# Translational research: Basic science to health care. Way forward

In the field of neurology as in other disciplines, there are several disorders without specific biological markers for diagnosis and lack of affordable, effective, and safe drugs either for treatment or for slowing down the relentless progression of the disease. There is a sense of urgency to develop novel therapies to meet the expectation of patients, their families, and treating doctors. To expeditiously harness the research leads for improving health care the concept of 'translational research" has recently been attracting increasing attention of scientific organizations and scientists across the world.[1] To achieve the set goals of translational research, scientific research at cellular and molecular levels needs to be translated to offer practical solutions in diagnosis and treatment, a philosophy ingrained in the term "from bench to bedside" implying a partnership between basic scientists and medical professionals.

It is critical to recognize that information flow is not always unidirectional from the research laboratory to the patient but is a two-way-street." There are numerous examples of astute observations of clinicians based on unique features in a group of patients or even an isolated case which led to path-breaking research. In the field of neurosciences the oft cited famous example is of the patient known as Henry Molaison who had bilateral temporal lobectomy for uncontrolled epilepsy at the age of 27 years in 1953.[2] Peculiar memory problems noted in the postoperative period were that he was able to recall events of his childhood but was unable to learn new facts, e.g., could not remember the faces or names of the treating doctors who therefore had to reintroduce themselves every day. When given a task he could execute it but if his attention was diverted by someone talking to him or a phone call, he had no memory of what he had been doing a few minutes ago. Brenda Milner, a distinguished neuropsychologist of Montreal Neurological Institute, conducted extensive studies and her observations led to the concept of "short term" and "long term memory" which are distinctive and are stored in different areas of the brain. Thus, this classical study of a single patient laid the foundation of modern concept of functional organization of memory.[3]

Reverting back to complexities of bridging the border between clinical and basic research, while new knowledge is rapidly accumulating from research in basic sciences, translation to clinical sciences is becoming more difficult and challenging. Development of drugs and medical devices based on research in multiple disciplines of biology, technology, bioinformatics, pharmaceutical sciences, molecular genetics etc., is of fundamental necessity to treat diseases which either have no proven therapies or do not have satisfactory effective agents. Further, the concept of translational research extends beyond the domains of laboratory not only to patients but to the community as a whole, necessitating health systems and operational research involving disciplines of epidemiology, behavior and social sciences, to incorporate the leads from the new research and technology in formulating public health policy and delivery strategy.

Translational research evolves from scientists and researchers with a broad knowledge base, who can concentrate on bringing together basic scientific innovations to clinical studies converging on human health. Recognizing the need to create greater opportunity to facilitate and enhance development of the new discipline of Translational research, an innovative approach in US by National Institute of Health was the establishment of Clinical and Translational Science Award in 2006. Networking of 12 institutions of health which was further expanded to 46 and by 2012, 60 institutions were expected to be funded. The aims are to nurture multidisciplinary and inter-disciplinary investigators, promote innovative research and information technologies so that new knowledge and techniques can be rapidly translated to patient care.

It is a happy augury that India has not lagged behind and the Government of India with an ambitious aim has already put in place the Translational Health Science and Technology Institute in the year 2010. The goals of this institute are: to create a conducive ambience for facilitating research, to initiate a multidisciplinary approach to research, to translate the emerging leads to scientific and technological output and to transform appropriate innovations to bring about a significant change in health care. The ultimate objective is to develop new strategies for diagnosis and management of diseases and also facilitate preventive and promotive health. Recognizing that there is a need to enhance and promote research capabilities in medical colleges, networking of research institutions with medical institutions and hospitals in India is planned. For creation of a cadre of clinicians who can straddle two roles of clinical practice and research and allow cross fertilization between basic and applied science, partnership is envisaged with Harvard-Massachusetts Institute of Technology Health Science Technology, which integrates excellent training programs for clinicians and researchers cutting across disciplines of science, engineering, and medicine.

Personalized medicine is an excellent example of translating

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the leads from basic science of pharmacogenomics to determine the "right drug to the right patient at the right dose". Determination of specific biomarkers or genetic tests to identify the individuals with a specified profile provides guidance in decision regarding treatment protocol or avoidance of life threatening side effects.[4] The recent observation of a significant association of HLA-B*1502 with Stevens-Johnson syndrome and toxic epidermal necrolysis induced by carbamazepine in Han Chinese has made a remarkable impact on prescribing pattern of drugs in treatment of epilepsy.[5] This association was not a universal phenomenon since it was not seen in White population[6] but was present in Asian population in, Malaysia, India,[7] and Thailand.[8] CYP2C9 is a major cytochrome P450 enzyme that is involved in the metabolism of phenytoin and mutation of CYP2C9*2 and CYP2C9*3 alleles leads to decreased hydroxylation of phenytoin and hence the mean dose required to achieve therapeutic serum concentration is 30-40% lower than in those without the mutation and toxic levels are easily attained with the conventional doses.[9-11] Therefore, it is important to recommend appropriate dose range for a particular genotype. The overall impact of personalized medicine will be on choice and delivery of appropriate therapy, avoidance or reduction of side effects of drugs thus resulting in optimization of cost of health care.

Seamless partnership between engineers, scientists, computer specialists and technologists has led to development of a range of appliances and the recent concept of 'brain-computer interface' is being increasingly exploited to provide mobility and communication skills to patients with a wide range of disabilities. Undeniably this is an excellent example of translational research integrating computer sciences and neurosciences to alleviate human suffering. Nanotechnology is the engineering of functional systems at the molecular scale, which involves designing and production of small electronic devices and circuits built from individual atoms and molecules. The application of nanotechnology to medical sciences, in particular to neurosciences, will initiate an exciting era with breakthroughs in treatment of disorders which are currently challenging. Convergence of nanotechnology and biotechnology will further accelerate the pace of research.

The rapid growth of translational research is reflected by the publication of a number of journals, to name a few: Clinical and translational Science, Journal of Translational Medicine, World Journal of Translational Medicine, American Journal of Translational Research, Translational Medicine etc., While basic science research and the translation to the realm of new therapies and technologies are emphasized in some journals, in others the focus is on implementation of interventions in the field.

For translational research to gain a firm footing a paradigm shift in the training of research scientists and clinicians has to occur with a clarion call to develop innovative training programs to bridge the gap and facilitate cross pollination. Interdisciplinary approach has to be focused and students and faculty encouraged going beyond borders of the standard teaching program and research and seek novel pathways to discovery. Master's program on Translational medicine is already in place in some universities and it is hoped that with a critical mass of researchers and establishment of a multi-sectoral network of scientific organizations, technology institutes, computer professionals, medical and health care institutes it would be possible to achieve the vision and goals of development of novel therapeutic agents, delivery systems and cutting edge treatment strategies transforming the health care scenario and effectively connecting science and society. A road map is necessary to foster translational research with a separate path for speedy processing and funding of projects with flexibility and expandability needed to meet the changing demands of translational research.

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