The Shanghai Institute of Hypertension, Shanghai, China

Qi-Fang Huang & Ji-Guang Wang

The Shanghai Institute of Hypertension, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

The Shanghai Institute of Hypertension was established in 1958 under the auspices of the municipal government of Shanghai. The Institute is dedicated to clinical, basic, population and translational research in hypertension. Inside the Institute, there are several research platforms, such as the Shanghai Key Laboratory of Hypertension, Cellular and Molecular Biology Laboratory, Centre for Epidemiological Studies and Clinical Trials, Centre for Vascular Evaluations, and Centre for Community Control of Hypertension. The clinical wing of the institution is the Departments of Hypertension in Ruijin Hospital and Ruijin North Hospital. The Institute offers postgraduate programs for master’s and doctoral degrees in cardiovascular medicine in Shanghai Jiao Tong University School of Medicine.

Over the years, especially in the past decade, the Institute had published a series of scientific papers in international literature. We performed genome-wide association studies in the Chinese population using various techniques with our own biological bank of more than 20,000 hypertensive patients and normotensive controls. Using the early technique of microsatellite markers, a susceptibility locus for hypertension was mapped to the chromosome region 2q14-q23. In subsequent association and functional studies, a rare variant Arg188Gln of the kynureninase gene (KYNU) located in this region was found to be associated with hypertension, and the KYNU protein with the mutation (Gln) showed less catalytic efficiency than the wild type enzyme. We also performed a genome-wide association study on the basis of SNPs, and participated in the Pan-Asia collaboration of genome wide association studies. This collaborative project confirmed seven loci that had been previously reported to be associated with systolic and/or diastolic blood pressure in populations of European descent. In addition, this project identified several new genetic variants (ST7L-CAPZA1, FIGN-GRB14, ENPEP, NPR3 and TBX3) associated with hypertension.

In our population- and patients-cohort studies, we reported a special form of masked hypertension, termed as “isolated nocturnal hypertension” and characterized by elevated night-time blood pressure and normal daytime blood pressure. This form of hypertension, though mild in the level of

Continued overleaf
blood pressure, does confer cardiovascular risk. In our China Ambulatory and Home BP Registry study initiated in 2009, participants underwent clinic, home, and 24-h ambulatory BP measurements. We investigated the accuracy of home blood pressure monitoring in the diagnosis of white-coat and masked hypertension in comparison with ambulatory blood pressure monitoring. We found home BP monitoring has high specificity, but low sensitivity in the diagnosis of white-coat and masked hypertension, and may therefore behave as a complementary to, but not a replacement of, ambulatory BP monitoring. In our elderly population study, by recording pulse waves at the left and right ankles by plethysmography and calculating the percentage of upstroke time per cardiac cycle, we found that upstroke time per cardiac cycle at baseline had an overall sensitivity and specificity of 86% and 80%, respectively, for the diagnosis of peripheral arterial disease (upstroke time per cardiac cycle, ≥21.7%) in comparison with computed tomographic angiography and significantly (P<0.0001) predicted total and cardiovascular mortality.

Our fundamental research focused on the role of inflammation, an immune response in vascular remodeling in hypertension, and on vascular adventitia. Our recent research has shown that adventitia and perivascular tissue are a complex and heterogeneous compartment of the vessel wall, and a dynamic mixture of several interactive cell types. We have found that fibroblasts secrete osteopontin (OPN) to induce macrophage chemotaxis and cause neointima formation. We have also found that perivascular adipose tissue (PVAT)-derived complement 3 (C3) induces differentiation of fibroblasts to myofibroblasts, which contribute to vascular adventitial remodeling processes. We have confirmed that deficiency of complement C3a and C5a receptors prevents angiotensin II-induced hypertension via regulatory T cells (Tregs). Tregs deletion blocks the protective effects of C3a and C5a receptor deficiency (DKO) against blood pressure elevation, suggesting complementing Tregs could be a novel strategy for the treatment of hypertension. Moreover, PVAT-derived PDGF-D contributes to aortic aneurysm formation via activating adventitial inflammation.

We found that brown adipose tissue (BAT)-derived fibroblast growth factor 21 (FGF21) upon adenosine A2A receptor (A2AR) activation, plays an important endocrine role in hypertensive cardiac remodeling. Recombinant FGF21 administration improves iBAT-depletion-induced dramatic cardiac remodeling in hypertensive mice. Brown adipocyte-specific FGF21KO blocks the effects of A2AR agonism in attenuating hypertensive cardiac remodeling. These provide the first line of evidence for a direct crosstalk between BAT activity and cardiac protection in hypertension. These studies suggest that inflammation and immunity-mediated adipose dysfunction may play an important role in hypertension-related target organ damage.

Hypertension affects approximately a quarter to a third of adult population. Hypertension control therefore requires joint efforts of the community, including patients themselves and their community and family physicians. The institute recently started a collaborative project in a community in Shanghai to do research on the management of hypertension. We established a web- and wireless-based system for the measurement, transmission, storage and analysis of blood pressure. This automated system might improve blood pressure control in this community, in the future hopefully will expand to the whole city of Shanghai or even other Chinese provinces, and in the long run will help reduce the risk of cardiovascular complications of hypertension.

Ji-Guang Wang
jiguangwang@aim.com

REFERENCES
7 Li XD et al. ATVB 2012;32:2250-2258 DOI:https://doi.org/10.1016/j.atvbaha.112.255216
9 Chen XH et al. Circ Res 2018;122:970-983 DOI:https://doi.org/10.1161/CIRCRESAHA.117.312153

Please get in touch with the author for further references.