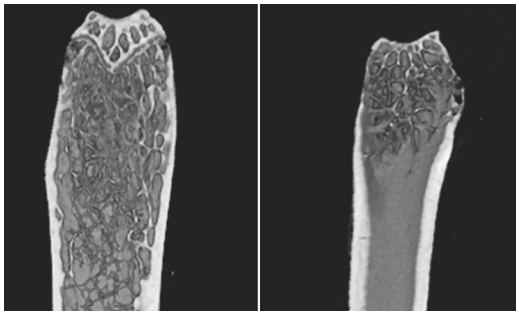


Femurs from 6-month-old mice from *Becn1* wild-type (left) and *Becn1* cKO (right) mice, showing a thickening of the cortical bone but diminished trabecular bone mass in cKO mice. Image courtesy of Reuben Kim/UCLA School of Dentistry.

> the bone-resorbing function of osteoclasts is decreased in *Becn1* cKO mice

"Targeting autophagy in osteoclasts would be a great strategic way to prevent pathologic bone loss; however, based on our findings, this strategy might come with a cost of inhibiting chondrocyte differentiation and long bone growth," concludes Kim. "Our future studies will aim to develop ways of inhibiting autophagy in an osteoclast-specific manner."

Shimona Starling

ORIGINAL ARTICLE Arai, A. et al. Beclin1 modulates bone homeostasis by regulating osteoclast and chondrocyte differentiation. *J. Bone Miner. Res.* https://doi.org/10.1002/jbmr.3756 (2019)

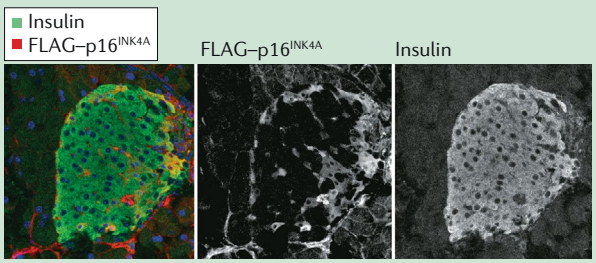


Image shows a mouse pancreatic islet, with insulin-positive β-cells (green) and FLAG–p16^{INK4A}-expressing (red) senescent cells. Image courtesy of Cristina Aguayo-Mazzucato/Harvard Medical School.

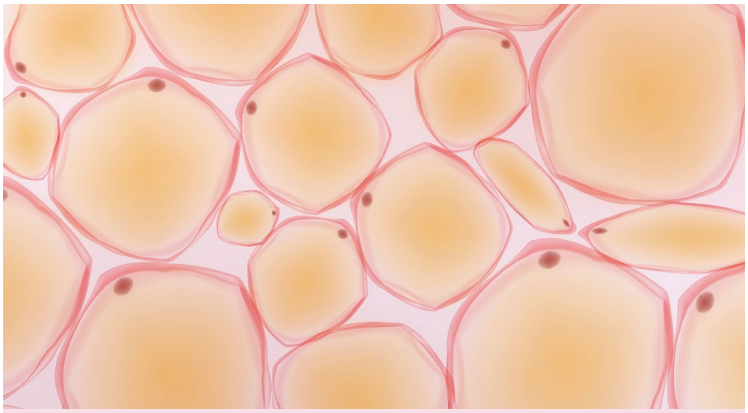
> β-cell senescence contributes to T2DM and … this process could be targeted with senolytic therapies

with a senolytic drug," says Aguayo-Mazzucato.

"Going forward, we would like to improve our understanding of β-cell senescence and its role in insulin secretion and limitations of β-cell proliferation," concludes Aguayo-Mazzucato. "Our ultimate goal is to take the principle of senolysis to the clinic as a new way to treat prediabetes and early onset T2DM."

Shimona Starling

ORIGINAL ARTICLE Aguayo-Mazzucato, C. et al. Acceleration of β cell aging determines diabetes and senolysis improves disease outcomes. *Cell Metab.* https://doi.org/10.1016/j.cmet.2019.05.006 (2019)



Credit: Benjamin Toth/Getty

ADIPOSE TISSUE

New role for adipocytes in tumour-associated bone disease

Adipocytes have traditionally been seen as fat storage cells, but studies from the past decade have highlighted a role for adipocytes in tumour growth. Now, a new paper published in *Science Translational Medicine* reports that these multifaceted cells also have a function in tumour-associated bone disease. Specifically, the authors show that following exposure to myeloma cells, adipocytes are reprogrammed and gain the ability to resorb bone.

"Our lab is interested in the pathogenesis of myeloma-associated bone disease, with a specific focus on how myeloma cells regulate bone remodelling," explains corresponding author Jing Yang. "While observing the bone marrow specimens from patients in remission, we could not overlook the prominent presence of adipocytes around the bone." This observation led the authors to hypothesize that adipocytes might have a critical role in the bone lesions themselves.

To investigate their hypothesis, the authors first recreated the adipocyte–bone phenomenon seen in patients in remission in a humanized mouse model. The mouse model reflects the different stages of disease whereby it first displays an active myeloma, then after treatment, the model stays in remission. The team found that mice that were injected with conditioned medium from adipocytes obtained from patients with newly diagnosed myeloma caused multiple large lytic lesions. By contrast, mice that were injected with control medium were found to have little bone resorption.

Next, Yang and colleagues created adipocyte-specific enhancer of zeste homologue 2 (EZH2)-knockout mice to evaluate the importance of EZH2 enzymatic activity in the failure of bone healing. To model myeloma in remission, the investigators injected murine myeloma into EZH2-knockout mice before treating them with chemotherapy. The team then evaluated the extent to which the myeloma was resolved by assessing levels of M-protein, which is an indicator of myeloma burden, and CD138$^+$ myeloma cell infiltration in marrow or other organs. Following an assessment of the mice 2 weeks after treatment, Yang and colleagues could only detect a few infiltrated CD138$^+$ cells and could not detect any M-protein, suggesting that the mice were almost free of myeloma.

"Our study provides an explanation for the mechanism of lytic bone disease development in patients with active myeloma, but questions regarding why bone lesions persist in patients after treatment — even when in remission — still remain," concludes Yang. "We are now planning to investigate how other stromal cells are involved in the failure of bone healing in patients in remission so as to get a complete picture within marrow niche."

Alan Morris

ORIGINAL ARTICLE Liu, H. et al. Reprogrammed marrow adipocytes contribute to myeloma-induced bone disease. *Sci. Transl Med.* https://doi.org/10.1126/scitranslmed.aau9087 (2019)