a study years ago "zombie cells" that was based on analyzing human vertebral of elderly both living biopsies and autopsies. It indicated that as much as 70% of old vertebral disks were made up of senescent cells

You're likely recalling the 2009 **Gruber et al.** human annulus study, rather than a study of "vertebrae" themselves. It examined cells from human intervertebral-disc annulus tissue, including surgical specimens and normal donor/control tissue, using senescence-associated β-galactosidase staining. [1]

What it found

- Across the study population, mean senescent-cell prevalence was **39.6% ± 21.1%**, with a broad **range of 0.002% to 76.4%**. Thus, the "about 70%" figure is plausible for individual highly degenerated discs—not an average for all elderly discs. [2]
- Two specimens were reported at **41.1% and 71.2%** senescent cells, accompanied by very low proliferation (3.3% and 3.0%). [2]
- More degenerated Thompson grade III–IV discs averaged **44.4% ± 20.0%** senescent annulus cells versus **18.8% ± 11.0%** in grade I–II discs. [1]

Citation

Gruber HE, Ingram JA, Davis DE, Hanley EN Jr. *Increased Cell Senescence Is Associated with Decreased Cell Proliferation In Vivo in the Degenerating Human Annulus.* **The Spine Journal.** 2009;9(3):210–215. [1]

Important qualification

The result refers specifically to **annulus fibrosus cells** in intervertebral discs and operationalized senescence primarily with SA-β-gal staining. It is strong evidence that a large fraction of cells in severely degenerated human discs can show a senescence-associated phenotype, but it does **not** establish that 70% of every old person's entire discs—or vertebral tissue—are senescent. Earlier human disc work likewise found degeneration-associated senescence, though reported much lower overall proportions in other sample sets and tissue compartments. [3] [4]

Gruber HE 2009 annulus senescent cells full text summary

Gruber et al., 2009 tested whether senescent-cell burden in the human annulus fibrosus tracks with the disc's already limited capacity for cell renewal. Their central finding was that more degenerated discs had substantially more SA-β-gal–positive cells, and discs with more such cells had fewer Ki-67–positive proliferating cells. [28]

Study

Citation: Gruber HE, Ingram JA, Davis DE, Hanley EN Jr. *Increased cell senescence is associated with decreased cell proliferation in vivo in the degenerating human annulus.* **The Spine Journal.** 2009;9(3):210–215. DOI: 10.1016/j.spinee.2008.01.012. [29]

- **Material:** 26 human discs from 24 people, predominantly lumbar, with two cervical specimens. Most material was obtained at surgery; three normal-donor/control specimens were included. Subjects were 16–68 years old (mean 42.3 ± 14.3 years). [28]
- **Degeneration distribution:** Thompson grade I: 1 disc; grade II: 4; grade III: 9; grade IV: 12. There were no grade-V discs. [28]
- **Tissue analyzed:** annulus fibrosus—not vertebral bone, and not a systematic whole-disc analysis of nucleus pulposus plus annulus. [28]
- **Assays:** paraffin-embedded sections were immunostained with anti-β-galactosidase as their senescence-associated marker and Ki-67 as the proliferation marker. Investigators counted about 410 cells per specimen for the former and 229 for the latter. [28]

Results

Measure	Healthier discs, Thompson I–II	More degenerated discs, Thompson III–IV
Senescence-marker-positive annulus cells	18.8% ± 11.0% (n=5)	44.4% ± 20.0% (n=21), $p = 0.011$
Ki-67-positive/proliferating cells	5.3% ± 1.9%	4.7% ± 1.6%; not significant

Across all 26 specimens, the mean estimated senescent fraction was **39.55% ± 21.1%**, ranging from **0.002% to 76.4%**. The high-end 70%-plus value is therefore real in this dataset, but it was a specimen-level observation rather than the reported mean for older adults or for all discs. [28]

The two cervical grade-IV specimens noted in the paper had senescence estimates of **41.08% and 71.2%**, alongside only **3.3% and 3.0%** proliferating cells. [28]

Interpretation

Proliferation was low throughout: 4.09% ± 1.76% overall, with a 1.81%–9.33% range; the normal donor discs were also low at 3.8%, 3.7%, and 1.8%. Thus, the key result was not that degeneration drastically reduced an otherwise vigorous annulus-cell proliferation rate; it was that a tissue with intrinsically sparse renewal capacity accumulated a much larger senescence-associated fraction as structural degeneration advanced. [28]

The full article reports a statistically significant inverse association between the percentage of senescence-marker-positive cells and Ki-67 positivity: the figure/text indicate $r = -0.476$, $p = 0.013$, with the model explaining roughly 22% of variation in proliferation. The PubMed abstract contains what appears to be a typographical error, stating $r = -0.013$; the article's Figure 4 and discussion give the interpretable value of -0.476. [29] [28]

Important caveats

- **Not elderly-only:** the cohort's mean age was ~42, the age range was broad, and the authors found *no significant association* of chronological age with either marker. Their principal association was with degeneration grade, not age per se. [28]
- **Marker limitation:** anti-SA-β-gal immunolocalization alone is not the modern multi-marker definition of cellular senescence. The result is best described as a high burden of **SA-β-gal–positive, senescence-associated annulus cells**, not definitive proof that every positive cell fulfilled a contemporary p16/p21, persistent DDR, cell-cycle-exit, and SASP phenotype.
- **Cross-sectional correlation:** the study cannot establish whether senescence initiated degeneration, accumulated secondarily to degeneration's mechanical/hypoxic/oxidative milieu, or both. The authors explicitly note that correlation does not establish causation. [28]
- **No direct SASP intervention:** it did not test senolytics, senomorphics, or whether removing these cells restored matrix homeostasis or disc function.

Follow-up molecular evidence

Gruber's 2010 follow-up used laser-capture microdissection to compare SA-β-gal–positive and paired non-positive annulus cells from 11 grade-3 to -4 human discs. Those specimens had 46.1%–92.0% marker-positive cells, making it a likely source of an even more striking "most of the disc cells are zombie cells" recollection. The microarray comparison found 292 upregulated and 321 downregulated transcripts in the putative senescent population, including increased p38/MAPK14, GADD45β, ING5, and RBAK, plus changes consistent with altered matrix turnover and inflammatory signaling. [30]

That molecular study supports the interpretation that the marker-positive cells were biologically different from neighboring cells, while still not resolving causality or demonstrating that broad senolysis would be safe or regenerative in human discs. [30]

⁂

Senolytics for intervertebral disc degeneration research

Senolytics are a credible **preclinical** strategy for intervertebral-disc degeneration (IVDD), with compelling human ex-vivo and animal results—but there is not yet a validated human clinical treatment for discogenic low-back pain or IVDD.

Why target senescence?

In a degenerating disc, senescent annulus and nucleus-pulposus cells can persist despite cell-cycle arrest and produce a SASP enriched in inflammatory mediators and matrix-degrading enzymes. The proposed therapeutic logic is to selectively remove these cells—or suppress their SASP—to reduce IL-6/MMP signaling, preserve proteoglycan/collagen homeostasis, and interrupt self-reinforcing degeneration.[36]

The key translational constraint is that discs are sparsely cellular, avascular, and poorly regenerative. A useful senolytic must therefore be selective enough not to deplete essential residual disc cells, must reach the appropriate compartment, and probably needs use at an early/moderate stage where viable matrix-producing cells remain.

Strongest studies

Approach	Model	Principal result	Translational reading
o-Vanillin + RG7112	Naturally degenerated human discs, ex vivo	Both selectively reduced senescence/SASP measures; a single treatment improved matrix-homeostasis measures in intact human degenerative discs	Best direct human-tissue evidence, but it is ex vivo—not a clinical outcome study.[37]
PLGA-encapsulated navitoclax (ABT-263)	Rat, injury-induced IVDD; intradiscal injection	A single local injection reduced senescent cells, pro-inflammatory cytokines and matrix proteases, slowed degeneration, and restored structural measures	Strong delivery concept; avoids much of the systemic exposure concern with navitoclax.[38]
o-Vanillin + RG7112	SPARC-null mouse model of disc degeneration/low-back-pain phenotype; oral dosing	Reduced behavioral pain indices, SASP release, senescent-cell measures in discs/spinal cord, disc-degeneration scores, and improved vertebral bone-quality measures	Important because it linked senescence targeting to pain-related phenotypes, but remains murine evidence.[39]
Dasatinib + quercetin (D+Q)	SM/J early-onset degeneration mouse model	D+Q lowered $p19^{ARF}$, p21, SASP markers, degeneration severity, fibrosis/remodeling; navitoclax did not achieve comparable benefit in this model	Suggests senolytic efficacy is context- and cell-state-specific rather than a class effect.[40]

Human-tissue evidence: Cherif et al.

The most relevant human study is **Cherif et al., eLife 2020**, *Senotherapeutic drugs for human intervertebral disc degeneration and low back pain*. It used cultured human IVD cells and intact, naturally degenerated human discs maintained ex vivo. **RG7112**—an MDM2 antagonist—and **o-vanillin** reduced senescence-associated cells and SASP outputs; in intact discs, a single treatment improved matrix-homeostasis readouts associated with less senescence/SASP.[37]

This work is promising because it used genuinely degenerated human discs rather than an exclusively toxin- or injury-driven rodent model. However, it does not show durable disc regeneration, restored human biomechanics, improved MRI endpoints, or reduced pain in people.[37]

Delivery is central

Local intradiscal delivery is arguably the more rational first clinical modality:

- It bypasses the disc's low perfusion and may achieve exposure with less total drug.
- PLGA nanoparticle delivery of navitoclax demonstrated proof-of-concept in rats after a **single** intradiscal administration. [38]
- It could reduce systemic risks, particularly relevant for agents such as navitoclax, whose on-target BCL-xL inhibition is associated with clinically significant thrombocytopenia.

Systemic D+Q or other systemic senolytics could potentially address multilevel disc disease and adjacent vertebral/endplate or systemic senescence, but exposure at the avascular nucleus pulposus is uncertain and their benefit-risk calculus is less favorable for isolated disc pathology. The 2026 mouse work specifically found D+Q benefit where navitoclax was ineffective, underscoring that target selection, delivery, and disc-cell subtype matter. [40]

Practical research status

No established human IVDD senolytic trial supports routine therapeutic use at present. D+Q has been evaluated clinically in other contexts, but that is not evidence of efficacy or safety for disc degeneration, and neither the 2020 human ex-vivo work nor the rodent studies establish an appropriate clinical dose, route, patient phenotype, biomarker threshold, or treatment interval for IVDD. [41] [36]

For a serious translational program, the most defensible near-term development package would be:

- Select patients with **early-to-moderate, phenotyped discogenic disease**, rather than end-stage collapsed/fibrotic discs.
- Establish a multiplex senescence baseline—p16/p21, persistent DNA-damage signaling, SASP profile, and preferably spatial cell-state analysis—rather than relying on SA-β-gal alone.
- Favor local controlled-release administration initially, with platelet and systemic safety monitoring if BCL-2-family targeting is used.
- Predefine clinical endpoints: pain/function, MRI hydration/structural measures, quantitative disc biochemical markers, and ideally biomarkers demonstrating target engagement.
- Compare senolysis with senomorphic approaches, because suppressing harmful SASP without eliminating scarce disc cells may be preferable in advanced hypocellular discs.

The evidence supports **a disease-modifying hypothesis**, not a treatment recommendation yet.

⁂

1. https://www.spine.org/Portals/0/Documents/ResearchClinicalCare/GrantWinners/Gruber06.pdf
2. https://link.springer.com/article/10.1186/1472-6750-10-5
3. https://pmc.ncbi.nlm.nih.gov/articles/PMC2335374/

4. https://pmc.ncbi.nlm.nih.gov/articles/PMC2206356/
5. https://www.mdpi.com/2218-273X/13/4/686
6. https://rheumnow.com/news/senescent-zombie-cells-and-low-back-pain
7. https://discoverysedge.mayo.edu/2023/11/16/health-and-zombie-cells-in-aging/
8. https://www.techexplorist.com/chronic-back-pain-new-drugs-show-promising-effects/99070/
9. https://www.cellularhopeinstitute.com/eliminating-zombie-cells-slow-down-aging/
10. https://event.fourwaves.com/fe9a2894-7998-4912-952e-2ef2668a26f7/abstracts/d5e2b2c8-f187-485d-bdbc-1c550ca7df77
11. https://www.youtube.com/watch?v=QIDgDPD4jiA
12. https://www.drugtargetreview.com/targeting-zombie-cells-a-new-treatment-for-chronic-back-pain/650015.article
13. https://pmc.ncbi.nlm.nih.gov/articles/PMC6248341/
14. https://onlinelibrary.wiley.com/doi/10.1155/2020/9503562
15. https://www.ijbs.com/v20p2370.htm
16. https://ouci.dntb.gov.ua/en/works/l1wamkB7/
17. https://www.sciencedirect.com/science/article/pii/S1063458415013333
18. https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2022.1038171/full
19. https://da.lib.kobe-u.ac.jp/da/kernel/0100490415/0100490415.pdf
20. https://www.fightaging.org/archives/2019/03/senescent-cells-as-a-contributing-cause-of-degenerative-disc-disease/
21. https://www.tandfonline.com/doi/full/10.1080/15384101.2016.1152433
22. https://www.oarsijournal.com/article/s1063-4584(15)01333-3/fulltext
23. https://pubmed.ncbi.nlm.nih.gov/17268263/
24. https://elifesciences.org/articles/107777
25. https://link.springer.com/article/10.1186/ar2198
26. https://www.biorxiv.org/content/10.1101/2024.02.22.581620v1.full
27. https://www.cedars-sinai.org/stories-and-insights/healthy-living/zombie-cells
28. https://www.spine.org/Portals/0/Documents/ResearchClinicalCare/GrantWinners/Gruber06.pdf
29. https://pubmed.ncbi.nlm.nih.gov/18440281/
30. https://pmc.ncbi.nlm.nih.gov/articles/PMC2828399/
31. https://www.sciencedirect.com/science/article/abs/pii/S152994300800048X
32. https://www.aging-us.com/article/100201/text
33. https://www.spandidos-publications.com/10.3892/mmr.2017.8322
34. https://www.sciencedirect.com/science/article/pii/S1063458415013333
35. https://www.oarsijournal.com/article/s1063-4584(15)01333-3/fulltext
36. https://pmc.ncbi.nlm.nih.gov/articles/PMC8924288/
37. https://elifesciences.org/articles/54693
38. https://pubmed.ncbi.nlm.nih.gov/34699690/
39. https://pmc.ncbi.nlm.nih.gov/articles/PMC11908501/

40. https://www.nature.com/articles/s41413-026-00526-4
41. https://pmc.ncbi.nlm.nih.gov/articles/PMC8417260/
42. https://www.fightaging.org/archives/2022/04/senolytics-as-a-treatment-for-intervertebral-disc-degeneration/
43. https://www.eurekalert.org/news-releases/1129421
44. https://www.drugtargetreview.com/study-suggests-senolytic-therapies-could-slow-spinal-disc-degeneration/2135596.article
45. https://europepmc.org/article/med/34699690
46. https://www.semanticscholar.org/paper/67ff0108bf73c434529bcc148a29bf04d4a45f24
47. http://biorxiv.org/cgi/content/full/2025.10.08.681005v1
48. https://www.frontiersin.org/journals/bioengineering-and-biotechnology/articles/10.3389/fbioe.2022.823945/pdf
49. https://www.news-medical.net/news/20260525/Senolytic-therapy-delays-early-disc-degeneration-in-mouse-model.aspx
50. https://www.drugdiscoverynews.com/drugs-that-slay-undying-cells-could-reduce-back-pain-16383
51. https://snu.elsevierpure.com/en/publications/local-delivery-of-senolytic-drug-inhibits-intervertebral-disc-deg/fingerprints/
52. https://advanced.onlinelibrary.wiley.com/doi/10.1002/advs.202522770
53. https://www.sciencedirect.com/science/article/pii/S2214031X24000172
54. https://lifespan.io/senolytics-decrease-low-back-pain-in-mice/