

High-throughput screening of 3D genome architecture using Plate-C

Stanford scientists have developed Plate-C, a high-throughput screening platform that captures genome-wide 3D chromatin architecture as a comprehensive cellular phenotype. Unlike traditional Hi-C methods that are costly and labor-intensive, Plate-C enables rapid, cost-effective screening of hundreds of perturbations in standard 96- or 384-well plates with minimal cell input, transforming 3D genome profiling from a specialized technique into a scalable screening tool.

Three-dimensional genome organization plays a critical role in gene regulation and cellular function, making it an attractive target for therapeutic intervention. However, systematically screening how different compounds affect genome architecture has been severely limited by the cost, complexity, and low throughput of existing chromatin conformation capture methods. Traditional Hi-C approaches require large cell numbers, extensive laboratory time, and significant financial investment, making them impractical for drug discovery or large-scale perturbation studies. This bottleneck has hindered the development of epigenetic therapeutics that could reversibly alter 3D genome organization for precision medicine applications, as well as the creation of standardized screening platforms for pharmaceutical and research applications.

Plate-C addresses these limitations by adapting the proven Dip-C single-cell chromatin conformation capture method for high-throughput screening in standard microplate formats. The platform enables comprehensive genome-wide 3D structure profiling directly in 96- or 384-well plates, reducing experimental time from weeks to approximately one day while dramatically lowering costs and cell input requirements. Unlike previous perturbation studies that were limited to analyzing a few genomic loci or small-scale screens using only cell lines at single time points, Plate-C can systematically screen hundreds of conditions across diverse cell types, including primary cells and post-mitotic cells that were previously difficult to study.

The platform has been validated using 157 epigenetic compounds on embryonic kidney cells, demonstrating its reliability for large-scale perturbation screens and its potential to transform 3D genome profiling from a specialized research technique into a practical tool for drug discovery and precision medicine.

Stage of Development

Research: in vivo

Continued research: optimization to streamline Plate-C for a robotics-based screening platform

Applications

- High-throughput screening of epigenetic drugs and compounds affecting 3D genome organization
- Development of precision medicine therapeutics targeting chromatin architecture
- Large-scale perturbation studies across diverse cell types including primary and post-mitotic cells
- Commercial screening services for pharmaceutical and biotechnology companies
- Research into developmental biology and cellular differentiation mechanisms
- Drug discovery platforms for neurological and oncological applications

Advantages

- Dramatically reduced experimental time from weeks to approximately one day
- Significantly lower cost compared to traditional Hi-C methods
- Minimal cell input requirements enabling studies of rare cell populations
- Scalable platform compatible with standard 96- and 384-well plate formats
- Comprehensive genome-wide coverage rather than limited genomic loci analysis
- Applicable to diverse cell types including primary cells and post-mitotic cells previously difficult to study
- Transforms specialized single-cell technology into practical high-throughput screening tool

Publications

- Bibudha Parasar, Achuthan Raja Venkatesh, Jonathan Perera, Lucas Sosnick, Siavash Moghadami, Yunji Seo, Jenny Shi, Lynette Chan, Satoshi Takenawa, Tetsuya Akiyama, Odilia Sianto, Takeshi Uenaka, Angela Hadjipanayis, Marius Wernig, Aaron D. Gitler, Longzhi Tan (2026). [Whole-genome 3D architectural screen reveals modulators of brain DNA structure](#). *bioRxiv* 2026.04.15.718501.

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