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Cytomegalovirus and age-related disease conditions——an interview with Prof. Patricia Price

Ying Li[a,*], Jianwen Chen[a], Yujing Fang[a]

[a] *Attending physicians, Department of Neurology, First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning Province, China.*

Abstract

The article is an interview with Prof. Patricia Price of the Curtin Medical School, Curtin Health Innovation Research Institute, Curtin University, Bentley, Australia conducted by Ying Li *et al*. from the Department of Neurology, First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning Province, China, on behalf of *Aging Pathobiology and Therapeutics.*

Patricia Price, MD

Prof. Patricia Price is a professor of immunology at University of Western Australia and an immunologist based at Curtin University in Perth. She has been engaged in immune related virus for over 40 years. The research has addressed the immunopathogenesis of viral diseases – notably Cytomegalovirus (CMV) and HIV. Since beginning her research in Asia in 2008, Professor Price has designed and run studies addressing co-infection with HIV and other viruses in a developing world setting. In addition, another research direction is to seek mechanisms that may alter the immune footprint of HCMV in individuals, providing new directions and ideas for further research and improvement of viral host interaction mechanisms. Patricia Price is also the author or editor of more than 300 articles in medical journals. (https://staffportal.curtin.edu.au/staff/profile/view/patricia-price-88ee06d7/)

Ying Li et al.: Hello, Prof. Price, nice to meet you. We are attending physicians from the Department of Neurology, First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning Province, China. Our team is now under the research field of immunosenescence on neurology, which is related to your research field. First of all, can you give a general introduction to your research direction?

Patricia Price: My research has addressed the immunopathogenesis of viral diseases – notably cytomegalovirus and HIV. This response will focus on CMV as 60-80% of all people in the world are CMV seropositive. The virus replicates the salivary gland so nobody can remain unexposed. CMV encodes homologues of several human genes implicated in immunoregulation and consequently affects the hosts immune system in a dose-dependent manner. In addition, successive CMV reactivations throughout life stimulate T-cell responses and hence drive immunosenescence. Hence CMV should be considered in all evaluation of the immune system in old age. These changes occur at a younger age in people living with HIV. Metrics of the burden of CMV associate with many diseases of aging – most notably cardiovascular disease.

Ying Li et al.: That sounds very interesting. Many patients in our department also have cardiovascular diseases. However, we never pay attention to their CMV burden. We have read many of your papers and know that you have done wonderful work on the interactions between CMV and cells of the immune system [1]. What made you switch to kidney transplant patients and evaluate the role of the

* Corresponding author: Ying Li
Mailing address: Department of Neurology, First Affiliated Hospital of Dalian Medical University, Dalian, Liaoning Province, China.
Email: nancy_942@163.com
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CMV footprint in cardiovascular health according to your publication [2]?

Patricia Price: Kidney transplant patients have a high burden of CMV so changes are likely to be most apparent in these people. The focus on CVD was partly driven by available funding, but is a logical progression. Issues with a clinical impact should be chosen when they are amenable to scientific study.

Ying Li et al.: Yes, we agree with that. Your work has pioneered the study of the relationship between cardiovascular disease and CMV, which is a huge field. When you were studying the pathological consequences of the CMV footprint, did you ever think that your work would become a landmark in the development of this field? Do you think there is still work to be done in this area? In future research, will your laboratory continue to explain individual differences in cardiovascular disease by CMV response according to your publication [3]?

Patricia Price: One always hopes to do work described as "landmark" but one should not give up hope as long as publications are passing peer review in acceptable journals. The important thing is to think hard about your own data and about what you are reading, and then write clearly so that every paper tells a story. I do believe that CMV influences CVD, but issues around assessment of the burden of CMV in an individual are too often overlooked.

Ying Li et al.: Yes. As attending physicians, it is a little difficult for us to publish many papers due to the little research time and hard clinical work. We will try to focus our work on a specific area as you have done. I think it would be helpful to use our limited research time. As we know, you started studying the pathogenesis of neurological disorders in HIV patients 20 years ago [4]. I think this is a huge and very important topic. What drives you to do this innovative and transformative work?

Patricia Price: HIV-associated neuropathy was presented to me as a topic that had received too little attention. We were eventually able to determine the risk factors in South Africans and South East Asia. This included genetic studies which shed light on the pathogenesis – made possible by some awesome collaborations. However the condition is now rare (as HIV is treated early), so the work has largely stopped. It will be interesting to see whether the pathogenic mechanisms that we identified influence other forms of neuropathy.

Ying Li et al.: As you know, in China, HIV patients are well managed and treated. In our department, we can hardly meet HIV patients with neuropathy. We agree that the mechanisms of HIV-associated neuropathy are interesting, although difficult. Meanwhile, we have noticed that you have had a remarkable career. How do you evaluate your journey so far? What are your future goals and other passions?

Patricia Price: My main goal now is to help the next generation of young scientists. It is their turn to take the work forward.

Ying Li et al.: Sounds great. We really need help from famous scientists like you. We also hope to have some collaborations in the future. In the area of aging research, how does the immune system change with age and what are the implications of these changes for aging?

Patricia Price: There is an abundant literature addressing this question. The usual mantra is that existing B-cell responses are maintained, whilst T-cell responses decline faster. This mirrors the effects of CMV on the immune system. Measures of the burden of CMV will be informative.

Ying Li et al.: Our research is related to immunosenescence. In your opinion, what is the significance and research value of immunosenescence in relation to clinical diseases?

Patricia Price: I am not clear what you are asking here, but it is pertinent to note that T-cells change their functional profiles as they differentiate. For example; T_{EMRA} (marked by the phenotype $CD28^-$, $CD45RA^+$) produce interferon-efficiently but proliferate poorly. Hence the term "immunosenescence" has gone out of favor.

Ying Li et al.: Since age-related diseases such as Alzheimer's and Parkinson's are associated with changes in the immune system, the COVID-19 pandemic poses a huge challenge to the immune system of the elderly. Can you talk about the impact of this pandemic on the progression of these age-related diseases?

Patricia Price: I am not an expert on COVID-19, but believe that it has potential to alter the immune system itself and to promote the replication of other viruses such as CMV. This highlights the importance of COVID-19 vaccinations.

Ying Li et al.: Since we know that changes in the immune system are associated with Alzheimer's disease, can you talk about whether damage to the blood-brain barrier plays a role in the process of Alzheimer's disease?

Patricia Price: The continuum between vascular dementia and Alzheimer's disease is a topic of extensive research in the last decade. Inflammation is likely to play a role, so there is a potential for enhancement by many viral diseases. Our research suggests a role for CMV, but the effect is complicated as CMV-reactive antibodies appear to be protective. CMV certainly crosses the blood brain barrier.

Ying Li et al.: Thanks for your time!

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