

## **GeoMx: a revolution for spatial transcriptomics in Alzheimer's disease**

Alzheimer's disease research has struggled in recent years to produce effective treatments from the results of bulk and single cell transcriptomic studies. A pivotal piece of information missing from these findings is spatial context. Cells do not exist in isolation, rather, they reside within complex cellular neighbourhoods where they may be in contact with differing cellular substrates, cell types or pathogenic agents such as beta amyloid. Consequently, cells within the same sub type may express differential RNA species depending on their spatial context. For example, microglia in direct contact with amyloid plaques may express differential RNA expression to microglia that are not. Understanding the spatial distribution of RNA expression could therefore help us understand disease mechanisms further and provide more targeted interventions. The GeoMx digital spatial platform (DSP) from Nanostring is a new tool in the transcriptomic arsenal which allows users to probe FFPE or fresh frozen tissue for RNA species for NGS analysis while simultaneously using morphology markers to select highly specific regions of interest. This technology utilises the power of UV-cleavable barcoded probes and a complex micro-mirror system, allowing UV light to illuminate specific regions of the tissue. Furthermore, GeoMx is a multi-omic platform capable of performing targeted RNA, whole transcriptome as well as protein differential expression analysis. In our group we aim to utilise the GeoMx platform to investigate whole transcriptome differential expression of RNA from microglia in contact with amyloid plaques in the medial temporal cortex from human Alzheimer's disease and control brain tissue.