

# Molecular Biology, A Revolutionary Science at Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad

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**Cite this editorial as:** Riazuddin S. *Molecular Biology, A Revolutionary Science at Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad. Ann Pak Inst Med Sci. 2019;15(4):134-137.*

Ever since the creation of living beings on this planet, Man has struggled to understand Life. However, the phenomenon of Life has remained shrouded in mystery. Philosophers in the times of Aristotle and Omar Khayyam discussed Life in abstract terms. During the second half of the last century and the first two decades of the present century, breakthrough researches {in the structure and function of DNA (1953), isolation of DNA polymerase (1958), reverse transcriptase (1969), restriction enzymes (1970) and use of restriction enzymes in gene mapping & gene cloning (1971-72), sequencing of DNA (1977) cracking the genetic code and use of plasmids as vectors for cell transformation (1983), gene amplification (polymerase chain reaction), sequencing of the human genome (2000), the discovery of the functions of RNA, micro RNA and non-coding DNA (1993), and more recently applications of tools of bioinformatics and artificial intelligence to solve complex biological problems} have enabled biologists to penetrate deep into the intricate web of life. As a consequence, a scientific concept of life has emerged that biological activity is the expression of information stored in DNA and its translation into RNA and proteins. The study of biologically active “molecules” is called "Molecular Biology".

The largest of all biologically active molecules, "DNA", determines the characteristics of a living being. The DNA of all living beings — be that a tiny bacterium, a giant elephant or a mammoth banyan tree — is made up of four nitrogenous bases, adenine, guanine, thymine and cytosine. It is the order in which these four organic molecules are arranged on a strand of DNA (nucleotide

sequence) that distinguishes one living being from another. In 1970's it became possible to generate new DNA molecules (recombinant DNA) by polymerizing individual nucleotides or joining together pieces of existing DNAs from different species, thus producing the molecular equivalent of a chimera, the legendary animal {part lion, part goat, and part snake} of Greek mythology. Such capabilities have helped biologists not only to learn more about how a living cell does what it does but also in harnessing living organisms to do more useful work for mankind. This has made molecular biology the most exciting of all sciences as well as a new endeavor called "Biotechnology."

Biology has been harnessed since antiquity to fulfill humanity's most fundamental needs — from increasing food supplies to improving health care. The availability of new and novel methodologies has greatly expanded the scope of applications of biology, limited only to the imagination of people using it. For the first time in the history of mankind, it seems within reach of human endeavors to custom make nutritionally improved foods, new pharmaceuticals, and novel vaccines. Identification of human pharmaceutical protein genes and their expression in bacteria and yeast has enabled the production of wonder drugs to fight against cancer, hepatitis, leprosy, AIDS, cardiovascular, viral and parasitic diseases. It is no more a dream but a reality to diagnose and treat (via gene therapy) human genetic disorders even before the birth of the affected child.

As coincidence would have it, another breakthrough was made in the 1980's and 1990's when it was discovered

that certain kinds of somatic cells possess inherent capability (or can even be induced) to develop into different lineages such as skin cells, brain cells, lung cells and so on. This revolutionary discovery has given birth to a new era of medicine called regenerative medicine, opening doors to new clinical applications. The promise of regenerative medicine to revolutionize medical care for a wide variety of diseases is beyond imagination. The vast panorama of applications of molecular biology and stem cell technology is already unfolding for the benefit of mankind

The challenge of applying innovative laboratory research to solve unique and specific problems of health and medicine requires the talents of soundly trained manpower which can define problems and devise strategies that will work in the local setting. To develop a researcher having "hands-on" experience of various molecular biological and stem cell techniques, training of manpower need to be carried out in local hospital situations to see how many things can go wrong and how to get around those hurdles and solve problems. The quality of human training will depend on the condition of training laboratories. Traditionally, our medical university laboratories that are the breeding grounds for future medical practitioners of new and revolutionary technologies, have been even more deficient than the laboratories of general universities and research institutes in the country. As a consequence, medical university training in Pakistan has suffered from laboratory experience that is so vitally important for building the intellectual maturity of future medical practitioners. It is exceedingly important, therefore, to improve the local laboratory infrastructure in order to promote therapeutic applications of new and revolutionary medical technologies in our tertiary care hospitals as well as improve the quality of training of our medical graduates.

As the global landscape for health and medicine is changing, new strategies are being developed that involve combining basic laboratory research and clinical practices. The question arises are we preparing ourselves to meet the challenges posed by new and revolutionary molecular and cellular technologies? The short answer is big "NO." The main reason is that we have neither recognized the impact of changing International scenario nor have we allowed our scientists to take bold initiatives. In 2006, Centre of Excellence in Molecular Biology (CEMB), university of the Punjab, Lahore took the first initiative to set up a cGMP compliance protein purification facility, which is an essential requirement for

the indigenous production of human pharmaceuticals proteins from genetically engineered microbes. The project was approved in pre CDWP but withdrawn "hours" before it was to be discussed for approval in the CDWP meeting. Consequently, the project died even before its birth and all relevant facilities and infrastructure at CEMB went down the drain. Regrettably, as of to-date, there is no USFDA or EMEA approved cGMP compliance protein purification and/or stem cell production facility in Pakistan, neither in the public sector nor in the private sector. Countries that are now leading in the world (including India and China) are the ones that established cGMP compliance facilities during 2000-2010. In 2008, Indian President Dr. Abdul Kalam inaugurated India's largest cGMP compliance biopharmaceutical laboratories complex at Wockhard Biotech Park, Aurangabad, India. This state-of-the-art complex comprises several dedicated facilities built following US FDA and EMEA standards. Since then the establishment of such cGMP compliance laboratories have proliferated from coast to coast forming a sound base for the production of clinical-grade materials in India whereas there is none in Pakistan.

Recognizing future needs in the health sector in a background of the above international scenario and to place Pakistan on a firm footing with regard to uses and applications of new and revolutionary medical technologies, the federal government has established Shaheed Zulfiqar Ali Bhutto Medical University (SZABMU), as a premier medical teaching and research university. Besides teaching undergraduate and postgraduate courses in Health Sciences and Allied Subjects, the university, with the approval of Higher Education Commission, has initiated a regular M.Phil. and Ph.D. program in Molecular Biology with a strong backup of basic medical research. A consortium, comprising the University of Punjab thru its centre of excellence in molecular biology, Lahore, university of health sciences, Lahore, Shaheed Zulfiqar Ali Bhutto Medical University, Islamabad and Jinnah Burn and reconstructive surgery center, Jinnah hospital, Lahore have joined hands to pool efforts in overcoming the inherent constraints of a shortage of specifically trained manpower and laboratory infrastructure. To this end, an autonomous laboratory unit is established on the fourth floor of Jinnah burn and reconstructive surgery centre, Jinnah hospital, AIMC, university of Health Sciences, Lahore, jointly managed by the partnering institutions. The said consortium laboratory unit is headed by Dr S.

Riazuddin, professor Emeritus, SZABMU, Islamabad. In addition to M.Phil/Ph.D. teaching, Dr Riazuddin's research team has initiated a program of high quality research in two areas.

Firstly; to elucidate the molecular and genetic basis of hereditary hearing & vision impairment and intellectual disabilities, in collaboration with Johns Hopkins University, Baltimore and University of Maryland, Baltimore, USA. As a consequence of input into these studies during the last five years, the group has published 36 research papers in well-reputed journals such as *Am J Hum Genet*, *J Clin Invest* and *Mol Psychiatry* with a cumulative impact factor of 178.16 (Ref 1-36).

Secondly; to investigate the therapeutic potential of adult stem cells in the repair of burnt skin, impaired vision and damaged cartilage, in collaboration with the University of Miami, Florida, USA. As part of these collaborative studies, researchers have been working on a variety of stem cells, including adult stem cells found in umbilical cord blood and /or in adipose tissues. As part of clinical studies, skin tissues or adipose tissues are collected from a patient and reprogrammed to give them desired characteristics and delivered back into the patient to treat his or her disease. Consequently, early clinical trials are emerging in this lab, individually and in collaboration with scientists at Johns Hopkins University, University of Maryland and University of Miami, USA.

The entire program of collaborative research in the consortium lab unit is financed by grant monies from HEC and PSF (Pakistan) and the National Institute of Health, Bethesda, Maryland (USA). As such there is no financial liability on the part of partnering Institutions except salaries of two Assistant Professors by SZABMU and laboratory infrastructure by Jinnah Burn and Reconstructive Surgery Centre, Allama Iqbal Medical College and University of Health Sciences, Lahore. Execution of the research program, as well as management of the laboratory unit, exhibits an excellent model of management and research output, evidenced by an impressive number of high impact factor/International publications as well as clinical applications in both areas of research. There is no non-academic services expenditure. It is envisioned that this consortium unit, located in Lahore will serve as a nucleus for the National Institute of Advanced Research to be established by SZABMU in Islamabad as part of its vision 2025.

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