QUANTITATIVE MICROSCOPY IN UNDERSTANDING NEURODEGENERATION UNDER HYPOXIA: SCOPE OF CONFOCAL MICROSCOPY IN LONG TERM MONITORING PROTEIN CONDENSATES

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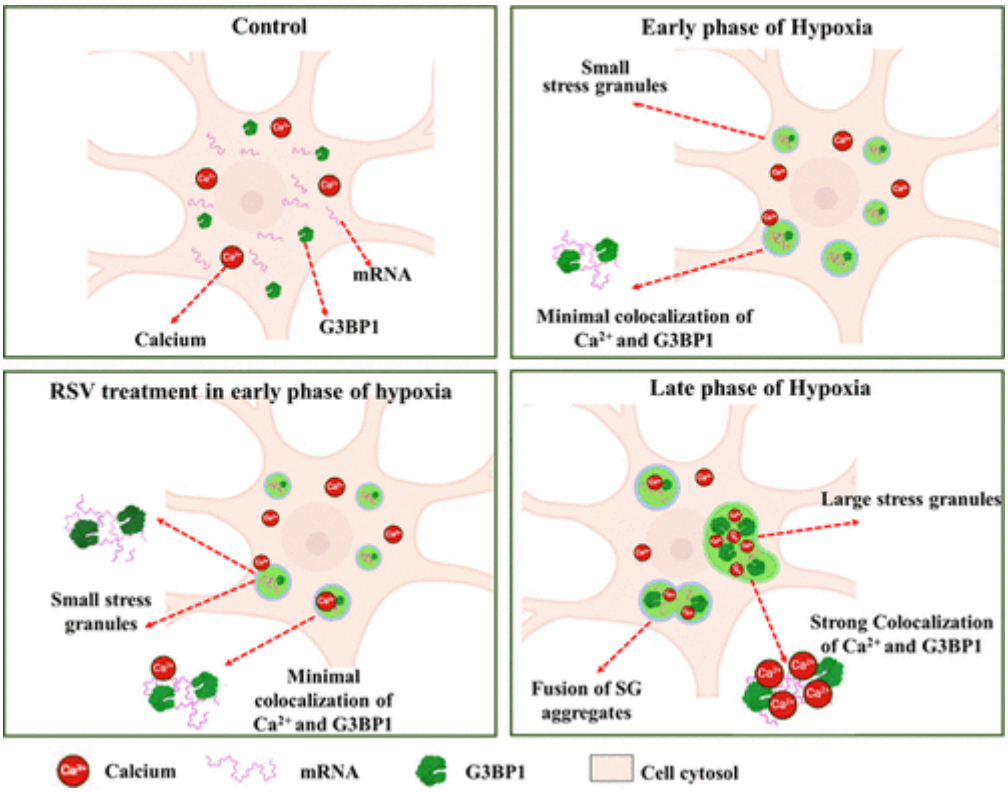
Abstract

The rising global impact of neurodegenerative diseases (ND), including Alzheimer's disease, other dementias, and Parkinson's disease, poses an escalating societal burden across the world. Statistical reports indicate that the world's aging population will rise to 1.5 billion by 2050, signifying an increase in the prevalence of NDs in future. Currently, therapeutics showed relatively low success rate, demanding the identification of potential therapeutics for neurodegenerative disorders that can control the protein aggregation. In this context, it is important to explore new compounds that may synergize with existing drugs. In this context, we propose live cell confocal imaging as a powerful tool which allows neuroscience researchers to observe cellular processes. Time lapse imaging can be used to monitor individual cells that provides insights into the cellular processes underpinning the neurodegeneration. Here, we have implemented a chronic hypoxia model in N2A cells and used genetic fluorescent sensors to monitor protein aggregation as well as cytosolic calcium at cellular level. Our results indicate the critical role of confocal imaging in simultaneous visualization of ion level and protein condensate formation during the process of degeneration. We demonstrated that real-time information on cellular and molecular events at the subcellular levels, provide critical insights into the progression of neurodegeneration. Additionally, we showed how imaging can also facilitate the assessment of therapeutic strategies and collect longitudinal data, thus holding significant promise for advancing the treatment protocols. Finally, we assess the limitations of confocal microscopes and the need to switch towards Raman Microscopy.



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