverse transcription.

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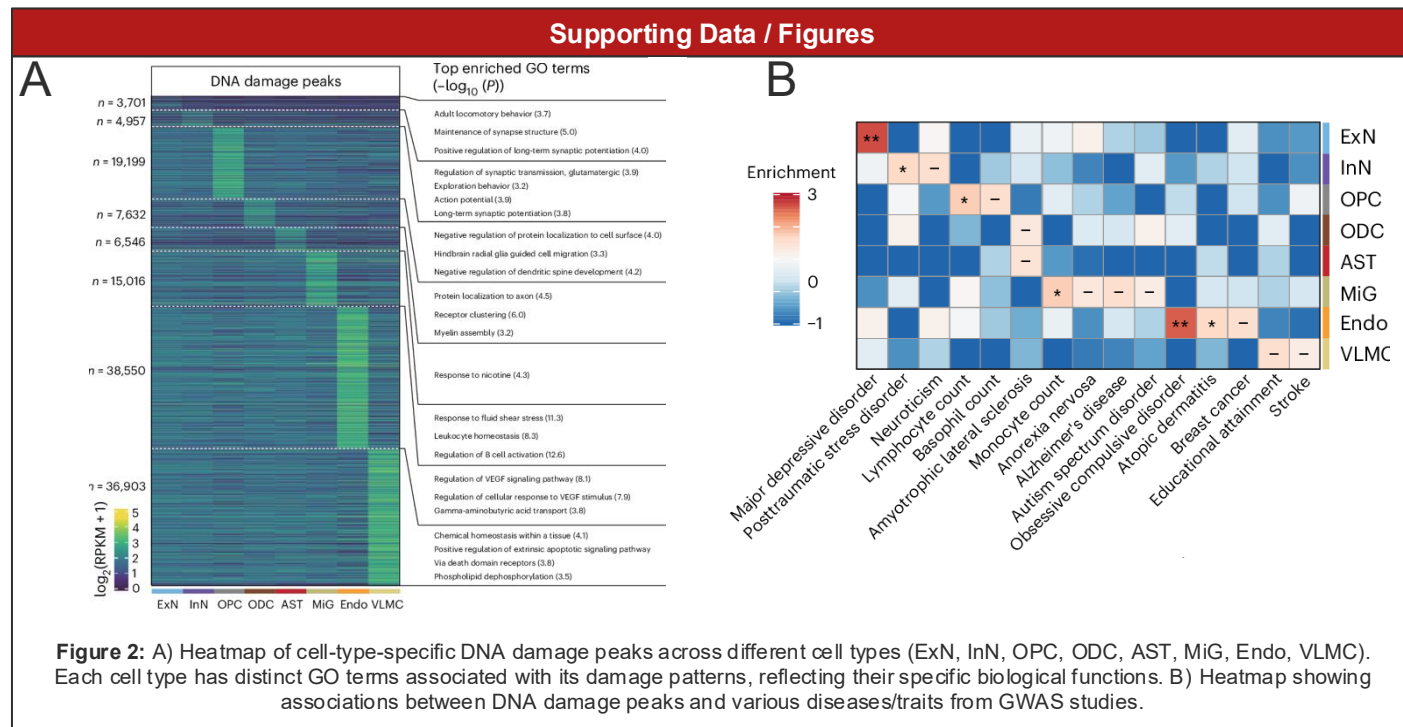
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