Preface

I came to know the word of "Immunity" in Chinese for the first time when I was given a shot of vaccine during my childhood years in my hometown, a small town called Poyang Town and named after the largest freshwater lake of China, Poyang Lake, near the middle of Yangtze River, in Jiangxi province, China. After elementary school, middle school and high school in Poyang, I was admitted to Sun Yat-sen University (SYSU), my first alma mater, after National College Entrance Exam. At university, I had a chance to learn the basic terms of immunology, such as antibody and antigen, with major in biology. After graduating from SYSU, I was awarded a government scholarship to study in the United States in 1985, and was eventually admitted to the Ph.D. program of Immunogenetics at the University of Illinois at Urbana-Champaign (UIUC), in 1986. Under Dr. Harris Lewin's supervision, I was fascinated by the complexity and diversity of animal and human immunity, which prompted me to quest from where this immunity came and how it was formed during the evolution. In addition to my scientific curiosity, my way to think about scientific questions and to conduct scientific experiments was completely shaped up by my Ph.D. mentor's hard training, which has ever since influenced my scientific career until today. After graduating from UIUC, my second alma mater, with both M.S. and Ph.D. degrees, I was fortunate to work with a world famous female physician scientist, Dr. Helen M. Ranney, Professor in the Department of Medicine, University of California San Diego (UCSD), in 1992 as her last post-doc, and then went with Dr. Ranney to work at a San Diego-based pharmaceutical company, Alliance Pharmaceutical Corp after post-doc research. Dr. Ranney has also made great influence on my scientific career like Dr. Lewin. In consultation with the two important persons in my scientific career, I decided to come back to my home country China to joint faculty of the Department of Biochemistry, College of Life Sciences, SYSU, my first alma mater, in 1996.

The first thing I decided to do for my scientific research after I came

back to China was to start something new which could utilize my scientific training in US and explore new avenue on immune research. I had many thoughts on my new research directions, and one of my top listed directions was to understand the origin and evolution of human immunity. However, I had no idea about which model species to pursue this very important quest. It took me one year to figure out that amphioxus was THE model organism to best address my question, and another two years to establish lab-based aquaculture system of amphioxus and the infection model for understanding host immune response to infections, which made my lab one of the pioneer labs in the world to study amphioxus immunity, although this species had been an iconic model for the evolutionary biology for more than 200 years. Instead of using conventional immunological methods only, my lab combined traditional immune methods with cellular, biochemical and molecular approaches, particularly genomic approach, to conduct a comprehensive survey on the immune response of amphioxus to bacterial infection from the beginning, which gave us a quick open-up for this brand new field. For last 10 years, my lab has contributed more than 30 papers related to amphioxus immunity. In summary, our contribution to the knowledge of amphioxus immunity, aiming to the understanding of origin and evolution of vertebrates immunity, especially human immunity, can be briefly described as followed:

1) Genomic analysis of the immune gene repertoire of amphioxus reveals extraordinary innate complexity and diversity, suggesting that our chordate ancestors had a remarkably elaborate innate immune system, but this system was somehow reduced in the vertebrate lineage. This finding provides an obvious evidence for the so-called "immunological big bang" for the explanation of the origin of vertebrate immunity.

2) Functional analyses of important innate immune genes involved in two basic innate immune signaling, TLR and TNF signaling, in amphioxus, suggest that the basic frameworks for these two signaling pathways have been established at the basal chordate which have laid foundation for the eventual formation of the two pathways in vertebrates.

3) Identification of lymphocyte-like cells along with related transcription factors and signaling molecules for lymphoid proliferation and differentiation indicates the emergence of adaptive immunity for vertebrates with the

presence of some basic components for adaptive immunity. Finding of extrinsic apoptosis pathway in amphioxus further substantiates the claim for the beginning of adaptive immunity in the basal chordate since extrinsic apoptosis pathway is generally believed to be co-evolved with adaptive immunity.

4) In addition to tracing the origin of existing system for immune response and regulation in vertebrates including humans, we may be in the position to reveal a novel mechanism involved in immune regulation which has never been described in other organisms by studying this model animal, such as findings of novel molecules for immune recognition and novel mechanism for immune regulation epigenetically by alternative 3'UTRs.

5) In immune signaling system, most proteins have characteristic and conserved multiple domains to exert specific functions to the proteins so as to interact with specific molecular partners. Our study on amphioxus immune signaling molecules indicates that different combinations of these domains (e.g. CARD, TIR, DFD, DEATH and etc) are the sources of evolution for the generation of new signaling molecules that can result in the interaction specificity. Understanding the evolution mechanism of these domains and their shuffling for the generation of new proteins with new functions should provide a novel vista to synthetic biology and insights that may help the treatment of diseases associated with mutated protein activity.

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