





Stress-induced ubiquitin-rich aggregates: identification and characterization in the yeast *Saccharomyces cerevisiae*

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Keywords: membraneless protein aggregates, ubiquitin, stress, yeast

By prevailing opinion, protein aggregation represents a dangerous phenomenon, being associated to age-related neurodegenerative disorders, such as Alzheimer's or Parkinson's Diseases^[1]. However, this event is not always a synonym of cellular failure or cell death. Indeed, protein aggregation is employed by healthy cells to overcome the presence of large amounts of misfolded polypeptides, generated in response to external stresses, which cannot properly be rescued by the overloaded proteolytic machinery. In this context, Dendritic cell Aggresome-Like Induced Structures (DALIS) function as transient deposits for ubiquitinated defective proteins in mammalian dendritic cells, also delaying antigen presentation and promoting a more efficient immune response^[2].

The yeast *Saccharomyces cerevisiae* is a well-established and powerful model organism to study aging and neurodegenerative disorders, also widely used for the research on cytoplasmic aggregates, including stress granules and processing bodies, and autophagy^[3]. Therefore, in this study, yeast cells have been engaged to detect the formation of stress-induced ubiquitin-rich structures, identifiable as DALIS-equivalent bodies. To this purpose, cells have been subjected to specific stresses, namely, heat shock temperatures, ethanol administration, nitrogen depletion and glucose starvation. Ubiquitin-rich aggregates were visualized by fluorescence microscopy, revealing the formation of structures comparable to the mammalian DALIS after the exposure to specific stress conditions. For further investigation, aggregates were isolated under the same experimental conditions and analysed by western blot, displaying a complex ubiquitin-rich pattern, which will be analysed by mass spectrometry in order to establish the exact protein composition and to identify its human counterpart.

References

- 1. Hipp MS, Kasturi P, Hartl FU (2019). Nat Rev Mol Cell Biol, 20, 421-435.
- 2. Lelouard H, Ferrand V, Marguet D, et al. (2004). J Cell Biol, 164, 667-675.
- 3. Decker CJ, Parker R (2012). Cold Spring Harb Perspect Biol, 4, a012286.