Dr. Amom Ruhikanta Meetei:

Discovery of new genes on *Fanconi anemia*

- Compiled by RIST, Imphal.

Dr. Amom Ruhikanta Meetei, an eminent Manipuri Scientist, working at the Cincinnati Children's Hospital Medical Centre, USA, showed his excellence in his research field by publishing a series of papers on ***Fanconi anemia*** (FA) in highly reputed International Journals, and the significance of his discovery was highlighted in the editorial column of the journal *Nature Genetics* (Ref: ***Nature Genetics, vol.37, No.9, September 2005)***. It is a highly commendable scientific discovery and a source of pride for the people of Manipur, and a great joy for all of us who love science here in Manipur.

Amom Ruhikanta Meetei was born on March 14, 1965, at Taobungkhok Awang Leikai, Imphal West to his parents, Shri Amom Chandramani Singh and Smt Amom (ongbi) Akoijam Akashini Devi. He is the eldest of four brothers and three sisters.

Amom Ruhikanta Meetei started his early schooling from Government Primary school, Taobungkhok Mayai Leikai, KEISAM BIRJIT High school, Patsoi, Imphal West and Model Higher Secondary School, Khamnam Bazar, Imphal West respectively. He then passed PUSc II year from D.M. College of Science under Manipur University. He completed his Bachelor of Science (B.Sc.) in Chemistry (Honors) from D.M. College of Sciences in 1989 and Master of Science (M.Sc.) in Biochemistry in 1992 from Manipur University respectively. He was born and raised completely in Manipur.

He joined his Ph.D. course at the Indian Institute of Science (IISc), Bangalore, India as Junior Research Fellow (CSIR) from 1993 to 1995, and then as Senior Research Fellow (CSIR) from 1996 to 1999. He completed his Ph.D. degree from Indian Institute of Science (IISc), Bangalore in 2000. During 2000 to 2004, he was a Visiting Fellow, National Institute on Aging, National Institute of Health, Baltimore, Maryland. During this period, he discovered three new genes related to Fanconi anemia. In 2004 he joined as Assistant Professor in Experimental Hematology, Cincinnati Children's Hospital Medical Centre, University of Cincinnati, Department of Pediatrics, Cincinnati, Ohio, USA. At present he is working as Professor in this hospital, and he is also a member of Division of Experimental Hematology and Cancer Biology.

Fanconi anemia is a chromosome destabilizing disorder. The affected persons are characterized by diverse congenital abnormalities, retarded growth, early predisposition to cancer and bone marrow failure. The Fanconi anemia cells have highly breakable chromosomes. The cells are easily killed by such agents as mitomycin C, cisplatin etc. (used as drugs) which make DNA interstrand crosslinks. The key biochemical defect of Fanconi anemia is lack of biochemical repair system of these toxic lesions.

The research works of Dr. Meetei and his team, involved the structural and functional elucidation of Fanconi anemia –associated core complex protein involved in DNA repair of normal individuals as well as individuals with FA. In this work another component of the core complex protein FAAP250 or FANCM has been found to be defective in individuals with Fanconi anemia. The result has brought one step nearer to the understanding and treatment of a long puzzled genetic

disease having adverse disorder effects. Researchers are also hoping that it will throw light on the mechanisms of other such dreadful diseases.

Dr. Meetei's clinical interest are Fanconi anemia, chromosome instability; DNA repair; multiprotein complex. His research interests include functional analysis of Fanconi anemia gene products; identification of new FA genes and signal transduction pathways that regulate DNA damage induced activation of the FA-core complex, biochemical purification of multi-protein complexes from human cell extracts, immune-precipitation, RNAi, and biochemical assays; Fanconi anemia as a model system to study some of the important fundamental questions of cancer biology in general. He has more than 100 publications, with more than thousand citations. He was a part of the NIA (National Institute of Aging) scientists who discovered a new gene FANCM, which sheds light on an important pathway involved in the repair of damaged DNA. Specially, mutation in this gene is responsible for one of the forms of Fanconi anemia (FA), a rare genetic disorder that primarily affects children. Like many rare, inherited diseases, understanding this gene's role in the development of FA provides insights into other medical problems – in the case, age-related conditions including ovarian and pancreatic cancers, as well as leukemia. Discovery of this gene and its protein provides a potential target for the development of drugs that can prevent or alleviate FA and a variety of cancers.

Dr. Meetei has been bestowed so far with so many international awards and honors, including "Discovery Award at the 2005 FARF Scientific Symposium for the cloning of the FANCB and FANCM genes", and delivered so many invited talks on Fanconi anemia and its related issues at many international conferences.

The other Manipuri Scientist who was part of a scientific group focusing on rare genetic disease, Fanconi anemia at Cincinnati Children Hospital Medical Centre, was Dr. Thiyam Ramsingh Singh, a Postdoctoral fellow working under Dr. Meetei, at Cincinnati Children's Hospital Medical Centre at that time. At present Dr. Thiyam Ramsingh Singh is working as a Professor of Biotechnology, Tezpur Central University, India. Another Manipuri scientist Dr. Nanaocha Sarma who was trained as postdoctoral fellow under Dr. Meetei, is now working at IBSD, Imphal.

Dr. Amom Ruhikanta Meetei is a man of very high moral value in life. He is leading a nice and simple family with his wife, Smt Amom (ongbi) Kebola Wahengbam who is also working at

Cincinnati Children's Hospital Medical Centre as laboratory technician, and two daughters. Prativa (Thoibi) Amom and Prety (Inaoba) Amom. Smt Kabola Wahengbam is also very popular and famous for her extraordinary performance in cooking and preparation of variety of Manipuri foods in the Youtube channel. Dr. Meetei has also played very important role in organizing "North American Manipuri Association" and its activities to help students coming from Manipur for higher studies in USA. His hobby is to sing old Manipuri songs, particularly patriotic songs. His philosophy in life is to believe in one-self and to be happy in life with the chosen profession. One needs to follow his own liking while choosing a profession, without any influence from other. About education, he opines that educational training up to Ph.D. in India, is not lesser than in any part of the world, even USA. For becoming successful person, honesty, self-confidence, integrity and perseverance are key words as life is a long marathon race. We appreciate his desire that there should be a world class research institute on the soil of Manipur where other scientists of Manipuri origin working all over the world, can contribute in their research experiences.

Conversations with People's Science Network (PSN):

Q1. PSN: How you land up working at present problem i.e. FA?

Reply from A.R. Meetei: As an International Fogarty Fellow at the National Institute on Aging, Baltimore, I was studying Bloom helicase, an ATP-dependent DNA unwinding enzyme involved in a cancer prone genome instability disease called Bloom's syndrome. While I was purifying bloom helicase complexes from the human cell extracts, I discovered for the first time a key biochemical link between two cancer prone genome instability diseases; i.e., Bloom syndrome and Fanconi anemia (published in 2003). During that time, very few Biochemists were working in the field Fanconi anemia (FA). I took that opportunity to utilize my expertise and was able to purify and identify all the components of the FA-nuclear core complex. Subsequently, we cloned and partially characterized three new FA genes (published in 2003, 2004 and 2005).

Q2. PSN: How will your work help to understand Fanconi anemia (FA) and other such similar diseases?

Reply from A.R. Meetei: Although we understand the genetic basis of the disease, we do not fully comprehend how these mutations cause FA. As we begin to understand the disease's progression more clearly, we hope to identify legitimate therapeutic targets that may delay or even prevent the development of FA. Finally, the enzymatic activity of FANCL (one of the 12 FA genes) suggests that small molecules could alter its activity. Such a compound may hold hope for preventing the disastrous consequences of genomic instability in individuals with Fanconi anemia. Conversely, inhibitors of FANCL activity would probably create a Fanconi anemia-like phenotype and would sensitize cells to DNA crosslinkers. DNA crosslinkers, such as cisplatin, are already among the best currently available cancer chemotherapy agents. One can easily imagine a potential use for drugs that would result in enhanced crosslinker sensitivity in specific target cells.

Q3. PSN: What is your advice to young scientists of Manipur?

Reply from A.R. Meetei: In my opinion, if you want to make a career in research you need perseverance, hard work and sincerity. Above all, one should enjoy doing research (if not, it does not worth 6 years of Ph.D. and 5 years of Postdoctoral training before you really become an independent scientist). To me, the most important quality of a good scientist is one's scientific integrity. Conducting research in any field of science is nothing but seeking for the truth. In other words, one's research finding should not only be just to publish in a high profile journal but also should stand the test of time. Finally, you don't need a Gold medal to be a successful researcher, what you need is a constant exertion at your maximum ability until you reach the final goal.

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