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CUSTOMER INTERVIEW

Decoding the Human Dopamine System – One Cell at a Time

Introduction

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Elina Nagaeva completed her PhD in Neuroscience at the University of Helsinki, where she characterised somatostatin-expressing neurons in the mouse ventral tegmental area (VTA) — revealing a previously unrecognised inhibitory microcircuit — and built a deep expertise in dopamine system heterogeneity, neuropharmacology, and VTA circuit function. She is now a postdoctoral researcher in Nathan Skene's Neurogenomics Lab at Imperial College London, a group focused on translating GWAS statistics into specific human cell types to identify the cellular basis of complex traits and brain disorders. Here, she is extending her experimental and computational approaches to human post-mortem brain tissue, combining single-nucleus RNA sequencing, spatial transcriptomics, and fluorescence-activated nuclei sorting with comparative rodent datasets, with the goal of building a cell-type-resolved atlas of the human midbrain with direct translational relevance to dopamine-related disorders.

Interview

Why is single cell sequencing important for your research?

Coming from patch-clamp single-cell electrophysiology, I have seen firsthand that every brain cell is unique. Single-cell sequencing is essential to my research because it is the most powerful way to deconstruct the cellular composition of brain nuclei. For regions like the human Ventral Tegmental Area and Substantia Nigra, which are too small to image in living subjects, single-cell and spatial transcriptomics on postmortem tissue are the only ways to map neuronal networks. By mapping transcriptomes, I can identify which cells release specific molecules and which express their receptors, helping us generate precise hypotheses about cell interactions. I also use these data to align human cell types with mouse models and translate physiological insights from animal studies back to human biology.

What biological questions are you trying to answer with single cell sequencing data?

I aim to understand how the human dopamine system works, specifically how excitatory and inhibitory neurons locally regulate dopamine neurons in the Substantia Nigra versus the Ventral Tegmental Area.

In rodents, the local VTA network is well characterized, including receptor expression and how substances like opiates alter dopamine release by inhibiting GABA neurons. Whether these same mechanisms exist in humans remains unclear.

We know even less about how GABA neurons regulate dopamine neurons in the Substantia Nigra or how drugs affect these interactions and motor-related dopamine signaling. My goal is to bridge mouse and human physiology across both regions using single-cell sequencing.

What made you decide to adopt Illumina single cell solution for your research?

I come from a patch-clamping background and have followed single-cell technologies since 2016, when I first used Patch-seq with the Karolinska Institute. Since then, I have worked with several platforms. Patch-seq is highly manual, while microfluidics platforms offer higher throughput but depend on specialized equipment and scheduling, which can reduce flexibility. I was initially skeptical that the Illumina cell prep solution could work with only basic lab equipment like a vortexer. But after trying it, I found it effective and easy to run independently, without relying on shared systems or coordinating schedules. It is also cost-effective. I used it in my previous lab, where it is still in use, and have since introduced it in my current lab with similarly strong results.

How did the hands on time and overall complexity compared to what you expected before starting?

The hands-on time closely matches what is described in the protocol. One of the main advantages is the flexibility built into the workflow, with several safe stopping points that allow you to spread the protocol across two or three days depending on your schedule.

It is also possible to collect samples at the start and process them later, which adds to the overall flexibility of the system.

Initially, some steps such as phase separation can seem challenging, as it is not immediately clear what to expect. However, once performed, these steps are straightforward, and the separation is clearly visible, making the process easier than anticipated.

How has the simplicity of the workflow affected the speed at which your lab can generate actionable data?

The simplicity of the workflow has significantly increased the speed of our research. In our lab, the Illumina solution is used as a quality control step to assess the success of our cell sorting.

We are able to prepare libraries within three days, which allows us to move quickly from experiment to decision-making. Even though sequencing turnaround time still applies, having libraries ready so quickly means we can evaluate whether an experiment worked and adjust our approach much sooner.

This has noticeably accelerated the pace at which we generate actionable insights.

What would you tell to your peers who are hesitant about adopting single cell technology due to workflow complexity?

I would say: do not hesitate.

Single-cell technology may have been complex and inaccessible a decade ago due to high costs and limited infrastructure, but today it is a well-established and accessible method.

With the Illumina solution, researchers are essentially using standard lab techniques like pipetting, vortexing, and PCR which makes the workflow much more manageable. It allows you to generate meaningful data quickly without requiring highly specialized setups.

Looking ahead three to five years, how do you hope single cell technologies like this will shape your research?

Because my research focuses on neural circuits, I see the brain as a system of interactions between different regions. For example, genetic studies may indicate that one cell type in the midbrain and another in the cortex are involved in a disease.

Single-cell technologies can help us understand how these cell types are connected by revealing whether one expresses receptors for molecules released by the other. This allows us to determine whether and how they interact, and how those interactions change in disease states.

Ultimately, these insights can be translated back into model systems, such as mice, where we can test potential strategies to correct dysfunctional interactions.

Learn more

Illumina Single Cell Technology