Leading presentations at the 20th International SHR Symposium

Symposium 1: Hypertension model research in the past, present and future

Yukio Yamori (Japan) - SHRSP research for cardiovascular disease prevention

"Nutrients effective on stroke prevention in SHRSP were epidemiologically proven to be inversely associated with cardiovascular risks in world-wide populations, and consistent with common merits of long-living Japanese and Mediterranean populations, compared with Euro-Western populations by 24-hour urinary biomarker analyses. SHRSP will contribute to healthy longevity by predictive-preventive medicine."

Giuseppe Bianchi (Italy) - MHS as a tool to disentangle the genetic complexity of human primary hypertension and contribute to the precision medicine

"In this symposium, I will summarize my achievements for approximately 30 years regarding the genetics of hypertension and its organ damages both in the Milan hypertensive strain of rats (MHS) and in patients with the contribution of rostafuroxin to establish causal relationships and precision medicine."

Yoram Yagil (Israel) - The Sabra hypertensive strain model

"We will present the story of the creation of the Sabra rat model of salt-sensitive hypertension and discuss its place as a unique model of salt-sensitivity among the abundance of other models of hypertension. We will provide details of physiological, pharmacological, genomic, transcriptomic, and proteomic studies designed primarily to resolve the pathophysiology involved and review their outcome. We will examine those research fields that have yet been untouched in this model and consider current and future challenges using this model, in our quest to identify novel mechanisms of salt-sensitive hypertension and its relevance to cardiovascular disease in humans."

Toru Nabika (Japan) - Mapping genetic determinants of hypertension and stroke in the SHRSP model

"SHRSP is a unique genetic model for cerebral hemorrhage and small-vessel disease as well as severe hypertension. Under the hypothesis that understanding the genetic mechanisms underlying cerebrovascular events in SHRSP would provide important clues to understand the human counterparts, genetic analyses were performed on SHRSP. In this presentation, I would like to summarize achievement of such studies, and to discuss about future challenges."

Symposium 2: Mechanistic understanding of hypertension

Norihiro Kato (Japan) - Genome scan and human homology of hypertension loci

"By integrative genomic analysis in a rat polygenic hypertension model, we successfully identified potential target genes, including rat homologs of human transcriptome-wide association study loci. Notably, five of these genes belong to the kallikrein–kinin / renin–angiotensin systems, supporting the presence of key disease pathways that regulate blood pressure and related phenotypes."

Stephen Harrap (Australia) - How does brief early renin-angiotensin system blockade prevent SHR hypertension – finally an answer?

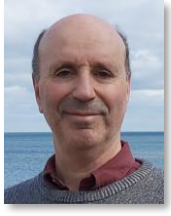
"The reprogramming of SHR hypertension to lifelong lower blood pressure by brief RAS inhibition is a well-established and fascinating phenomenon. Despite 30 years of research, the explanation has remained mysterious. Our recent detailed molecular studies in the kidney show that the answer is simple and elegant and has been hiding in plain sight."

Michal Pravenec (Czech Republic) - Sodium accumulation and blood capillary rarefaction in the skin predispose SHR to salt sensitive hypertension

"Increased Na^+ storage in the skin without parallel water retention has recently been suggested to predispose to salt-sensitive hypertension. To examine this, we compared tissue Na^+ storage between salt-sensitive SHR and salt-resistant Brown Norway (BN-Lx) rats. Storage of osmotically inactive Na^+ was found to be increased, concomitant with blood capillary rarefaction, in the skin of SHR but not of BN-Lx rats. After salt treatment, mRNA expression of genes involved in angiogenesis and proliferation of endothelial cells was significantly up-regulated in BN-Lx rats contrary to SHR. Since the skin harbors most of the body's resistance vessels, skin blood capillary rarefaction may lead to increased peripheral resistance and salt sensitivity in SHR."

Dominique Gauguier (France) - Architecture and metabolic function of the rat gut microbiome

"The gut microbiota contributes to multiple biological functions for the mammalian host. Dysbiosis has been associated with increased risk of inflammatory and cardiometabolic diseases. I will discuss complementary strategies designed to understand the contribution of disrupted gut microbiome architecture and products of bacterial metabolism to cardiometabolic phenotypes in the laboratory rat."



Tim Aitman (UK) - My personal journey with the SHR

"I'm profoundly grateful to the creators of the SHR, a model organism which dominated my research activities for more than 20 years. From my first days as a group leader, I recognised the value of SHR as a model for insulin resistance and the metabolic syndrome and applied all my resources, personal, intellectual and financial, to resolving the genetics and cellular mechanisms of the SHR phenotype. For this talk, I will give my personal view of the research that I undertook in these 20 years, and will attempt to put it in the context of model organism research and genetic analysis of complex traits more broadly across species and phenotypes."

Christian Delles (UK) - Uromodulin: New mechanistic insights into an old player in hypertension and kidney disease

"Uromodulin is the most abundant protein in urine. Genetic variants of the UMOD gene but also urinary uromodulin levels have been found to be associated with hypertension and kidney diseases. Uromodulin interacts with renal sodium excretion and inflammatory cascades, and possibly has direct vascular effects. The pathways from gene to biological function are complex, particularly because of posttranslational modifications affecting protein trafficking. We will summarise recent findings derived from in vitro experiments, preclinical models and human studies, highlighting multiple facets of this important player in the pathogenesis of hypertension."

Symposium 3: Recent progress in the pathophysiology of hypertension

Fadi Charchar (Australia) - Non-coding genome in hypertension research

"The Non-coding genome is an expanding repertoire of regulatory and non-regulatory RNA. Some of the latest research in the SHR and humans point to contribution of this RNA to hypertension and cardiovascular disease. I will discuss some or findings including evidence for circular RNA."

Yoshitaka Hirooka (Japan) - Sympathetic nerve system in hypertension

"Activation of the sympathetic nervous system is one of the major etiologies of hypertension. It is also responsible for the development of hypertension and target organ damage related to hypertension. The brainstem and hypothalamus are key areas, which determine central sympathetic outflow. Imbalance of nitric oxide, oxidative stress and immune-inflammatory abnormality are suggested to be involved in higher levels of sympathetic activity in hypertension. I will show these data and current topics in this field of research."

Anne Kwitek (USA) - Rat genome resources and the Rat Genome Database

"The generation of genome-scale data in the rat is witnessing another surge, including a vastly improved BN rat reference genome assembly, over 16 million variants from over 90 different strains, and strain-specific genome assemblies with companion transcriptome data in rat strains studied by the rat research community. These community-generated genomic and additional 'omic' data are being integrated with comprehensive phenotype data (qualitative and quantitative) in the Rat Genome Database (RGD) to support the hypertension research community."

Peter Doris (USA) - Reference quality de novo assembly of SHR and WKY genomes using HiFi long reads and long range scaffolding

"Alignment of short read genome sequences to a reference genome introduces reference bias: insight into the query genome is limited to genomic regions that are generally similar to the reference. Using a combination of approaches, we generated de novo genome assemblies for SHR-A3, SHR-B2 and WKY, which are chromosome level, highly contiguous, complete and correct. These assemblies provide insight into genetic variation associated with several SHR phenotypes, including those arising from structurally complex and variable regions of the genome in which the existing rat reference is uninformative."

Hiroki Ohara (Japan) - Genome editing in SHRSP and SHR to reveal molecular mechanisms of hypertension and its complications

"We have been aiming for identifying genetic determinants of hypertension and stroke in SHRSP by congenic strategy. Genome-editing technologies that can create gene-targeted knock-out or knock-in rats enabled us to verify pathophysiological implications of the candidate genes on hypertensive phenotypes in this model in vivo. In this symposium, I will introduce our recent findings obtained from phenotyping of knock-out or knock-in SHRSP (or SHR) models."

Jens Titze (Singapore) - Crosstalk among skin, immune system, and kidney (TBD)

"TBD"

Symposium 4: Bridging the gap between bench and bedside

Patricia Munroe (UK) - GWAS of hypertension: Deciphering effector genes and opportunities for clinical translation

"The genome-wide association study (GWAS) approach has now successfully identified over 2000 independent signals, explaining about 40% of common variant heritability of blood pressure traits. Rare genetic variants also contribute to hypertension in the general population, highlighting select candidate genes. I will describe some of our latest work on fine mapping and leveraging "omics datasets to identify causal variants and effector genes, discuss druggability of candidate genes and the utility of blood pressure polygenic risk scores."

Anna Dominiczak (UK) - Precision medicine

"Precision Medicine is one of the most impactful opportunities in healthcare, bringing the prospects of pre-symptomatic diagnosis, more effective treatment, and better patient outcomes. All the above is supported by the "triple helix" collaborations between the health service, academia, and industry. My presentation will give examples of bench to bedside research on the Uromodulin, leading to precision medicine clinical trial."

Noboru Fukuda (Japan) - Transcriptional regulation of TWIST1-C3 system for the cardiovascular and renal remodelings in hypertension

"Mesenchymal organs and tissues show the undifferentiated and the synthetic phenotype in SHR. We have demonstrated that TWIST1-C3 system is responsible for the synthetic phenotype inducing the cardiovascular and renal remodelings. In this symposium I will present the transcriptional regulation of TWIST1-C3 system for the cardiovascular and renal remodelings in hypertension."

Akira Nishiyama (Japan) - Future research in onco-hypertension

"Owing to aging populations, the prevalence of hypertension and associated cardiovascular disease has been increasing worldwide. The morbidity and mortality due to cancer have also been increasing with aging populations. Several small-molecule inhibitors have been used in cancer therapy, which have a positive impact on the prognosis and survival of cancer patients. Consequently, the number of cancer survivors with hypertension has been rapidly increasing. However, both clinical and laboratory evidence are lacking regarding optimal blood pressure control in hypertensive patients with cancer. We will discuss our proposed "Onco-Hypertension" at this symposium."

Theodore Kurtz (USA) - Mechanism-based strategies for preventing salt-induced hypertension in humans: lessons learned from animal models

"This presentation will discuss the use of animal models for identifying the hemodynamic mechanisms of salt sensitivity and developing effective strategies for preventing salt-induced hypertension in humans. New data will be presented showing that primary aldosteronism increases salt sensitivity by promoting salt-induced increases in vascular resistance, not increases in cardiac output."