Journal club

CELLULAR SENESCENCE CAUSES AGEING

In my view, the study published by the van Deursen group in 2011 (Baker et al.), reporting that the elimination of senescent cells can delay ageing-associated disorders, transformed this research field. First, it provided evidence for cellular senescence having a role in ageing, a hypothesis that had been around for about 50 years. But also crucially, it exposed the unexpected potential for the selective elimination of senescent cells to be of benefit for treating diseases as diverse as cancer, atherosclerosis, osteoarthritis or glaucoma — taking research on cellular senescence to new heights.

Senescence defines a stable growth arrest that is induced when cells reach the end of their replicative potential or are exposed to different stressors. This cell state was discovered serendipitously by Leonard Hayflick when culturing primary human fibroblasts to grow viruses. He stumbled upon something unexpected: primary cells could be cultured for a while but eventually stopped proliferating. This was the first suggestion that cellular senescence might be linked to ageing. But the excitement was followed by high levels of scepticism. Could cell senescence be just an artefact resulting from non-physiological cell culture conditions rather than a defined physiological cell state?

In 1997, the discovery by Serrano et al. that cellular senescence can be ‘prematurely’ triggered by the expression of oncogenic Ras sparked new interest as it suggested that senescence is associated with cancer. But, the physiological relevance of oncogene-induced senescence (OIS) was disputed. It wasn’t until 2005 senescent cells were identified in premalignant lesions but not in more advanced lesions; an observation consistent with OIS being a mechanism for tumour suppression. This breakthrough led researchers to re-focus on the role of senescence in cancer rather than ageing.

Baker et al. not only settled a looming question of half a century, it also provided a tool (the INK-ATTAC mouse model to eliminate senescent cells) to validate the causative role of senescence in a myriad of diseases. In addition, the paper also formulated a new concept: that the elimination of senescent cells has widespread benefits. It is not often that a paper spearheads such a revolution. A decade has not yet passed and there are already multiple investments on therapeutic strategies based on the idea that selective elimination of senescent cells can improve healthspan. We can safely say, more than 60 years since senescence was first discovered, that research on cellular senescence looks anything but arrested.

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