Cancer research is a very broad term. It encompasses basic research, translational research, epidemiological research and therapeutic research, all with overlapping boundaries. While the ultimate goal for all forms of cancer research is to have a direct or indirect impact on reducing the morbidity and mortality from cancer, the objectives, triggers and also the measures of success are very different for these four broad areas of cancer research. The Journal of Cancer Research and Therapeutics aims to provide a forum for basic, translational, epidemiological and therapeutic research. To set our priorities it is necessary to restart a round of discussion on emerging issues related to the goals, triggers, trends and measures of success for these four broad areas of cancer research.

BASIC AND TRANSLATIONAL RESEARCH

As for basic research in any discipline, the driving force behind basic research related to cancer is the human quest for new knowledge and to some extent frustration with gaps in our knowledge. The key questions for basic research in cancer biology are centred around the mechanisms for malignant transformation of a cell, how it evades the cellular gate keeping and housekeeping machinery, signalling pathways, replication and growth, angiogenesis, invasion, metastases, immunological aspects and the molecular basis of resistance to cytotoxic agents. New knowledge emanating from basic research is intellectually satisfying and a satisfying measure of success in itself. However, it is being increasingly linked with the secondary objective of demonstrating how it could also lead to improved diagnostic and therapeutic approaches for cancer. This secondary objective is laudable and often increases the chances of obtaining funding and enables the research programme to climb up the priority ladder. However, it should compliment and follow rather than sideline novel basic research which may have no clinical application in the near future. There are numerous examples of important diagnostic or therapeutic approaches in the clinic evolving from basic research that were initiated without clinical applications in mind. Creating new knowledge or understanding biological processes is sometimes more challenging than deciphering how to apply it for human well being. While we had to wait for centuries for someone to discover naturally occurring radioactivity and the x-rays, finding its applications for human health took only a few years. The same is true for modern organic chemistry.

The secondary objective referred above is essentially the ‘Translational Research’ which is triggered and sustained by interesting leads from basic research in biology, chemistry or physics. It deals with the application of new research leads for better diagnosis, prognostic classification or therapy of cancer. The ‘Omics’ era from the genome to proteome has arrived and is likely to infuse much life in the biological translational research programmes. Translational research is truly speaking a melting pot of various philosophies, biological, technological and computational concepts and to some extent opportunism. The bench to bedside ‘Translational’ approach is certainly welcome and some would argue that it best justifies the taxpayers money spent on research. Nevertheless it should not assume the centre stage for its sheer potential for generating excitement and some revenues for the mushrooming biotechnology or bio-equipment industry. Being in the driving seat of translational research, industry is making inroads and perhaps setting the agenda for basic research by a form of reverse engineering. Industry is likely to promote basic research which will have a shorter gestational period for commercially successful applications. This underscores the need for continued public funding for basic research in view of its importance in the long term interests of science, medicine and human health. The alchemists of the middle ages epitomise the translational research approach where leads from chemistry set several generations on the gold hunt and finally the effort was abandoned out of sheer frustration. The public perception that it was greed that sus-
tained alchemy for so long may not be wrong. The modern biological translational research programme should learn from history and should be innovative, pragmatic and most importantly based on well proven biological concepts.

**EPIDEMIOLOGICAL RESEARCH**

Epidemiological research is not as glamorous as the cutting edge basic, translational or therapeutic research for obvious reasons. It is often tedious, expensive and generally takes a long time to demonstrate efficacy. Nevertheless, observational or interventional epidemiological research provides initial clues for hypothesis generation and sometimes starts a whole new area of basic or clinical research. In addition, it is a vital link for providing the data on population trends in morbidity and mortality and the real impact of new diagnostic or therapeutic approaches on the population at large.

Epidemiological research and public health measures can have a profound effect on human health. Let us not forget that for the infectious diseases, even in the industrialised nations, improved sanitation and hygiene in the late nineteenth and early twentieth century had a far greater impact on population mortality than the discovery of antibiotics. Is this true for other non communicable but often lifestyle related complex diseases like cancer? Can we rightly take the major credit for reduction in the population mortality from some of the common cancers due to our better understanding of the biology of cancer and ‘spectacular’ advances in therapeutics. Here also changes in the lifestyle, early detection due to increased public awareness, better diagnostic tools and perhaps screening have had a far greater impact in reducing the mortality of some cancers at the population level. Major reduction in the population mortality from cancer of the cervix was achieved with public health measures much before we knew the role of HPV in its causation or the experimental HPV vaccines. While this may not be the perceived wisdom, the facts imply that epidemiological research and population based interventions for changing lifestyle or more cost effective and sensitive screening tools are more likely to reduce cancer mortality than most of the new therapeutic tools. There is a need for more innovative, need based and adaptive epidemiological research in cancer all of which would require increased funding and trained manpower.

**THERAPEUTIC RESEARCH**

Here I am using Therapeutic Research as a broad area of clinical research conducted with the aim of more refined cancer diagnosis, improved survival or quality of life or reduced treatment toxicity. Clinical research is at the forefront of the medical research as its findings can have a direct and immediate impact on human health.

Clinical research in oncology has a rich tradition. Randomised controlled trials (RCTs), the punch line in the modern Mantra of Evidence Based Medicine were initiated in the field of cancer in the 1940’s. While a lot of ground has been covered, for a substantial amount of our clinical practice in oncology we still do not have unequivocal or the so called ‘Level I evidence’. In the absence of major breakthroughs in the way we diagnose or treat cancers, the law of diminishing returns is now clearly evident in clinical research. The modern and expensive clinical trial machinery is like a juggernaut which often draws thousands of patients in huge trials with the hope of showing a small improvement in survival. The increasing use of disease free survival as the primary endpoint rather than the hard endpoint of overall survival perhaps may be a reflection of the frustration, and impatience of clinical researchers.

The golden era of modern clinical cancer research was in the latter half of the twentieth century when major improvements in the survival of most childhood cancers (exemplified by the Wilms’ tumour studies) and some adult cancers with combination chemotherapy was established. By comparison, the clinical cancer research today is predominated by phase I-III trials of newer cytotoxic or designer drugs that have a far less impact on survival. Though cooperative research groups have produced robust data on the survival benefit with adjuvant chemotherapy in several solid tumours, the increasing influence of the multi-billion pharmaceutical industry on chemotherapy research is evident. New and very expensive molecules are being inducted in routine practice based on clinical trials which sometimes demonstrate survival improvement by only a couple of months or just better quality of life.

The trends in clinical research in cancer surgery or radiotherapy are also not very exciting. The major breakthrough in these fields was through clinical research conducted in the eighties and nineties that led to the emergence of organ and function preservation with conservative surgery and radiotherapy for several cancers. Most of the current research in cancer surgery is comparative (with other modalities) or exploiting improvements in material sciences and instrumentations. Clinical research in radiotherapy centres around combined modality treatment, tumour dose escalation and normal tissue protection. This was made possible with newer radiation technology and faster computational methods that allow more conformal dose delivery. The DAHANCA sequential trials in head and neck cancers could serve as a model for radiotherapy clinical trials exploiting novel fractionation schemes and cost effective radiosensitisers like nimorozole. It is an irony that these robust results have failed to influence practice outside Denmark while very expensive and labour intensive new techniques such as IMRT are being increasingly used worldwide without any level I evidence.
It is difficult to sum up cancer research and see through the exponentially rising research activities. However most would agree that basic research in cancer is very central to cell biology and continues to excite even if it fails to sustain the translational bandwagon. Translational research though fashionable should not have a free run and merely a conduit for starting new companies. Which leads from basic research should go in the translational mode needs a careful rethink and a more sound scientific basis. The much needed epidemiological research and public health measures are somewhat neglected, under funded and still as difficult as they were fifty years ago. Breaking free from the law of diminishing returns in clinical research will remain a daunting task and is a real challenge. It is a sobering thought and perhaps an inspiration for being more creative that despite the great efforts by several generations of clinicians and scientists the common epithelial cancers when advanced or disseminated are still incurable.