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Editorial

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Leonard Hayflick (1928-2024) – obituary

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On August 1, 2024, the aging field lost one of his pioneers, Leonard Hayflick. Dr. Hayflick was Professor of Anatomy at the UCSF School of Medicine, and Professor of Medical Microbiology at Stanford University School of Medicine. He served as president of the Gerontological Society of America and as a founding member of the Council of the National Institute on Aging (NIA).

Dr. Hayflick was born in Philadelphia in 1928 and received a PhD from the University of Pennsylvania. He then spent a brief period at the University of Texas as a postdoctoral fellow before returning to Philadelphia to work at the Wistar Institute. There, he developed an interest in studying how cells can be cultured ex vivo, and how this could be important for the manufacturing of vaccines.

When Hayflick pursued his initial research, the extensive laboratory use of cancer cells, many of which are immortal, led scientists to believe that individual cells do not age when cultured outside the organism. In 1961, Leonard Hayflick, together with Paul Moorhead, reported in a seminal paper that cultures of human fetal fibroblasts, comprising a total of 25 independent isolates, were not immortal and degenerated after approximately 50 sub-cultivations[1]. The work included other insightful observations, such as the fact that cultivation history was not affected by freezing/thawing cycles, which he interpreted as reflecting some kind of molecular memory of the age of cells. In a follow-up paper in 1965[2], Hayflick reported that, for adult lung fibroblasts (mostly from donors aged 58–87 years), the number of doublings was substantially lower than that of fetal lung fibroblasts (approximately 20 doublings for adult fibroblasts and approximately 50 for fetal fibroblasts). He also mixed female cells at an early passage with male cells at a high, non-proliferative, passage and observed that the 'old' cells did not affect the proliferative lifespan of the 'young cells'. Based on these and other observations, Hayflick reached two remarkable conclusions: (1) "intrinsic factors" in actively proliferating cells are progressively depleted (or accumulated) until they reach a critical threshold that limits further growth and (2) this phenomenon also operates during organismal aging. This marked the beginning of a new field of research, cellular senescence, a process that plays a major role in human aging and disease, and that remains an extremely active topic of research.

Today, 60 years after the above discoveries, cellular senescence is regarded as an evolutionarily ancient response that can be activated in almost all types of cells by the accumulation of multiple types of cellular damage. Cellular senescence allows cells to self-restrain their own proliferation in a stable manner, while simultaneously modifying their microenvironment through the secretion of soluble factors. The secretome of senescent cells, discovered by Judith Campisi, another giant in the field who sadly passed away this year, has complex effects on neighbouring cells depending on the tissue context. These effects can be positive, for example, assisting in tissue repair, but very often senescent cells promote fibrosis and chronic inflammation, thereby becoming pathological. Understanding these intricacies and how to manipulate them therapeutically is one of the most pressing challenges in the current field of cellular senescence.

In addition to his important fundamental discoveries, Leonard Hayflick also represents a role model for the translation of basic research into medical applications. The fetal lung fibroblasts that he isolated at the Wistar Institute, particularly the isolate named WI-38, became the cell line of choice for many pharmaceutical companies to grow viruses for manufacturing vaccines[3]. This cell line was carefully characterized by Hayflick and was specially attractive because of its chromosomal stability and absence of pre-existing infectious agents, both of which were major problems in vaccine manufacturing. The 'Hayflick cells', WI-38, have been the basis for producing vaccines for poliomyelitis, measles, mumps, rubella, varicella, adenovirus, rabies, and hepatitis A. Over the last 50 years, the number of people benefiting from these vaccines has been estimated to be several billion worldwide[3]. Regrettably, the success of WI-38 was also a cause of great frustration for Hayflick. Given the high demand for WI-38 and the lack of support from his funders (Stanford University and the NIH), he decided to create a company to cover maintenance and shipping costs. This led to years of legal battles and litigation with the NIH that were eventually resolved exonerating Hayflick of any wrongdoing[4].

During the last decades of his career, Hayflick has been a visible member of the cellular senescence and aging research community, playing an active role as consultant for several companies and scientific societies. The International Cell Senescence Association (ICSA) presented him on August 17, 2021, with a plaque naming him the First Honorary Member of ICSA. This was a well-deserved tribute from a lively community of researchers, both young and senior, who continue to build on the scientific legacy of Leonard Hayflick.

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Competing interests

The author declares no competing interests.

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