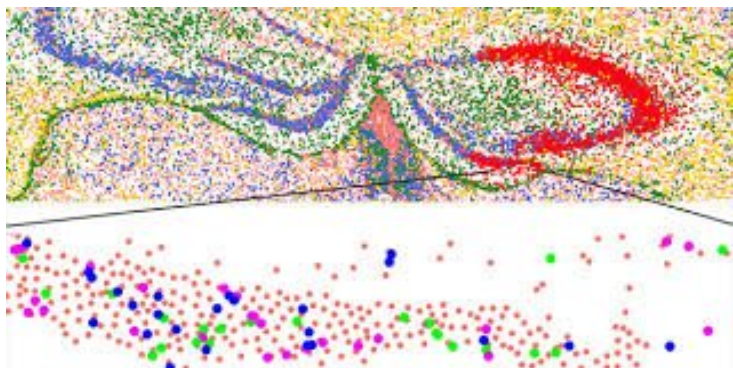


A*STAR GIS Develops Technology to Map Gene Mutations Inside Living Tissue

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New Functional Genomics Technology Preserves Tissue Architecture to Unlock More Precise Therapeutic Targets



Researchers at A*STAR Genome Institute of Singapore (A*STAR GIS) have developed a breakthrough functional genomics technology that enables scientists to study how genes function within intact living tissue, offering an unprecedented view into how diseased cells interact with surrounding healthy cells.

The new technology, called Spatial Perturb-Seq, overcomes a major limitation of conventional genomic methods, which typically require tissues to be broken down into individual cells. While effective for analysing isolated cells, these approaches lose critical information about how cells communicate and influence one another within their natural environment.

By preserving tissue architecture and cellular positioning, Spatial Perturb-Seq allows researchers to observe not only how genetic mutations affect individual cells, but also how those effects ripple through neighbouring healthy tissue. The findings have been published in the journal *Nature Communications*.

Using the gene editing tool CRISPR-Cas9, researchers introduced mutations into selected brain cells and assigned each edited cell a unique barcode. This enabled precise tracking of multiple genetic modifications simultaneously while maintaining the tissue in its native state. Scientists could then visualise exactly where each edited cell was located, identify its neighbouring cells, and examine how the mutation altered surrounding cellular behaviour.

The research team applied the technology to 18 genes associated with neurodegenerative diseases including Parkinson's Disease, Alzheimer's Disease, and Amyotrophic Lateral Sclerosis. Importantly, the study revealed not only how the genetically altered cells responded, but also how nearby healthy cells were affected through cell to cell communication networks within the brain.

These findings provide important insights into how diseases develop and spread within tissue environments. In the brain, neurons operate through highly interconnected signalling networks, meaning mutations in one cell can influence the behaviour of many others. Spatial Perturb-Seq uncovered previously unknown biological mechanisms linked to genes involved in neuronal signalling and tissue level interactions.

The implications extend beyond neurodegenerative disorders. Researchers believe the same principles could transform cancer research, where tumour cells continuously interact with and reshape surrounding healthy tissue environments.

Dr Kimberle Shen Yanyin, Senior Scientist at A*STAR GIS and first author of the study, said:

“We built Spatial Perturb-Seq as a powerful technology that is easily used, so that we can now literally see each gene mutation and its consequences in the tissues and organs. This enables new target discovery and mechanistic study important for new drugs.”

Dr Chew Wei Leong, Senior Principal Scientist at the Laboratory of Synthetic Biology & Genome Editing Therapeutics at A*STAR GIS and lead author of the study, added:

“For the first time, we are not just reading genes, we are revealing the full picture of where and what they do within the organs. This shows us precisely what disease mutations to target. That is the answer that matters for patients.”

The A*STAR GIS team is currently extending the application of Spatial Perturb-Seq into tumour models to better understand how cancer cells communicate with surrounding healthy tissues and how these interactions influence disease progression and treatment response.