

Cellular Senescence

Cellular senescence is a state of cell cycle arrest that occurs in response to various stressors or stimuli. It is considered an important factor in the development of many age-related diseases and thus has become an important therapeutic target. Focus Biomolecules has assembled an extensive portfolio of small molecule research tools which includes inducers as well as senolytic and senomorphic agents.

Senescence Inducers

Senescence can be initiated by a large variety of stress-inducing agents (DNA damaging agents for example) some of which are listed below.

2',3'-cGAMP	Endogenous STING agonist	10-1639
Abemaciclib	CDK4/6 inhibitor	10-4833
Actinomycin D	Transcription inhibitor	10-2054
Aphidicolin	DNA polymerase inhibitor	10-2058
Decitabine	DNA hypomethylation agent	10-2412
BIBR1532	Telomerase inhibitor	10-3920
Bleomycin	Induces DNA double strand breaks	10-2623
Daunorubicin HCl	DNA damaging agent	10-2429
Entinostat	HDAC inhibitor	10-2131
Etoposide	Topoisomerase II inhibitor	10-1123
Ingenol-3-angelate	PKC activator	10-1244
Mitomycin C	DNA damaging agent	10-1170
Nutlin-3	MDM2 antagonist	10-1350
PMA	PKC activator	10-2165
Ribociclib	CDK4/6 inhibitor	10-4807
RITA	p53 activator	10-3385
SN-38	Topoisomerase I inhibitor	10-2425
Temozolomide	Autophagy inducer	10-2390
Tenovin-1	SIRT1/2 inhibitor	10-2982
WM-1119	KAT6A HAT inhibitor	10-4013

Senolytics

Senolytics are agents which target various prosurvival signaling pathways resulting in the elimination of senescent cells⁴. A variety of senolytic agents are shown below.

17-AAG	HSP90 inhibitor	10-1097
ABT-263 (Navitoclax)	Bcl-2 family inhibitor	10-3141
ABT-737	Bcl-2 family inhibitor	10-3661
BPTES	Glutaminase GLS1 inhibitor	10-5414
Dasatinib	Src kinase inhibitor	10-2126
Enzastaurin	PKC, PI3K/Akt inhibitor	10-2132
JQ1	BRD4 inhibitor	10-1584

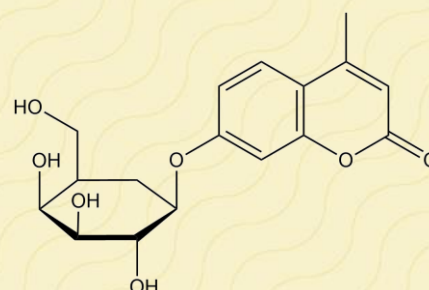
Senomorphics

Senomorphic agents are designed to suppress (senostasis) the proinflammatory senescence-associated secretory phenotype without killing senescent cells.

BAY 11-7082	IKK inhibitor	10-1296
FK866	NAMPT inhibitor	10-1109
I-BET762	BET Bromodomain inhibitor	10-4122
Metformin	AMPK activator	10-2469
ML324	KDM4 histone demethylase inhibitor	10-1455
Rapamycin	mTOR inhibitor	10-1104
Ruxolitinib	JAK/STAT pathway inhibitor	10-4511
SB 203580	p38MAP kinase inhibitor	10-2173
SR9009	REV-ERB agonist	10-1511
SRT1720 HCl	SIRT1 activator	10-4628
Zileuton	5-LO inhibitor	10-1098

Detection of Senescent Cells

The most widely used biomarker for senescent cells is senescence-associated β -galactosidase (SA- β -Gal) which has been identified as being of lysosomal origin¹. Although some doubts have been raised about specificity SA- β -Gal staining has gained broad acceptance as a marker for senescence^{2,3}. 4-MUG or 4-methylumbelliferyl- β -D-galactopyranose is a versatile fluorogenic substrate for SA- β -Gal and is converted to the blue fluorescent 4-methylumbelliferone, Ex: 342 nm and Em: 441 nm.



4-MUG For senescence detection 10-3879

REFERENCES

1. Lee et al. (2006) *Aging Cell* **5** 187
2. Gary and Kindell (2005) *Anal. Biochem.* **343** 329
3. Sosinska et al. (2014) *Biogerontology* **15** 407
4. Kirkland and Tchkonja (2020) *J. Int. Med.* **288** 518