



**CSIR - INDIAN INSTITUTE  
OF TOXICOLOGY RESEARCH**



**COUNCIL OF SCIENTIFIC  
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## Golden Jubilee Lecture

**February 29, 2016**



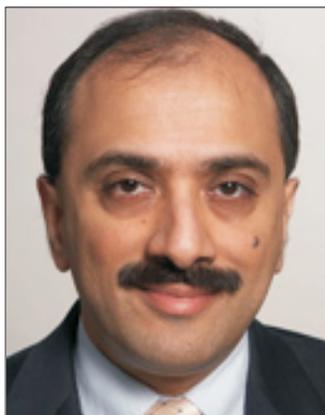
### **Professor Mone Zaidi**

MD, PhD, FRCP, FRCPI, FRC Path, MD (h.c.), DSc (h.c.)

**Professor of Medicine and  
Structural and Chemical Biology  
Mount Sinai School of Medicine  
New York, USA**



*50 Years of Service to the Nation*



**Mone Zaidi,**

MD, PhD, FRCP, FRCPI, FRC Path, MD (h.c.), DSc (h.c.)

Mone Zaidi has been Professor of Medicine and Structural and Chemical Biology and Director of the Mount Sinai Bone Center since 1999. He obtained his medical degree from King George's Medical College in Lucknow, India, completed his clinical training under Professor Iain MacIntyre, FRS, at the Endocrine Unit of the Royal Postgraduate Medical School, Hammersmith Hospital, in London and his PhD from the University of London. He was appointed University Senior Lecturer and Consultant Physician at St. George's Hospital Medical School, University of London, in 1990. Dr. Zaidi's group has made seminal discoveries on the mechanisms of skeletal homeostasis in health and disease. These have included the first description of calcium sensing in the osteoclast; the discovery that nitric oxide regulates bone remodeling; the definition of a novel pituitary-bone axis; and more recently, the elucidation of pathophysiological mechanisms in Gaucher Disease. He has published over 360 papers and has been funded since 1987 initially from the Medical Research Council of the UK and since 1997, from the US National Institutes of Health (NIH). He has received many honours, including being elected to the Association of Professors of Medicine, Association of American Physicians, American Society for Clinical Investigation and William Osler Interurban Clinical Club (where he serves as Secretary-Treasurer). He has also served as the Chair NIH, for the Musculoskeletal Sciences Grant Review Panel. He also chairs the New York Skeletal Biology and Medicine Conferences, the premiere research meetings in the field. Dr. Zaidi has lectured worldwide and most prominently delivered the Sreebny Distinguished Lecture at the State University of New York, the James Platt White Memorial Lecture, the Marookian Lecture at the University of Pennsylvania and Steven Goodman Lecture at Yale School of Medicine. He was also Kramer Visiting Professor at Dartmouth Medical School, Highlight Speaker at the National Institutes on Aging Council and Guest Lecturer at the Japanese Bone and Mineral Society. He was awarded an Honorary Doctorate of Medicine (*Laurea Honoris Causa*) from the University of Bari and an Honorary Doctor of Science from the Postgraduate Institute of Medical Sciences, India.

## Genes, Diseases and New Medicines

Mone Zaidi, MD, PhD, FRCP, FRCPI, FRCPath, DSc (h.c.), MD (h.c.)  
Professor of Medicine and Structural and Chemical Biology  
Mount Sinai School of Medicine  
New York, USA

The cataloging of human mutations, the use of genetically engineered mice to recapitulate human disease and the rapid evolution of genomic sciences over the past decade has had a major impact on how basic research is translated into clinical care. However, the fundamental questions to be asked have invariably arisen from the bedside and. It is this vibrant and purposeful interaction between bench and bedside that I shall focus on as I describe three sets of our own scientific observations. First, I will comment on work, primarily achieved through the combination of mouse genetics and classical biochemistry and pharmacology, that has allowed a better understanding of the pathophysiology of a crippling disease of public health proportions – osteoporosis. In doing so, we have revealed new therapeutic targets, besides altering our clinical management. Most notably, we have discovered a new connection between bone and the pituitary gland, through which pituitary hormones, *hitherto* thought solely to act on master endocrine glands, can affect skeletal remodeling directly and with remarkable precision. In the second part of this talk, I shall describe the application of modern genomics and computational biology that has helped us understand and treat rare monogenic disorders, notably Gaucher disease and congenital adrenal hyperplasia. Specifically, I will describe our unraveling the genetic basis of the high incidence of lymphoproliferative malignancy in Gaucher disease and the use of next-generation deep sequencing of DNA in the plasma of pregnant women to obtain a genetic diagnosis as early as 6 weeks of pregnancy. I will also describe *in silico* dynamic modeling that has allowed the swift and effective prediction of the clinical consequences of newly identified gene mutations. Finally, using connectivity mapping, I will highlight a new concept in drug development – repurposing old drugs for new uses. Our data using complementary genomic, computational, biophysical and mouse-based technologies have revealed that bisphosphonates – the most commonly used drugs for osteoporosis and skeletal metastases – can be repurposed for the primary treatment of cancers driven by the EGF receptor family of tyrosine kinases. These drugs, we find, bind directly to the kinase domain of the EGFR family and inhibit tumour growth, in essence preempting their use for the primary treatment and prevention of EGFR-driven lung, breast, colon, gastric and head and neck cancers.





# सीएसआईआर-भारतीय विषविज्ञान अनुसंधान संस्थान CSIR-INDIAN INSTITUTE OF TOXICOLOGY RESEARCH

वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद्  
COUNCIL OF SCIENTIFIC & INDUSTRIAL RESEARCH



CSIR-IITR, Lucknow is the only multidisciplinary research institute in the field of toxicology in South-East Asia with the motto:

***"Safety to environment & health and service to industry".***

## R&D Areas

- Food, Drug & Chemical Toxicology
- Environmental Toxicology
- Regulatory Toxicology
- Nanotherapeutics & Nanomaterial Toxicology
- Systems Toxicology & Health Risk Assessment

## Services Offered

- GLP certified for pre-clinical toxicity studies
- Safety / toxicity evaluation of NCEs
- Water quality assessment and monitoring
- Analytical services
- Environmental monitoring and impact assessment
- Epidemiological studies
- Information on chemicals / products

## Recognitions

- Scientific & Industrial Research Organizations (SIROs)
- UP Pollution Control Board (Water & Air)
- Indian Factories Act (Drinking Water)
- Bureau of Indian Standards (Synthetic Detergents)
- Food Safety & Standards Authority of India (FSSAI)

## Technologies Developed / Available

- Water Analysis Kit
- Mobile Laboratory Van for on spot water quality analysis
- Argemone Detection Kit for rapid screening of Argemone in mustard oil
- CD-Strip for detection of butter yellow, an adulterant in edible oils
- Arsenic Detection Kit



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50 years in the service of the nation



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Toxicity Testing: GLP Test Facility