**Aging Pathobiology and Therapeutics** 2022; 4(3): 90-92 ***90***
DOI: 10.31491/APT.2022.09.094



# On the frontier of immunogerontology—an interview with Prof. Graham Pawelec

Xiaodong Li[a]

[a] *The Africa Hepatopancreatobiliary Cancer Consortium (AHPBCC), Mayo Clinic, Jacksonville, FL, USA.*

## Abstract

The article is an interview with Prof. Graham Pawelec of the Department of Immunology at the University of Tübingen, conducted by Xiaodong Li of the Mayo Clinic African Hepatobiliary Cancer Consortium (AHPBCC), on behalf of *Aging Pathobiology and Therapeutics*.

**Graham Pawelec, PhD**

Graham Pawelec received an MA in Natural Sciences in 1978 and a PhD in Transplantation Immunology in 1982 from the University of Cambridge, UK, and the Dr. habil and Venia Legendi from the University of Tübingen, Germany, where he became Professor of Experimental Immunology in 1997. From 1999 to 2017 he led the Tübingen Ageing and Tumour Immunology (TATI) group within the Second Department of Internal Medicine, University of Tübingen Hospitals System. He remains affiliated part-time Faculty at the Department of Immunology, University of Tübingen. He is currently affiliated with the Cancer Solutions Program, Health Sciences North Research Institute of Canada, Sudbury, ON, and is a Visiting Professor at Nottingham Trent University, UK, King´s College London, London, UK, and is an Honorary Professor at Manchester University, UK.

***Xiaodong Li:*** Let's have everyone get to know you first, can you tell us how you got into the field of immunology research and where were your early passions?

***Graham Pawelec:*** After studying a mixture of preclinical and biology subjects as an undergraduate at Cambridge University (which did not have a Clinical School at that time), I stayed in Cambridge and graduated with a History & Philosophy of Science, MA 1976 (Cambridge was the only British University offering this specialty at that time). Although I retain an interest in this fascinating topic, I felt that I needed to do something of more practical relevance to humanity and so embarked on a job as Research Assistant in the Dept. Surgery at Cambridge, which was pioneering solid organ transplantation and immunosuppression at that time. This was on the front lines of medical interventions to save lives and was very exciting in the late 1970s. I registered for a Ph.D., finally submitted in 1982, four years after I left Cambridge and moved to Germany to continue work in human transplantation - but in the even more demanding and difficult area of bone marrow transplantation for leukemia (Tübingen was one of the first medical schools in the country to set up a BMT unit). This aroused our interest in anti-tumor immunity in general due to the anti-leukemia effects of the transplant; culturing T cells in vitro for adoptive immunotherapy and use as agents for tissue matching then aroused interest in the aging of cells in culture, and eventually in immune aging in general. And after all these years, the issues of specific transplantation tolerance, anti-cancer immunity, immunosenescence, and vaccination efficacy in the elderly are all still open and exciting and crucial for enhancing the health and longevity of older adults worldwide. So that is still my passion.

* Corresponding author: Xiaodong Li, PhD
Mailing address: The Africa Hepatopancreatobiliary Cancer Consortium (AHPBCC), Mayo Clinic, Jacksonville, FL, USA.
Email: shuiliuhefang@163.com
**Accepted: 08 August 2022 / Published: 30 September 2022**

***Xiaodong Li:*** You have a legendary career. You achieved great success in multiple countries. Can you share your experience in achieving that?

***Graham Pawelec:*** Actually, I have been very sessile, based only in Cambridge, and then for more than 40 years in Germany. My work in Canada and visiting professorships in the UK did not involve lengthy stays, but mostly shorter-term visits. Nonetheless important for collaborations and mentoring, especially the Canadian collaboration on influenza vaccination in the elderly. Very important to have international collaborations. It is crucial to be able to maintain these across borders that do not exist in science.

***Xiaodong Li:*** Much of your work has remained centered on immunogerontology, vaccination, and cancer immunology/immunotherapy. What are some highlights of your research findings in this field?

***Graham Pawelec:*** 1. My earliest contributions were addressed to transplantation immunology and how to prevent graft rejection and induce immunological tolerance. We were the first to demonstrate the immunosuppressive properties of Cyclosporin A and that it preferentially inhibited T cells, not B cells. The introduction of this new-generation immunosuppressive agent revitalized organ transplantation in Cambridge and allowed the re-introduction of pediatric kidney transplantation.

2. We pioneered techniques to establish long-term cultured human T cell clones (TCC) and undertook extensive characterization of their properties in vitro. We established that such clones possessed finite lifespans in culture (unexpected at the time). In attempts to parallel longitudinal in vitro models of immune aging during long-term culture of TCC, we began to analyze younger and older people for characteristics of immunosenescence. Using the biomarkers established from cultured TCC, we asked which were also seen ex vivo. Early on, this drew our attention to the role played by a chronic viral infection, especially and unexpectedly with the common herpesvirus Cytomegalovirus (CMV). We hypothesized that chronic antigenic stimulation "exhausted" T cell immunity and that this could contribute to decreased immunosurveillance against pathogens and cancer. We showed that CMV was part of a cluster of simple immune parameters predicting survival in the very elderly, the "Immune Risk Profile" (IRP). We studied this in the context of different populations and ethnicities, and under different circumstances (*e.g.*, variable socioeconomic status, psychosocial status, health status). We have examined these issues in well-characterized European (Germany, Holland, Belgium, Sweden, Britain) and non-European (Pakistan, Singapore) populations.

3. When performing immune monitoring studies of cancer patients undergoing experimental immunotherapies, we were aware of the potential impact of age and CMV on immunocompetence potentially impinging on the success or failure of such therapies. We showed that the melanoma patients´ functional T cell responses against certain tumor antigens predicted survival. Together with assays of regulatory T cells and myeloid-derived suppressor cells, these studies began to provide powerful tools for predicting patient outcomes and stratifying responders and non-responders. We recently extended these studies to breast cancer patients—specifically, investigating older women and showing that their "immune signatures" measured as outlined above also predicted survival, as they did for younger patients.

4. In the context of vaccination, as well as our contributions in the cancer immunotherapy field, including the first study to show a clinical benefit of multi-peptide vaccination in renal cancer patients, we dissected the detrimental effect of age-vs-CMV infection on influenza vaccination in the elderly. These studies included findings on the influence of CMV infection on antibody responses of older people to the first seasonal influenza vaccine to be licensed specifically for use in the elderly and studies directed at identifying mechanisms responsible for weaker memory responses to viral core proteins.

***Xiaodong Li:*** Can you share with us your current focus and what you most want to achieve?

***Graham Pawelec:*** Currently, I am focusing on mentoring, consulting, editing, and reviewing. These interactions range from work in mentoring programs such as that of the Gerontological Society of America, and the new peer-review mentoring program of the Society for Immunotherapy of Cancer (very important in my view) to consulting for biotech startups, reviewing grant and fellowship applications for international bodies, and attempting to teach colleagues and doctors that the immune systems of older adults are not intrinsically incapable of responding adequately to vaccines as is commonly believed. I am arguing for a paradigm shift away from the "received wisdom" that immunosenescence is inevitably responsible for decreased responses to vaccination, and for increased susceptibility to infectious disease and cancer–especially for the latter there is very little actual evidence.

***Xiaodong Li:*** You continue to publish highly impactful work over your long career. Any advice for junior colleagues on how to build and maintain that productivity for so long?

***Graham Pawelec:*** I think that if someone is enthusiastic about science and discovery from a young age, this never changes over the years. Experimental science is not "just another job" - it demands sacrifice, social and often financial, and someone who is not fully committed to an ongoing uphill battle should consider a different career from the beginning.

***Xiaodong Li:*** At what point in your career did you begin to get involved with editorial roles?

***Graham Pawelec:*** Mid-level, I guess. My first Editorial Board membership invitation was some time around 1990 I guess.

***Xiaodong Li:*** (Follow up) Do you think it's beneficial for early career investigators? If yes, Any advice to help junior faculty/early career researchers obtain editorial roles?

***Graham Pawelec:*** I think it is essential to learn how to act

as a competent peer reviewer, starting at the predoctoral level. Reliable work for a particular journal may then eventually result in a meaningful invitation to join the Board. However, Board membership has less meaning nowadays when journals invite anyone who has acted as an ad hoc reviewer to join the Board and end up with hundreds of members. Editing special issues may still be of interest if the guest editor can solicit invitations and oversee the reviewing process, but this would usually require more seniority.

***Xiaodong Li:*** Thank you, Prof. Pawelec. Lastly, I would like to take the chance to thank you for mentoring and advising us.

***Graham Pawelec:*** Thank you for asking.