-Breaking the Samurai Law of Biology-
Translational Assays for Aging and Age-Related Diseases

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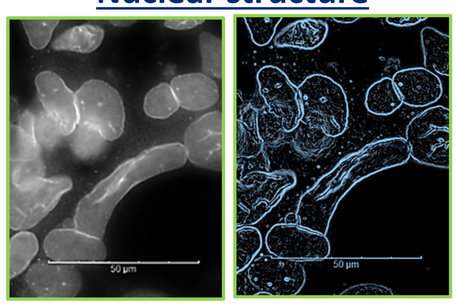
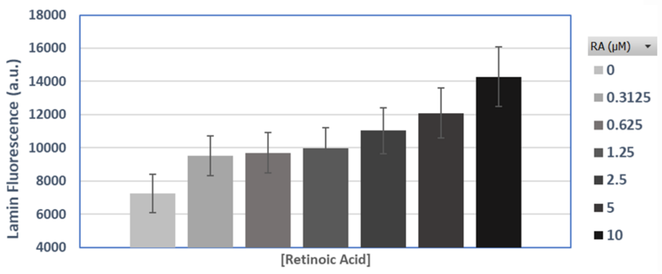
The cruel "Samurai law of biology", that is better to die than to be wrong suggests aging and cell death are unavoidable. However, growing evidence shows that modulating key pathways—such as autophagy, mitophagy, mitochondrial function, and inflammation—can delay aging and extend healthspan. At Axxam, we offer high-throughput and high-content assay services to evaluate compounds and/or targets directing to these processes. Our expertise spans toxicology, DNA damage, neurodegeneration, metabolism, dermatology and other pathways, using disease-relevant cell models including iPSC and 3D assays. Supporting target validation and hit-to-lead programs, we help partners identify new targets, mechanisms of actions and accelerate the development of anti-aging therapeutics designed to overcome biological decline.

Primary Hallmark: Genomic Instability

Nuclear structure



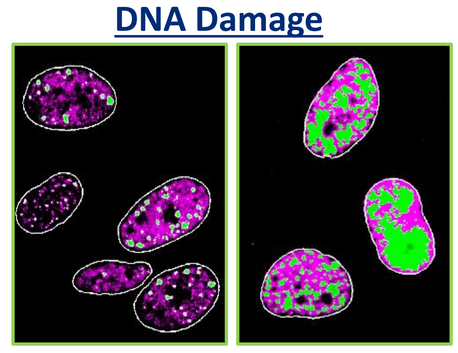
Lamin B1
Segmented Nuclei



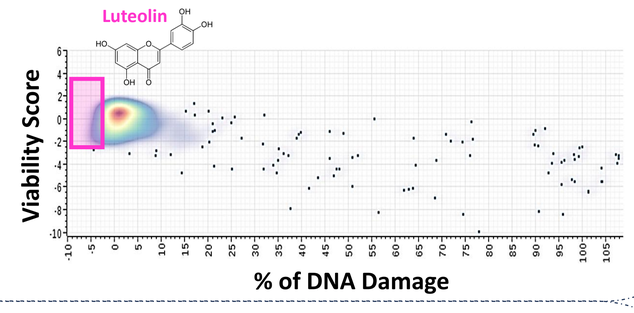
Left side: differentiated SH-SY5Y cells treated with retinoic acid (RA) and stained for Lamin B1 to visualize nuclear architecture. Structural alterations in the nuclear envelope, driven by stress-induced damage to Lamin, are phenotypes frequently associated with genomic instability

Right side: compound library screening of human osteosarcoma cells (U2OS) and DNA damage evaluation by means of phosphorylated H2AX staining. Luteolin appears to reduce/protect from DNA damage

DNA Damage

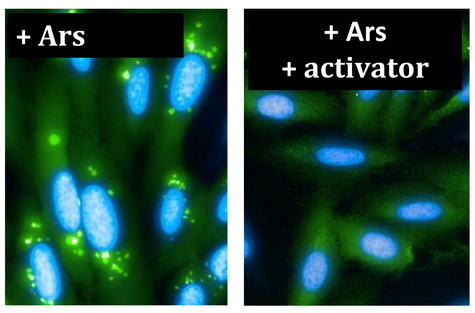


Green= γH2AX
Pink= Dapi



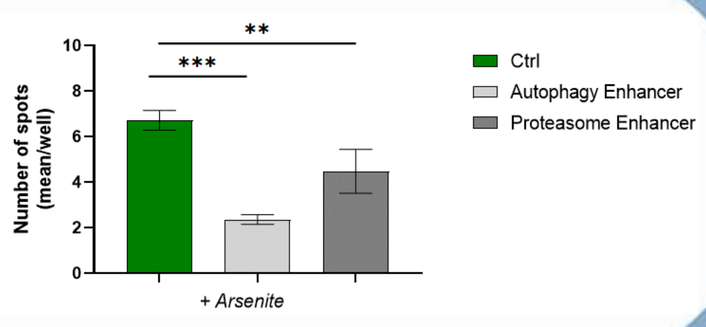
Primary Hallmark: Loss of Proteostasis

Neurodegeneration



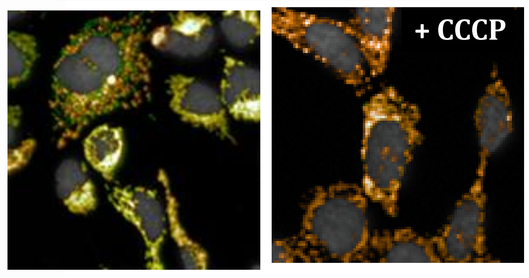
TDP43
Hoechst

Oxidative stress, occuring during aging, contributes to neurodegeneration. U2OS cells overexpressing NLS-mutated TDP-43 (green) show cytoplasmic mislocalization and pathological aggregates formation in presence of arsenite (Ars), mimicking age-related dysfunction. Treatment with proteostasis activators reduce TDP-43 aggregates

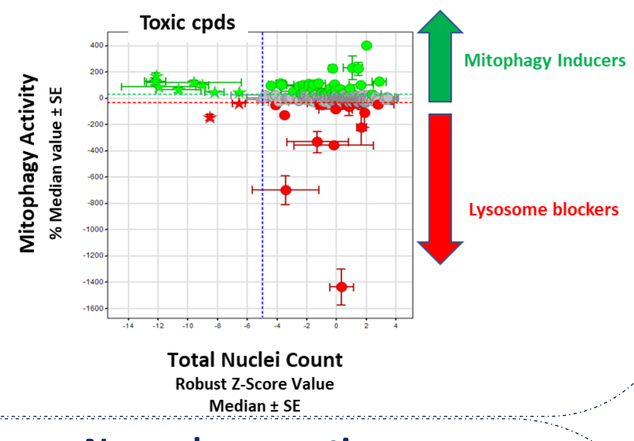


Aging impairs autophagy, leading to toxic aggregates and defective mitochondria. Here, a mitophagy reporter cell line was used to screen for compounds that restore mitophagy.

Autophagy Functionality

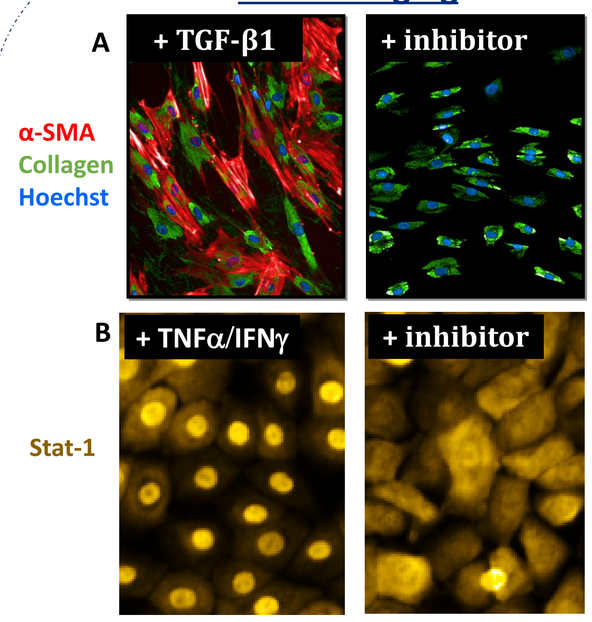


Red and Geen autophagic vesicle signals



Integrative Hallmark

InflammAging



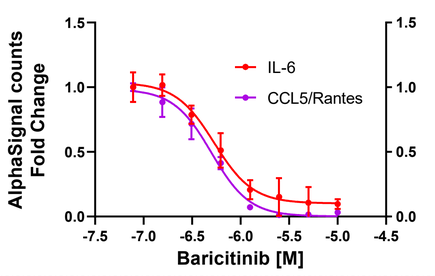
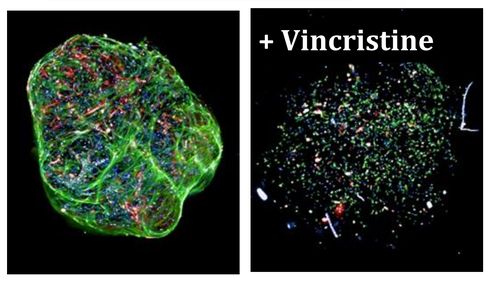


Figure A: Primary human fibroblasts stained for α-SMA and collagen I show TGF-β1–induced myofibroblast activation. Marker deposition is reduced in the presence of a specific inhibitor. This model reflects fibrotic responses that contribute to aging-related tissue dysfunction.

Figure B and C: Recombinant or primary human keratinocytes stained for STAT1 show nuclear translocation after TNF-α stress, which is reverted by an inhibitor. This models age-associated inflammatory signaling and altered intercellular communication.

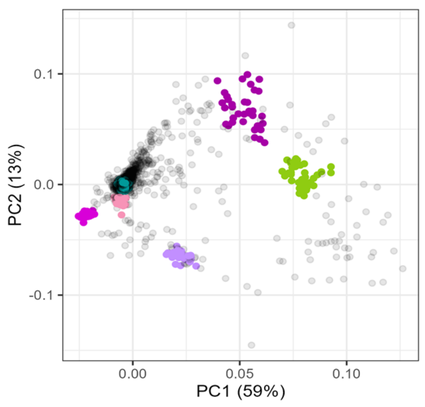
Oxidative stress contributes to aging-related neurodegeneration. A 3D minibrain model (iPSC-derived neurons and glia, developed by Tessara Therapeutics treated with vincristine shows neurite loss and altered morphology. The model can recapitulate key neurodegenerative features.

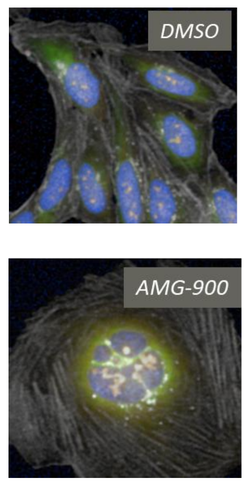
Neurodegeneration



Glial cells
Neurons
Hoechst

Cell Painting





Cell Painting enables high-content profiling of aging-related phenotypes, such as mitochondrial dysfunction, nuclear abnormalities, and cytoskeletal changes—supporting exploratory toxicology and assays linked to key aging hallmarks.

Conclusion: Advancing healthy aging requires strategies that enhance cellular viability and target key aging mechanisms.

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Literature:. 1) López-Otín et al. Cell, 2023. 2) MatiasI. Et al. Aging Cell, 2022 3) Lin Y. Et al. Neurochem Res, 2010 4) Ash P. et al, Nature Neuroscience, 2010 5) Chandrasekaran, S.N et. Cell Reports, 2021.