## Life Sciences Seminar

# Single-cell transcriptomic analysis of Alzheimer  s disease reveals cell type- and sex-specific pathophysiology

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Host: Sandra Siegert

Alzheimers disease is a pervasive neurodegenerative disorder, the molecular complexity of which remains poorly understood. Here, we analysed 80,660 single-nucleus transcriptomes from the prefrontal cortex of 48 individuals with varying degrees of Alzheimers disease pathology. Across six major brain cell types, we identified transcriptionally distinct subpopulations, including those associated with pathology and characterized by regulators of myelination, inflammation, and neuron survival. The strongest disease-associated changes appeared early in pathological progression and were highly cell-type specific, whereas genes upregulated at late stages were common across cell types and primarily involved in the global stress response. Notably, we found that female cells were overrepresented in disease-associated subpopulations, and that transcriptional responses were substantially different between sexes in several cell types, including oligodendrocytes. Overall, myelination-related processes were recurrently perturbed in multiple cell types, suggesting that myelination has a key role in Alzheimers disease pathophysiology. Our single-cell transcriptomic resource provides a blueprint for interrogating the molecular and cellular basis of Alzheimers disease.

**Wednesday, October 16, 2019 02:30pm - 03:30pm**
Mondi Seminar Room 2, Central Building

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