Exploring the 'zombie cells' in cancer evolution
Welcome to Cell Fate Dynamics Group

Group Research Focus

Cells constantly face challenges, from stress signals to metabolic fluctuations, that shape their destiny. In our lab, we study how **replication stress (RS) and metabolism interact to drive senescence**, a state where cells stop dividing but remain active. While senescence can act as a barrier against cancer, some cells find ways to **escape this arrest**, leading to aggressive, therapy-resistant tumors.

Our research focuses on:

🔬 **How chronic replication stress rewires metabolism** to maintain the senescent state.
🧬 **The molecular switches that allow cells to escape senescence** and fuel disease progression.
💊 **Targeting these vulnerabilities** to prevent cancer cells from becoming more aggressive.

By combining high-content imaging, metabolic profiling, and functional genomics, we **decode the mechanisms that lock cells in senescence, or set them free.** Understanding these processes could lead to **new therapeutic strategies** that stop cancer cells before they evolve into resistant, more dangerous forms.
Join us in exploring how cell fate decisions shape disease and how we can control them! 🚀
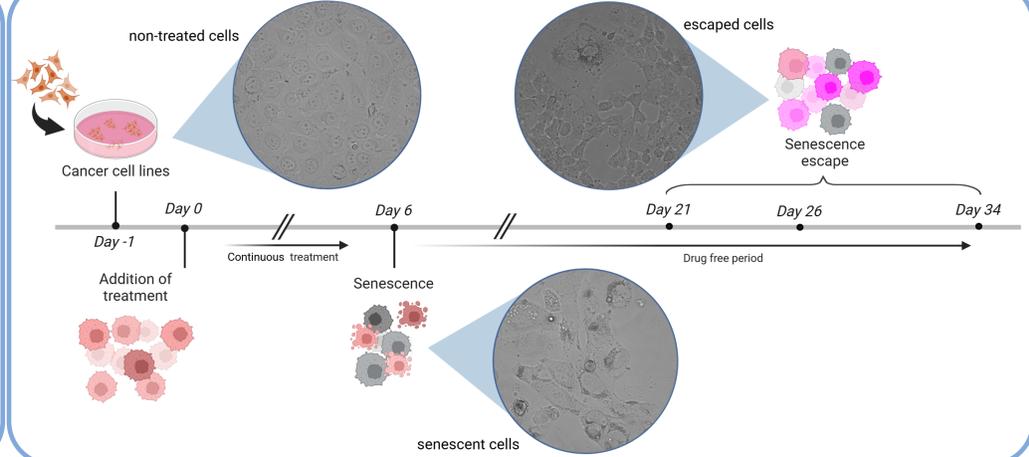
If you are interested in joining the Galanos Group, please contact Panos:
panos@bmb.sdu.dk

Model of cancer evolution
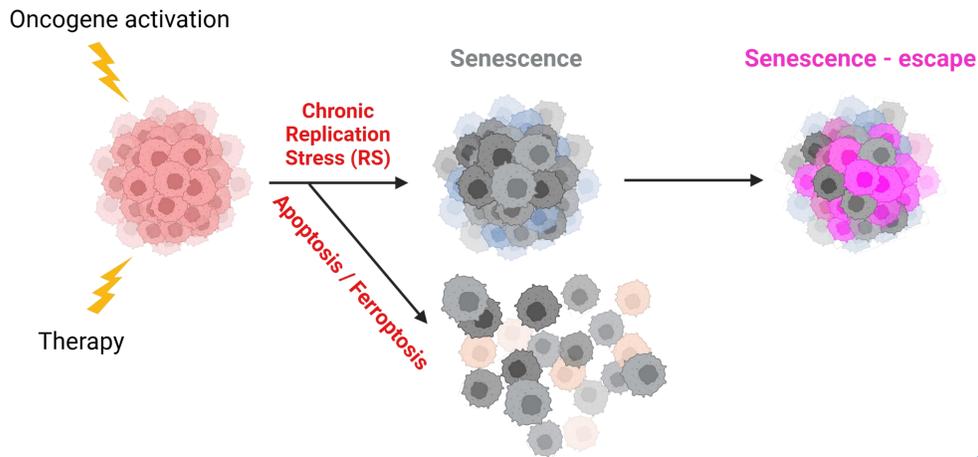

Experimental set up

Projects

1 **Metabolism & Senescence**
How do changes in **metabolism** help cells stay in senescence?

2 **Escape from Senescence**
What makes cells **escape senescence** and become aggressive?

3 **Targeting Senescent Cells**
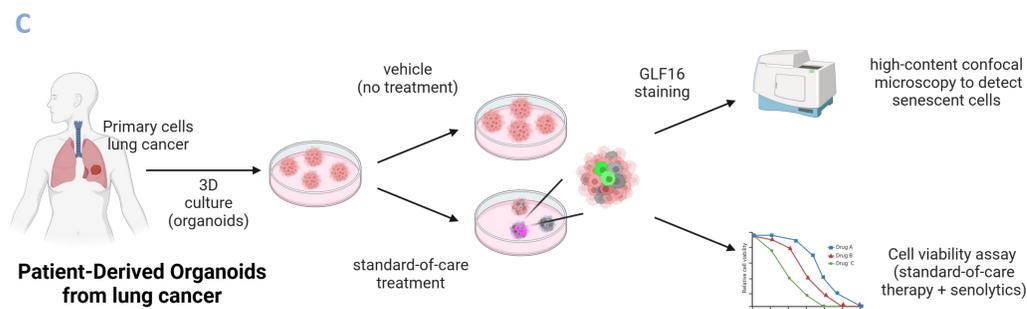Can we **block senescence escape** to stop cancer from becoming resistant to therapy?

Why It Matters?

By understanding how **senescence works** and how cells escape it, we can find **better ways to treat cancer** and prevent relapse.
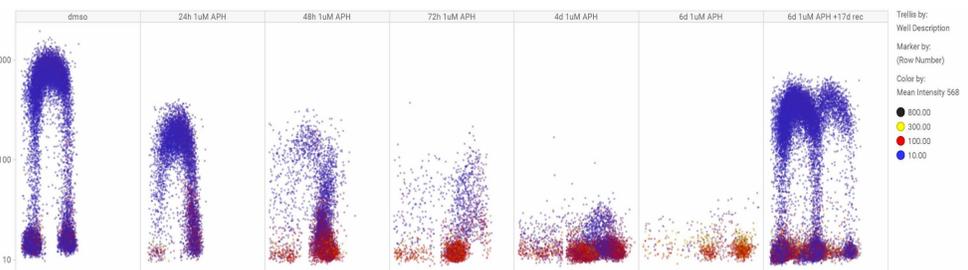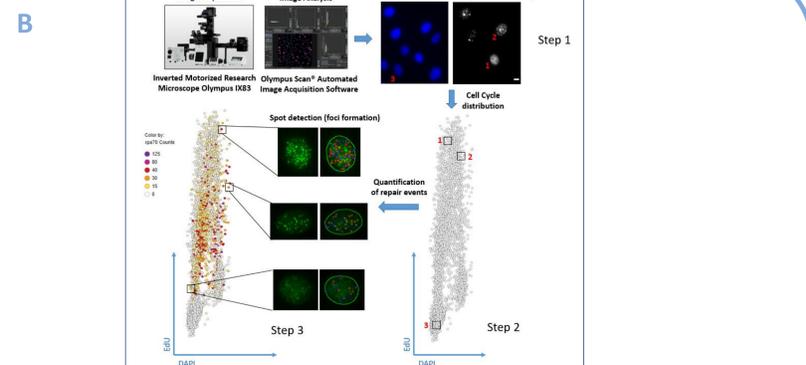
Technical approaches
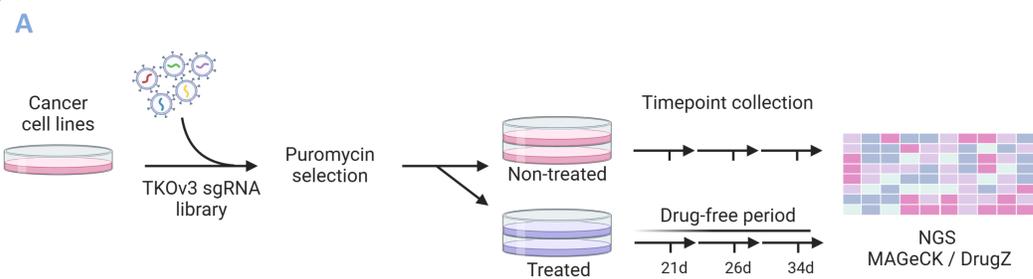
A genome-wide CRISPR/Cas9 knockout screen is used to identify key regulators of senescence maintenance and escape. Cells are induced into senescence, transduced with a pooled sgRNA library, and monitored for survival and escape. Enriched sgRNAs in escaping cells reveal potential drivers of senescence bypass, which are validated using functional assays.

High-content automated microscopy is applied to detect RS and DNA damage events with the surrogate markers, coupled with the cell cycle distribution by measuring EdU incorporation.

Patient-Derived Organoids (PDOs) provide a clinically relevant model to study senescence and therapy resistance. Lung cancer PDOs are established from resected tumors, treated with standard-of-care therapies, and analyzed for senescence markers. This system allows us to test new strategies to block senescence escape, preventing tumor progression and therapy resistance.

Available Reading Material

1. Chronic p53-independent p21 expression causes genomic instability by deregulating replication licensing. **Nat Cell Biol (2016)**
2. Mutational signatures reveal the role of RAD52 in p53-independent p21-driven genomic instability. **Genome Biology (2018)**
3. A recurrent chromosomal inversion suffices for driving escape from oncogene-induced senescence via subTAD reorganization. **Molecular Cell (2021)**
4. A fluorophore-conjugated reagent enabling rapid detection, isolation and live tracking of senescent cells. **Molecular Cell (2023)**
5. Protocol for image-based monitoring of de novo RNA synthesis at DNA double-strand breaks in human cell lines. **STAR Protocols (2025)**