# Transcriptomic signatures of brain regional vulnerability to Parkinson's disease

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**Résumé**

The molecular mechanisms underlying the caudal-to-rostral progression of Lewy body pathology in Parkinson's disease remain poorly understood. Here, we identified transcriptomic signatures across brain regions involved in Braak Lewy body stages in non-neurological adults from the Allen Human Brain Atlas. Among the genes that are indicative of regional vulnerability, we found genes known as genetic risk factors for Parkinson's disease: *SCARB2*, *ELOVL7*, *SH3GL2*, *SNCA*, *BAP1*, and *ZNF184*. Results were confirmed in two datasets of non-neurological subjects, while in two datasets of Parkinson's disease patients we found altered expression patterns. Co-expression analysis across vulnerable regions identified a module enriched for genes associated with dopamine synthesis and microglia, and another module related to the immune system, blood-oxygen transport, and endothelial cells. Both were highly expressed in regions involved in the preclinical stages of the disease. Finally, alterations in genes underlying these region-specific functions may contribute to the selective regional vulnerability in Parkinson's disease brains.

**Mots-Clés:** Allen Human Brain Atlas, Braak Lewy body stages, Gene coexpression, Selective vulnerability, Spatial transcriptomics

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