Neurology

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Major Scientific Interests of the Group

We explore biomarkers and treatments for Parkinson's disease, other neurodegenerative diseases, and REM sleep behaviour disorder using state-of-the-art multi-omic analyses. We have revealed alterations in fatty acid β-oxidation, polyamine and caffeine metabolism as well as changes in sebum mRNA in Parkinson's disease. Based on these findings, we develop a) new methods for early diagnosis and treatment evaluation, b) mechanistic understanding of the pathology and c) drug candidates for disease-modifying therapy. In this context, our particular interest is autophagy, an intracellular degradation system mediated by sequestration of cellular components into autophagosomes, followed by lysosomal degradation. Compromised autophagy has been implicated in the pathology of myriad human disorders including neurodegenerative diseases, and thereby restoring autophagic capacity is a promising therapeutic strategy. We investigate, in the context of neurodegenerative diseases, a) how autophagy is impaired, b) how autophagy dysfunction determines cell fate (such as apoptosis, ferroptosis and senescence), and c) develop small molecules to combat these diseases, using molecular cell biology techniques.

Projects for Regular Students in Doctoral or Master's Programs

1) Presymptomatic physiological biomarker identification for Parkinson's disease.
2) Liquid biomarker identification for Parkinson's disease and REM sleep behaviour disorder.
3) Mechanisms and treatments of Parkinson's and rare neurodegenerative diseases.
4) Mechanisms and interventions of ageing, the biggest risk factor of neurodegenerative diseases.

Study Programs for Short Stay Students (one week – one semester)

1) Autophagy flux assay to monitor autophagic activity in cultured cells.
2) Various cell death assays to evaluate cytotoxicity, apoptosis or ferroptosis in neuronal cells.

Selected Publications

1) Kelly G† & Kataura T† et al., Suppressed basal mitophagy drives cellular ageing phenotypes which can be reversed by a p62-targeting small molecule. ***Developmental Cell*** (in press).
2) Date Y et al. & Saiki S*, Novel autophagy inducers by accelerating lysosomal clustering against Parkinson's disease. ***eLife*** 13:e98649 (2024).
3) Kataura T†* & Sedlackova† L et al., Targeting the autophagy-NAD axis protects against cell death in Niemann-Pick type C1 disease models. ***Cell Death & Disease*** 15(5):382 (2024).
4) Zhu Y† & Fujimaki M† et al., Loss of WIPI4 in neurodegeneration causes autophagy-independent ferroptosis. ***Nature Cell Biology*** 26(4):542-551 (2024).

5) Miyamoto K, Saiki S* et al., Systemic metabolic alteration dependent on the thyroid-liver axis in early PD. ***Annals of Neurology*** 93:303-316 (2023).
6) Kataura T et al., NDP52 acts as a redox sensor in PINK1/Parkin-mediated mitophagy. ***EMBO Journal*** 42: e111372 (2023).
7) Sasazawa Y et al. & Saiki S*. Oxidative stress-induced phosphorylation of JIP4 regulates lysosomal positioning in coordination with TRPML1 and ALG2. ***EMBO Journal*** 41:e111476 (2022).
8) Kataura T† Sedlackova L† et al., Autophagy promotes cell survival by maintaining NAD levels. ***Developmental Cell*** 57:2584-2598 (2022).
9) Kataura T et al., A chemical genomics-aggrephagy integrated method studying functional analysis of autophagy inducers. ***Autophagy*** 17:1856-1872 (2021).
10) Saiki S†* & Sasazawa Y† et al., A metabolic profile of polyamines in Parkinson's disease: a promising biomarker. ***Annals of Neurology*** 86:251-263 (2019).
11) Fujimaki M et al., Iron Supply via NCOA4-Mediated Ferritin Degradation Maintains Mitochondrial Functions. ***Molecular and Cellular Biology***, 39(14): e00010-19 (2019).
12) Fujimaki M, Saiki S* et al., Serum caffeine and metabolites are reliable biomarkers of early Parkinson's disease. ***Neurology*** 90:e404-e411 (2018).
13) Korolchuk VI† & Saiki S† et al., Lysosomal positioning coordinates cellular nutrient responses. ***Nature Cell Biology*** 13:453-60 (2011).
14) Saiki S, et al., Caffeine induces apoptosis by enhancement of autophagy via PI3K/Akt/mTOR/p70S6K inhibition. ***Autophagy*** 7:176-87 (2011).