Help The Cell Is Under Stress!

Furthering Our Understanding of Stress Granules

Authors
ALEKSA KOMLJENOVIC[1], THOMAS STEVENSON[2], Suhma-Nagaraja Grellschied[2,3]
[1]Department of Biology, UiB. 2. Department of Biomedicine, UiB. 3. Department of Informatics UiB

Contact
alkom6463@uib.no

Background

This study aims to the interaction between **stress granules** and their constituent protein**,** respectively.

The study utilizes a special technique called **APEX-mediated proteomics** to explore how a main stress- related protein, G3BP1 connects with other protein in cells that are under stress or aging. In this project we used human bone cancer cells (U2O) to make them **Senescence** (*senescence was induced via incubation in 2 µM etoposide for 9 days*) and form stress granules (*SGs induced using 200 µM sodium aresnite, for 60 minutes*).

The proteins that were studied are as followed: **LSM7**, **CASP4**, **SNW1**, **BCL10** and **EIFC3**

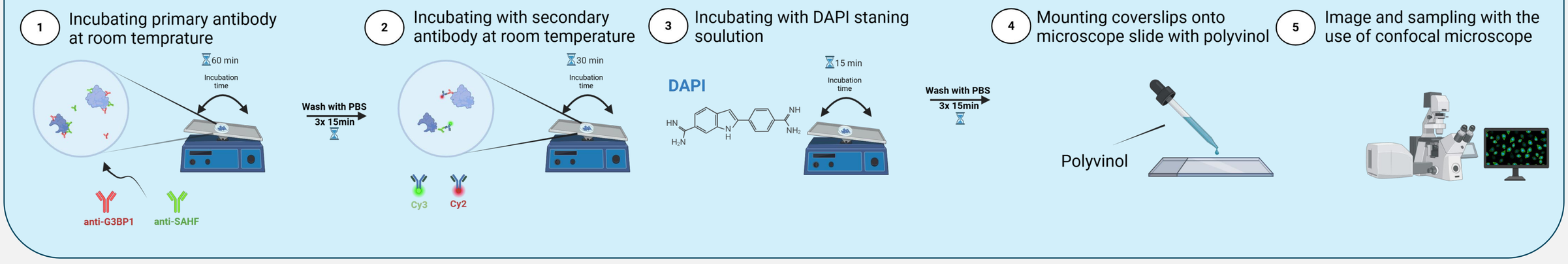
Cellular Senecence

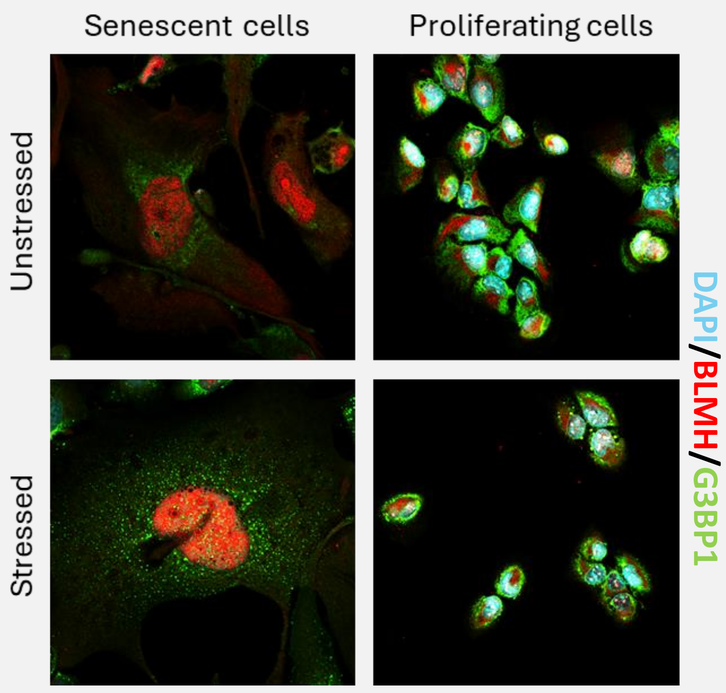
Cellular senescence is when a cell stops dividing forever, usually because of stress or damage, like when its DNA gets damaged, or it ages to much. Even though these cells don't divide anymore, they stay active and release chemicals that cause inflammation(1). This can be helpful at first glance, like stopping damaged cells from turning into cancerous ones, but as more senescent cells build up over time, they can cause aging and problems in tissues by making them less healthy. It can play a role in age-related diseases.

What Are Stress Granuels?

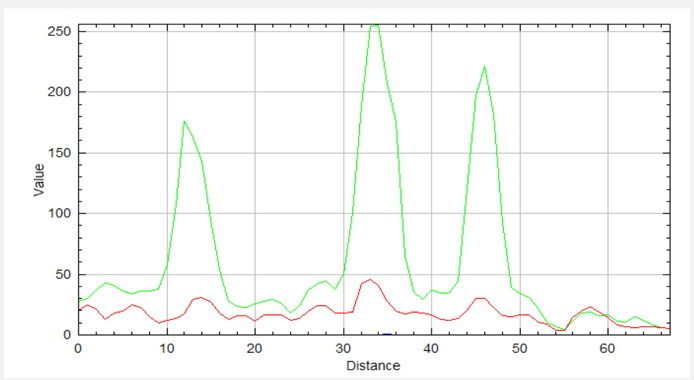
Stress granules are small structures that form inside cells when they are under stress, such as lack of nutrients, heat shock, or exposure to toxins(2). These granules are made up of proteins and RNA molecules that "cluster" together temporarily to protect the cell. When stress occurs, normal cell processes like protein production are disrupted, and stress granules help by pausing the production and storing these important molecules safely until the stress is gone. This way, the cell can focus on surviving the stressful conditions and later return to normal function. Disordered stress granule formation is linked to diseases, including neurodegenerative disorders like ALS and Alzheimer's.

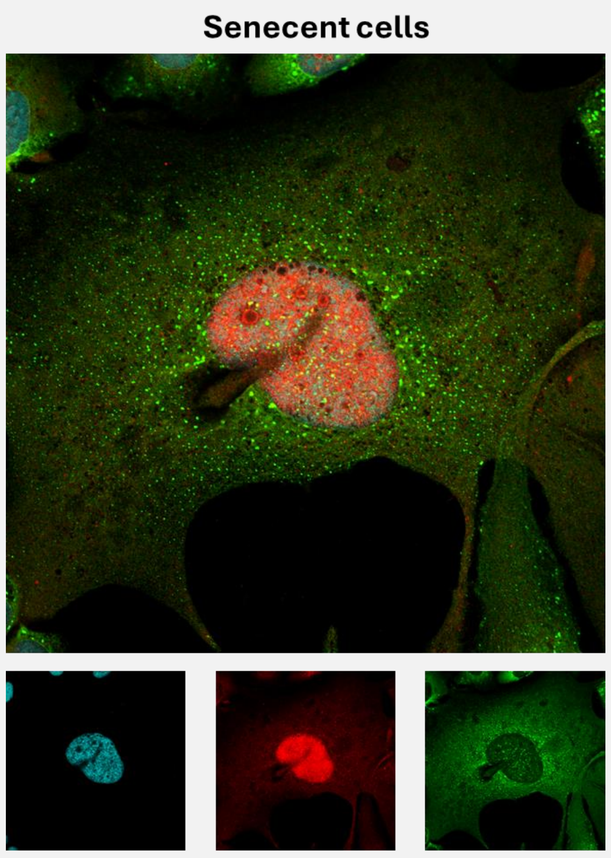
Methodology





BCL10 (protein) immunofluorescent staining in senescent and proliferating cells. Cells are stained with DAPI (blue) to indicate nuclei, BLMH (red) to label bleomycin hydrolase, and G3BP1 (green) to label the stress granule protein.





Top figures -High-magnification image of a senescent cell (BCL10) under stress, with clear staining of DAPI (blue), BLMH (red), and G3BP1 (green). This image highlights the localization of BCL10 in relation to other markers, with accumulation near stress granules or close to the nucleus

Graph-Intensity profile graph showing the distribution of BLMH (red) and G3BP1 (green) staining across a senescent cell. This graph shows insight into the co-localization and relative intensity, helping to understand the behavior of BCL10 in stressed conditions.

Why Are Stress Granuels Important

Studying stress granules is important because they play an important role in how cells respond to and withstand stressful conditions, which is essential for understanding cellular health and disease. When stress granules function correctly, they help protect cells by managing the temporary halt of protein translation and ensuring the cell can recover. However, issues with stress granule formation or clearance are linked to various diseases, including neurodegenerative disorders like Alzheimer's, ALS, and Parkinson's, as well as certain cancers (3). By researching stress granules, we can discover how cells cope with stress and identify potential therapeutic targets to treat or prevent these diseases, making this a vital area of study for improving human health.

BIO_299_4

References:

(1)Campisi, J., & d'Adda di Fagagna, F. (2007). Cellular senescence: When bad things happen to good cells. *Nature Reviews Molecular Cell Biology*, 8(9), 729-740
(2) Anderson, P., & Kedersha, N. (2009). Stress granules. *Current Biology*, 19(10), R397-R398
(3) Li, Y. R., King, O. D., Shorter, J., & Gitler, A. D. (2013). Stress granules as crucibles of ALS pathogenesis. *The Journal of Cell Biology*, 201(3), 361-372
Figure Created with BioRender. (2024)