



CASCADE 2027 NON-CONFIDENTIAL SUMMARY »

Multi-Omic Single-Cell Platform for Genetic and Epigenetic Discovery

Overview

Every cell in the human body accumulates its own unique set of small genetic and chemical changes over a lifetime, and these cell-by-cell differences are increasingly linked to cancer, aging, and neurological disease. Today's research tools force scientists to choose: they can sequence a cell's DNA, or measure its chemical modifications (methylation), or read out which genes it is actively using, but not all three from the very same cell at meaningful scale. This forces researchers to infer connections between a cell's genetic makeup and its behavior indirectly, rather than observing them together directly, and existing methods that attempt multiple measurements are often slow, expensive, low-throughput, incomplete coverage or destroy some of the information they are trying to capture. This UW innovation is a single-cell platform that captures genetic variants, DNA methylation, and gene expression from the same individual cell in one streamlined workflow, giving researchers a direct, cell-by-cell view of how genetic and chemical changes drive biological outcomes.

- **Unified measurement:** combines three types of single-cell data (DNA sequence, DNA methylation, and RNA expression) from the same cell in a single workflow, rather than requiring separate experiments or samples.
- **Preserves native information:** uses a single-step gentle conversion process to prepare cells from their native tissues that avoids destroying the DNA methylation signal, a limitation of most existing single-cell genome sequencing methods.
- **Built to scale:** is compatible with high-throughput, droplet-based cell processing as well as long-read sequencing platforms, provide flexibility to perform either global or target-specific analysis, positioning it for use in large research studies rather than small pilot experiments.

Description

The platform processes intact single cells or nuclei through a five-step workflow: cells are gently permeabilized to keep their membranes intact; genomic DNA is uniformly exposed and fragmented in place; DNA and RNA molecules from each individual cell are tagged with a matching cell-identifying barcode; the barcoded DNA undergoes a conversion step that reveals methylation information directly, without the harsh treatment used by conventional methods; and the resulting DNA and RNA libraries are sequenced using standard high-throughput or long-read sequencing instruments. Because the barcoding step links DNA, methylation, and RNA data back to the same originating cell, researchers can directly connect a genetic variant or structural

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change in a cell to its methylation state and its gene expression pattern, rather than inferring the connection statistically across separate datasets.

The technology is differentiated from existing single-cell genomic and epigenomic tools in several respects. Most current methods that attempt to combine DNA and methylation profiling rely on chemical treatments (such as bisulfite conversion) that damage DNA and are typically limited to low-throughput, plate-based workflows requiring manual cell sorting. Other approaches that avoid this damage generally sacrifice the ability to also capture gene expression, or cannot generate the long, uniform DNA fragments needed for accurate variant detection in lower complexity sequence contexts. This platform's gentle nuclear preparation chemistry preserves methylation signal while remaining compatible with both droplet-based, high-throughput cell processing and short- or long-read sequencing, allowing researchers to detect subtle structural DNA variants that are otherwise difficult to resolve.

- **Modality:** research tool for single-cell genomic, epigenomic, and transcriptomic profiling, with downstream applications in research, diagnostics and translational research.
- **Proof of concept:** a working prototype has been demonstrated in human blood cells and glioblastoma tumor samples, showing uniform genome coverage, accurate detection of genetic variants, reliable methylation calling, and coherent linkage between a cell's genetic, epigenetic, and expression profile.
- **Development status:** the prototype has also been extended to long-read sequencing platforms and to a scalable, plate-based cell-barcoding format that does not require specialized microfluidic instruments, broadening its potential deployment settings.

Technology Readiness Level (TRL)

TRL 4 — System or subsystem components tested in a laboratory environment. A working prototype has been demonstrated using human blood cell and glioblastoma tumor samples, with proof-of-concept results benchmarked against standard whole-genome and orthogonal sequencing methods. Testing to date has occurred in a research laboratory setting; the platform has not yet been validated in a large-scale tissue study or a clinical or commercial operational environment.

Value Proposition

- **Single-workflow efficiency:** captures DNA sequence, DNA methylation, and gene expression from the same cell in one experiment, eliminating the need for separate assays and samples.
- **Preserves native methylation data:** avoids the harsh chemical treatment used by most competing methods, protecting data quality and expanding the types of genetic variants that can be reliably detected.
- **Scalable and flexible:** is compatible with both droplet-based, high-throughput processing and lower-cost, instrument-free plate-based barcoding, giving research groups flexibility depending on budget and cell numbers.
- **Long-read compatible:** supports long-read sequencing platforms, enabling the detection of complex structural variants that are difficult to resolve with short-read-only methods.
- **Broad research applicability:** provides a foundation for studying somatic mosaicism in cancer, neurodevelopmental disorders, and aging, an area of biology that is difficult to study with existing single-cell tools.

Intellectual Property Position

Patent application pending.

Market Opportunity

- **Single-cell genomics tool market:** academic research labs, pharmaceutical and biotech R&D groups, and genomics core facilities represent the primary near-term customers for a research-tool platform of this kind.
- **Cancer and neuroscience research:** investigators studying tumor evolution, clonal heterogeneity, and neurodegenerative or neurodevelopmental disease represent a natural early-adopter community, given the platform's ability to link rare somatic variants to cell behavior.
- **Unmet need in existing tool landscape:** published single-cell multi-omic and methylation-profiling methods are predominantly plate-based, low-throughput, and reliant on DNA-damaging chemical conversion steps, leaving an open opportunity for a scalable, damage-free alternative.
- **Sequencing platform partnerships:** compatibility with both droplet-based cell processing and long-read sequencing instruments positions the platform for potential partnership or licensing pathways with instrument and reagent providers in the single-cell genomics space.
- **Downstream diagnostic potential:** while initially positioned as a research tool, the ability to connect rare genetic variants to functional cellular consequences may create longer-term opportunities in translational and diagnostic applications.

References

Peer-reviewed publication(s) describing the validation study referenced in this profile are anticipated but not yet publicly available; citations will be added upon publication.