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Editorial: Women in cell death research

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Editorial on the Research Topic
Women in cell death research

Cell stress responses represent one of the most fascinating frontiers in modern biology, as they stand at the delicate interface between adaptation and demise. When cells cope with environmental challenges, metabolic imbalance, or developmental cues, the outcome of stress signaling can determine survival, transformation, or programmed death. The five articles collected in this Research Topic shed light on this complexity, providing fresh perspectives on cellular and molecular checkpoints, evolutionary models, and disease implications.

The review "Die Hard: Necroptosis and its Impact on Age-Dependent Neuroinflammatory Diseases" by Smith et al. addresses a form of programmed non-apoptotic cell death, known as necroptosis, that is increasingly recognized as a driver of neurodegeneration. The authors review necroptosis from its historical background to recent insights into signaling and regulatory mechanisms in several age-dependent neuroinflammatory diseases. They also examine therapeutic inhibitors and their outcomes and discuss *in vitro* methods to induce necroptosis, thereby contributing to the expansion of knowledge on the necroptotic signaling pathway that has potential therapeutic benefits across neuroinflammatory diseases.

The review by Seyrek et al., "Glycans on Death Receptors as Sweet Markers and Signaling Checkpoints", provides an overview of current understanding in cell signaling modulation through glycosylation of death receptors (DRs). The activation of the DRs triggers the extrinsic death pathway. Glycans attached to DRs have a structural diversity and understanding their involvement in signal transduction is crucial to decipher the role of specific glycan signatures, namely "glyco-code". Glycans act as functional modulators capable of shaping DRs activities and intracellular signaling. This view opens exciting avenues for future therapeutic strategies, where glycosylation could be targeted to fine-tune DR pathways.

Complementing this perspective, Guaragnella et al., in "Mitochondrial (dys)function: a double edge sword in cell stress response" revisit mitochondria not only as energy producers but as pivotal decision-makers in stress adaptation. The authors focus on mitochondrial communication and its relevance for cytoprotective strategies aimed at controlling synthesis, degradation and recycling processes in the yeast *Saccharomyces cerevisiae*. The latter is proposed as a suitable model organism to gain insights into the retrograde response pathways and autophagic/mitophagic processes to either promote metabolic remodeling to compensate mithochondrial function loss and provide building blocks for amino acid and protein synthesis or remove damaged/impaired organelles.

The theme of metabolic stress is further expanded in "Exploring Sugar-Induced Cell Death (SICD) in Yeast: Implications for Diabetes and Cancer Research" by Parbhudayal and Cheng, which uses yeast as a powerful model to dissect how sugar excess can trigger lethal signaling cascades. The Authors summarize the current understanding of SICD in yeast, a phenomenon first described in 1991 in *S. cerevisiae*. They highlighted studies showing the presence of a similar phenomenon in mammalian cells, High Glucose Induced Cell Death (HGICD) with a focus on the mechanisms used by cancer cells to evade HGICD.

Looking through the evolutionary lens, Deidda et al. in "The sea urchin embryo and the cell stress responses: new perspectives", focused on the cell stress response within a whole organism, namely, the sea urchin embryo, a well-known model used worldwide in many research fields. The authors provided an update on current knowledge of sea urchin embryo genes involved in the cellular stress response following exposure to different environmental conditions and pollutants. A selection of studies using high-throughput screening approaches was taken into consideration. The perspective is to identify panels of modulated genes to be exploited as biomarkers of embryotoxicity providing new approaches for monitoring and intervention strategies.

Taken together, these five contributions illustrate the richness and complexity of cell stress biology. From glycans to mitochondria, from yeast to humans through the sea urchin, and from cancer to neurodegeneration, they converge on a central message: cellular fate under stress is determined by finely orchestrated networks, whose perturbation can lead to pathology but whose understanding holds the promise of innovative treatments and intervention strategies in many different fields.

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