How Does Stress Affect Our Cells?

Uncovering the Role of Stress Granules

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Background

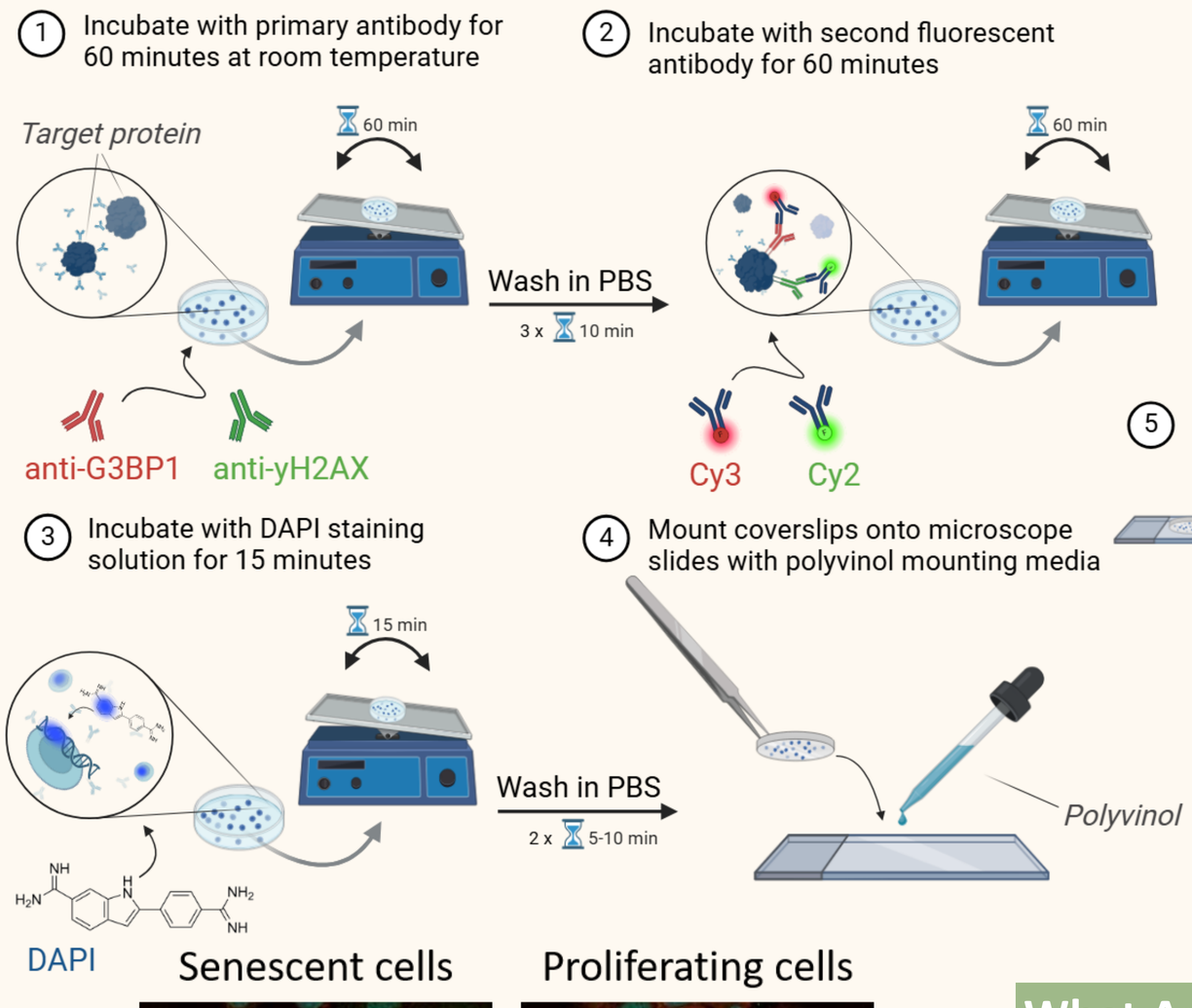
In this experiment, we aim to explore the relationship between stress granules (SGs) and **cellular senescence**. Using APEX-proteomics, our research group identified novel proteins associated with SGs. From this dataset, we selected several proteins for further validation to confirm their presence in SGs and investigate their potential roles in cellular stress responses

Cellular Senescence

Cellular senescence is a process where cells enter a state of permanent cell cycle arrest, meaning they stop dividing but remain metabolically active[1]. Senescence is often triggered by various types of cellular stress, such as DNA damage and oxidative stress. While senescence is a natural mechanism to prevent damaged or potentially cancerous cells from proliferating, it also plays a complex role in aging and age-related diseases.

From the APEX study, we chose to investigate the following proteins: **BLMH, APMAP, ACAT1, DESP, LAP3, SMU1**
Figure 2 shows a representative example for one of those proteins

Immunofluorescence Staining



Senescence was induced in U2OS by incubation with 2 µM **etoposide**, a DNA damaging agent, for 9 days. This DNA damage leads to a cell cycle arrest, inducing a state of senescence.

5 Image and analyse using confocal microscope

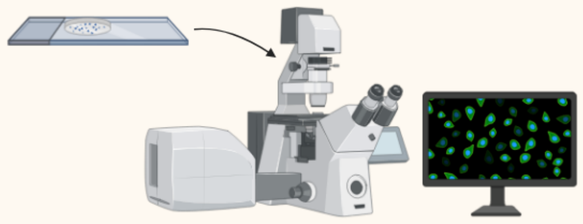


Figure 1. Stress granules forming from both senescent and proliferating cells after incubation with 200 µM sodium arsenite for 60 minutes.

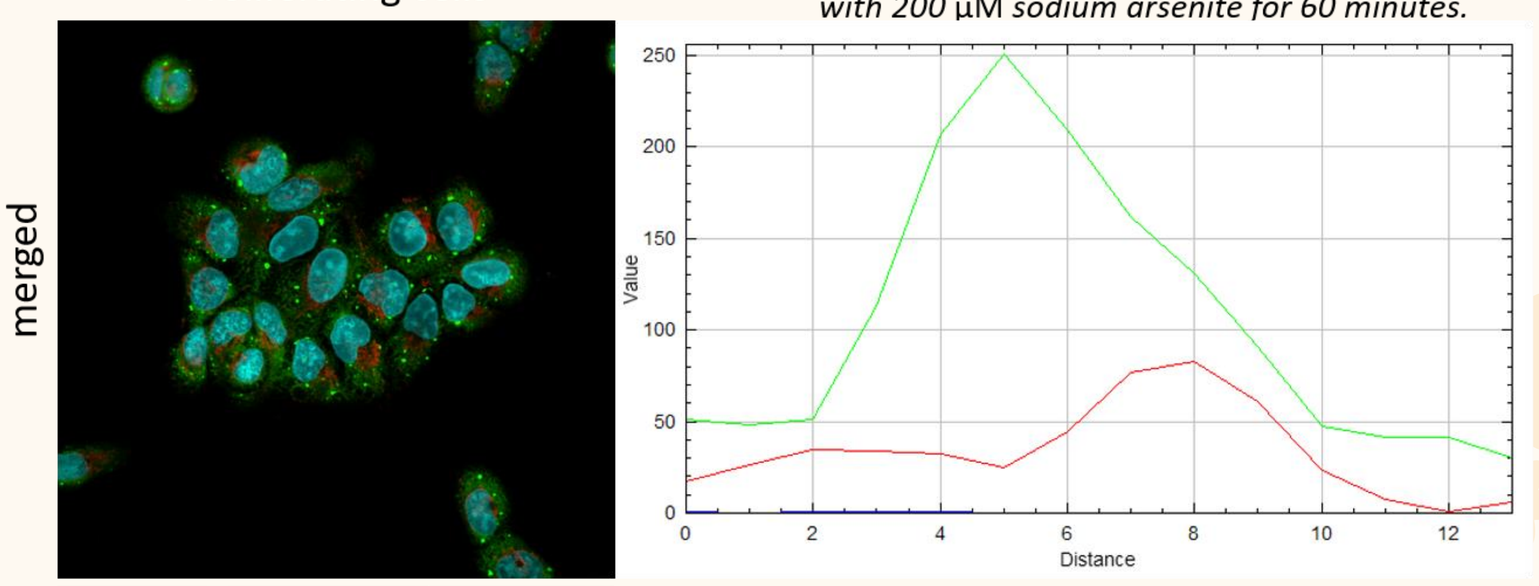


Figure 2. Co-localization of the target protein BLMH (red) together with fundamental stress granule protein G3BP1 (green). The plot shows the degree of colocalization of the target protein with G3BP. Line color corresponds to the color of the figure.

What Are Stress Granules?

Stress granules (SGs) are dynamic membrane-less organelles that form in response to stress, such as heat shock, hypoxia and viral infections[2]. The SGs are held together trough lipid-lipid phase separation, a process that enables their rapid assembly and disassembly based on cellular needs. These organelles are composed of untranslated mRNAs, RNA-binding proteins, and other stress response proteins, serving as temporary storage sites for cellular components during periods of stress.

Why Study Stress Granules?

The study of stress granules is important due to their role in cellular stress management and their involvement in several neurodegenerative diseases such as ALS, Alzheimer's, and Parkinson's disease[3]. In these conditions, SG-associated proteins may misfold or fail to disassemble properly, leading to toxic protein aggregates that disrupt cellular homeostasis.

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4. *Figure produced with* ***Biorender***