

## **Hypertension Unit**

The main focus of this unit is to understand the interactions of nitric oxide (NO), reactive oxygen species (ROS) and vasoactive hormones in the development of hypertension and its complications such as renal failure. To address this issue, we employ a multidisciplinary approach involving biochemical, physiological, pharmacological and molecular biological techniques. Our most recent approach in this issue is to explore the role of transcription factor peroxisome proliferator activated receptors (PPARs) in the regulation of blood pressure and vascular tone. Previously we have shown that both PPAR $\alpha$  and PPAR $\gamma$  play an important role in blood pressure regulation via modulation of vasoactive hormones and NO as it involves the role of PPAR $\alpha$  in the salt- and angiotensin-dependent models of hypertension using PPAR $\alpha$  knock-out mice. In SHR and DOCA-salt hypertension, our studies suggest that blood pressure regulation is a concerted effort between activation and desensitization of G-protein coupled receptors (GPCR) with a transcriptional regulatory role by PPAR $\gamma$  on GPCRs. Since GPCRs are tightly regulated by GPCR kinases (GRKs), ongoing studies are investigating the influence of PPAR $\gamma$  in the regulation of GRK activity in SHR.

**Mohammad Newaz, M.D., Ph.D.** is a Senior Scientist and Head of Hypertension Unit in the Center for Cardiovascular Diseases.. Dr. Newaz received his MD from University of Chittagong (1991) and PhD from the National University of Malaysia (1998). He has held faculty positions at the University of Science and Technology Chittagong, Bangladesh, National University of Malaysia and International Islamic University Malaysia before joining the Center for Cardiovascular Diseases in 2000. His laboratory focuses primarily on hypertension and vascular physiology using integrated investigative approach with special emphasis on understanding molecular events contributing to the pathogenesis of hypertension and its complications.

He is a member of many professional societies, including the American Heart Association, American Physiological Society. He has received many honors and awards, including the Young Investigator Award from High Blood Pressure Council of American Heart Association, Young Investigator Award from the renal section of American Physiological Society, Caroline Tun Suden professional opportunity award from American Physiological Society, Young Investigator Award from International Society of Hypertension, FASEB MARC fellowship and Grant-in-Aid from American Heart Association TX affiliate. He has published more than 30 papers and book chapters in the field of hypertension and vascular biology and extensively presented his research works in local and international conferences.

## **CURRENT RESEARCH**

### **1. Interaction of PPAR $\gamma$ , NAD(P)H oxidase and nitric oxide in glycerol-induced acute renal failure**

the aims of this study are:

1. To Investigate the role of NAD(P)H oxidase in the oxygen free radical mediated pathology of glycerol-induced ARF.
2. To determine the role of PPAR $\gamma$  in the regulation of NAD(P)H oxidase dependent oxygen free radical generation in glycerol-induced ARF.
3. To investigate the interaction of oxygen free radical, NO and NAD(P)H oxidase in the glycerol model of ARF.

## **2. Role of PPAR $\gamma$ in acrolein-induced vascular toxicity**

The aims of this study are

- (1) To determine the role of PPAR $\gamma$  in acrolein-induced impaired vascular response.
- (2) To investigate the role of PPAR $\gamma$  in acrolein-mediated NAD(P)H-dependent superoxide generation.
- (3) To establish the involvement of inflammatory process in acrolein-mediated vascular toxicity
- (4) To determine the PPAR $\gamma$ -NAD(P)H- and NO/NOS-dependent regulation of inflammation in acrolein-induced vascular toxicity.

## **3. Transcriptional regulation of vascular aging**

The aims of the study are:

1. To establish the role of PPARs in vascular aging.
2. To investigate the affect of PPAR induction on prevention of oxidative stress-induced vascular aging.
3. To establish the relationship between PPARs and klotho gene in vascular aging.

## **4. PPAR $\gamma$ -dependent regulation of GPCR activity in hypertension**

Specific Aims of this study are as follows:

1. To investigate the role of PPAR $\gamma$  in the regulation of vascular reactivity and blood pressure.
2. To understand PPAR $\gamma$ -mediated regulation of GRK-2 activity
3. GRK / GPCR signaling mechanism in the regulation of vascular reactivity and blood pressure.