Title: Differential SUMO-1 Distribution in Parkinson’s Disease Patient Neurosphere-Derived Cells in Response to Proteolytic Stress

Authors and Affiliations:

Mathew Wong\(^1\), Anthony L. Cook\(^2\), Alan Mackay-Sim\(^3\), Dean L. Pountney\(^{1,2}\)

\(^1\)Griffith Health Institute, Griffith University, Queensland.

\(^2\) School of Human Life Sciences, University of Tasmania, Tasmania.

\(^3\) National Centre for Adult Stem Cell Research, Eskitis Institute for Cell and Molecular Therapies, Griffith University, Queensland.

Abstract:

We compared human olfactory mucosa-neurosphere (hONS) derived cell lines from patients with idiopathic PD to those from healthy control donors to investigate differences in the response to proteolytic stress. Immunotyping of these cells has revealed a phenotype that shares features with neural stem cells and bone marrow mesenchymal stromal/stem cells. We used hONS cell cultures to reveal differences in the histological distribution of the small ubiquitin-like modifier (SUMO-1) and \(\alpha\)-synuclein between Patients and Controls. Using immunofluorescence, we found specific labelling of a high-proportion of lysosomes with SUMO-1 in both PD (25.5\%\pm6.5; n=5) and Control (17.3\%\pm4.8; n=5) cell lines after 24hrs treatment with the proteasome inhibitor, MG132 (5 \(\mu\)M), compared to sham-treated (15.3\%\pm4.2 and 7.4\%\pm2.7, respectively). This is consistent with the lysosomal SUMO-1 labelling found recently in post-mortem human diseased tissue. There was a significantly \((p = 0.025)\) greater proportion of SUMO-1-positive lysosomes in treated PD compared to treated Control cells, but a greater proportionate increase in SUMO-1-positive lysosomes at 24 hrs post-treatment in Control (2.3-fold) compared to PD cells (1.7-fold). Conversely, \(\alpha\)-synuclein aggregates were observed more frequently in PD than Control cells in response to proteasome inhibition \((p = 0.03)\), but were not significantly different in untreated cells. Total lysosome counts were increased in MG132-treated cells, but were equal in both PD and Control cells. This implicates both SUMO-1 and the regulation of the lysosome-autophagy pathway as being different on a disease basis in hONS cells.