

charnwood
discovery

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ONCOGENE INDUCED SENESCENCE

DNA DAMAGE/TELOMERE STRESS INDUCED SENESCENCE

SENESCENCE ASSOCIATED SECRETORY PHENOTYPE (SASP)

MUTATION

RAS

OXIDATIVE STRESS

ROS

TELOMERE SHORTENING

REPLICATIVE EXHAUSTION

UNREPAIRED DNA DAMAGE

CDKN2A GENE

G1 PHASE

S PHASE

M PHASE

G2 PHASE

p53

p16

pRB

SAHF

IL6

IL8

IL1A

SENESCENT CELL

The diagram illustrates the role of senescent cells in aging and disease. A central circle labeled "Aging tissue" contains "Primary senescent cells" (red) and "SASP factors" (blue and yellow dots). Arrows point from this central circle to six surrounding panels, each showing a different outcome of senescent cell activity:

- Paracrine senescence:** Shows a senescent cell (red) releasing SASP factors (blue and yellow dots) that influence neighboring cells.
- Impaired regeneration:** Shows a senescent cell (red) releasing SASP factors that inhibit the differentiation of progenitor cells (blue and yellow dots) into new cells.
- ECM degeneration:** Shows a senescent cell (red) releasing SASP factors that lead to the breakdown of the extracellular matrix (ECM).
- Inflammation:** Shows a senescent cell (red) releasing SASP factors that trigger an inflammatory response, indicated by red dots.
- Fibrosis:** Shows a senescent cell (red) releasing SASP factors that lead to the accumulation of blue collagen fibers.
- Cancer:** Shows a senescent cell (red) releasing SASP factors that promote the proliferation of precancerous cells (green).

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graph TD; A[Examining cellular proliferation] --> B[Senescence-associated β-galactosidase activity (SA-β-Gal)]; B --> C[Cell Cycle Analysis]; C --> D[Are these responses in the absence of cell death?]; D --> E[Functional readout]; E --> F[Scratch wound assay];
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Examining cellular proliferation

Senescence-associated β -galactosidase activity (SA- β -Gal)

Cell Cycle Analysis

Are these responses in the absence of cell death?

Functional readout

Scratch wound assay

A)

B)

C)

Doxorubicin induced cell stalling of WI-38 cells.

Phase Object Count (Per Image) vs. Time (min)

Time (min)	DMSO Control	Doxorubicin 3uM	Doxorubicin 1uM
48	55	55	55
60	65	55	55
72	75	55	55
84	85	55	55
96	95	55	55
108	105	55	55
120	115	55	55
132	125	55	55
144	135	55	55
156	145	55	55
168	155	55	55

Microscopy Images:

- DMSO:** Shows a high density of cells at Day 4 and Day 6.
- Doxorubicin:** Shows a significant reduction in cell density and stalling at Day 4 and Day 6.

Figure 1: Viability of MCF-7 cells treated with Doxorubicin

The graph displays Luminescence counts (Y-axis, 0 to 1,200,000) over time (X-axis, 0 to 72 hours). Three conditions are compared: Doxorubicin 3 μ M (purple triangles), Doxorubicin 1 μ M (orange squares), and DMSO Control (black circles). The DMSO Control shows a significant increase in luminescence over time, while the Doxorubicin treatments show a much slower increase, indicating cell death or reduced viability.

The schematic illustrates the principle of the assay: A Viable cell reduces the MCF Cell Viability Substrate, which is then detected by NanoLuc® luciferase to produce Light. A Dead cell does not reduce the substrate, resulting in No Reduction and No Light.

Wound closure in FW-38 cells subject to conditioned media from senescence cells.

Relative Wound Density (%)

Time (h)

Legend:

- Doxorubicin
- Cyclochalasin D
- Doxorubicin + Quercetin
- DMSO control

Wound Closure Images:

0-hour **24-hour** **72-hour**

Doxorubicin

Doxorubicin + Quercetin

Cyclochalasin D

DMSO



A leading CRO provider of drug discovery services, from standalone customized solutions through to fully integrated programs