





DALIS in aging, inflammation and neurodegeneration

Torinesi R.S.¹, Gatti E.², Grandori R.¹, Vai M.¹, Orlandi I.¹

E-mail: r.torinesi@campus.unimib.it

¹Dipartimento di Biotecnologie e Bioscienze, Università degli Studi di Milano Bicocca, Piazza della Scienza 2, 20126 Milano (MI), Italy

²Centre d'Immunologie de Marseille-Luminy, CNRS-INSERM-Université de la Méditerranée, Campus de Luminy, 13288 Marseille Cedex 09, France

Keywords: DALIS, dendritic cell, protein aggregate, Saccharomyces cerevisiae

Neurodegenerative diseases are debilitating pathologies with a common underlying pathogenic mechanism, involving incorrect protein folding processes and protein aggregation. The exposure of the cell to particular stress conditions (e.g. heat stress or oxidative stress) stimulates the accumulation of misfolded proteins into aggregated structures, which can interfere with the proper proteostasis, possibly leading to failures in cellular functions and to cell death¹. Nevertheless, in healthy cells, protein aggregation is one of the mechanisms adopted to overcome the presence of misfolded polypeptides². Among the cytoplasmic aggregates, DALIS (<u>D</u>endritic cell <u>Aggresome-Like Induced Structure</u>) are transient deposits for ubiquitinated defective polypeptides formed during dendritic cell (DC) maturation in response to several stresses³.

Yeast cells will be employed to evaluate the role of protein aggregates in aging and neurodegenerative diseases. The budding yeast *Saccharomyces cerevisiae* displays a range of different dynamic granules, such as P-bodies and stress granules, that are demonstrated to be conserved between different species, despite the increased complexity in protein composition and function in multicellular eukaryotes⁴. Moreover, yeast is a well-established and powerful model organism to study metazoan proteins associated to aging and neurodegenerative diseases, since many pathways that are relevant for these conditions in humans, including protein folding, proteostasis and stress response, are conserved in yeast⁵. Therefore, yeast cells will be subjected to the same stress conditions that were shown to induce the aggregation of DALIS in mammalian cells, in order to characterize and isolate yeast aggresome-like induced structures (yALIS), with the aim of understanding their composition and physiological role.

Reference:

- 1. Fulop T, Larbi A, Dupuis G, Le Page A, Frost EH, Cohen AA, Witkowski JM, Franceschi C (2018). *Front Immunol*, **8**, 1960.
- 2. Johnston JA, Ward CL, Kopito RR (1998). J Cell Biol, 143, 1883-1898.
- 3. Pierre P (2005). Immunol Rev, 207, 184-190.
- 4. Saarikangas J, Barral Y (2016). Curr Genet, 62, 711-724.
- 5. Longo VD, Shadel GS, Kaeberlein M, Kennedy B (2012). Cell Metab, 16, 18-31.