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Editing genes to tackle neurological conditions

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ABOUT THE LECTURE

There are multiple gene networks that impact how brain cells form early on in life, but genetic variants can disrupt this process, sometimes leading to different disorders or developmental disabilities. In her lecture, Xin Jin discussed how her lab is developing cutting-edge technologies to uncover the different genes, cells and brain regions involved in these neurological conditions, such as autism spectrum disorder. With these novel tools—including the gene editing method Perturb-seq—Jin shared how her lab is mapping the brain's genome, one cell at a time.

TOP TAKEAWAY POINTS

- Approximately one in every five adults in the U.S. will experience a serious mental illness in their lives. Studies have identified specific genes involved in these neurological conditions, but it has remained challenging to map these genes to their cellular processes, cell types and tissue types. Without this key information, it is impossible to understand the complex interplay of factors that lead to these brain disorders.
- 2. Jin and her lab have **developed a new technology to classify disease gene functions within each cell type**. The gene editing tool, called in vivo Perturb-seq, enables detailed, high-resolution mapping in a systematic and scalable way. Jin and her colleagues have since accelerated the Perturb-seq platform, and they can now analyze tens of thousands of cell types in a single experiment.
- 3. For example, Jin has been **studying the mechanisms underlying distinct genetic factors associated with autism spectrum disorder (ASD)**. Harnessing Perturb-seq, they could systematically dissect risk genes involved in ASD and developmental delay. This includes the gene FOXG1, which they have shown plays a specific role in determining brain cell fate in the developing brain.
- 4. The Jin lab is also revealing how genetic variants impact the cytoarchitecture, which is the brain's cellular composition under the microscope. Using another novel tool called Perturb-map, they can now **concretely view how these disease-risk genes alter cells in the intact brain**.
- 5. With these novel insights into the inner workings of the developing brain, Jin and her team are helping **uncover actionable drug targets for a spectrum of neurological diseases**. Their research is paving the way toward genomics-inspired therapeutics and diagnostic tools.



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