Turning laboratory findings into therapy: a marathon goal that has to be reached

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ABSTRACT

The mission of translational research involves difficult tasks to be accomplished for its ultimate goal, i.e. the introduction of novel, effective therapeutic strategies in the clinic to diminish human suffering and cure life-threatening diseases. Translational research (also referred to as translational medicine) facilitates the translation of investment in biomedical research into successful medical treatment. This includes the transfer of diagnostic and therapeutic advances by proving their efficacy in large evidence-based trials. Through the study of humans novel insights about disease are brought back to the laboratory to identify new, observation-based strategies. This "two-way road" ("bench to bedside and bedside to bench") process includes formulating guidelines for drug development and principles for new therapeutic strategies; initiating clinical investigations that provide the biological basis for new therapies, and related clinical trials; defining therapeutic targets and clinical endpoints. It requires a systematic approach beginning with specimen sampling, patient data collection, laboratory investigations, data analysis, preclinical testing, clinical trials, treatment efficacy monitoring, and finally the evaluation of therapeutic result. The marathon well symbolizes the enormous efforts undertaken by clinicians, scientists, regulators, ethicists, patient advocates, drug developers, and others, coordinately attempting to overcome obstacles along this road toward the final "marathon goal in medicine".

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Introduction Turning laboratory findings into therapy is the golden reward in a marathon for which most scientists and physicians train day after day. Indeed, "translational medicine" or "translational research" (the latter term emphasizing an essential aspect) might be considered as a great marathon run starting from scientific discovery and pre-clinical testing (training), through safety and human relevance testing during early-phase clinical experimentation (starting the race) to final validation, licensing and delivery of a clinically useful product (reaching the goal) (FIGURE).

Thus, as there is no successful marathon without rigorous training, the goals of translational medicine can be attained only by following the discovery process through the hurdles of guidelines and regulations with outmost dedication. Careful scientific and clinical planning of experimentation, achievable despite scientific, financial, ethical, regulatory, legislative, and practical difficulties, are the basis for success. Thus, the success of translational efforts will be dependent upon uncompromising efforts to break traditional barriers. As we previously suggested "traditional boundaries among basic research, clinical research and patient-oriented research are yielding to a single, continuous, bidirectional spectrum commonly termed *translational research* or *translational medicine*".[1] Traditional academic clinical research and translational research that emphasizes strategies to expedite successful implementation, though similar in intent, need to be distinguished. Translational research aims at providing

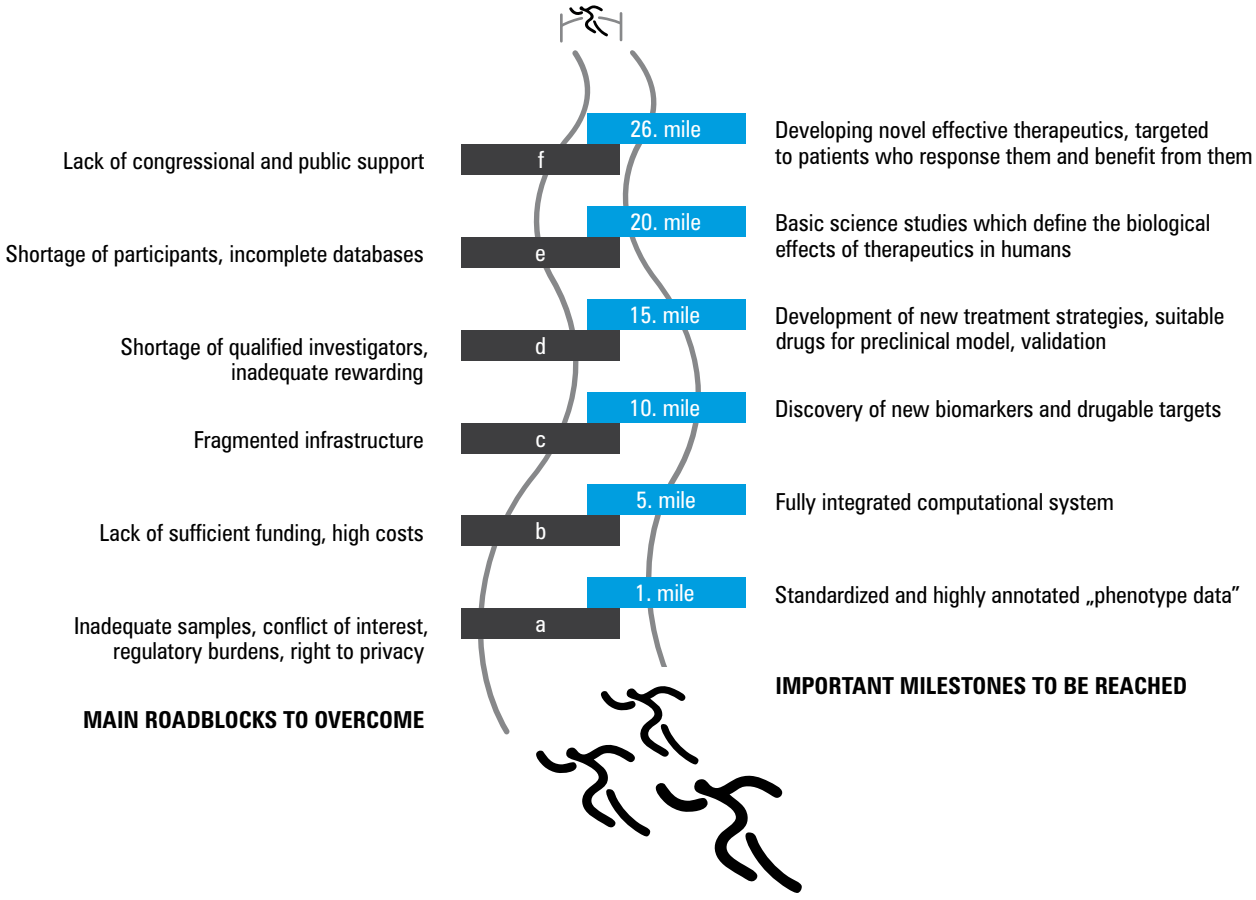

FIGURE The marathon goal of turning laboratory findings into therapy. Some of the important milestones (1–26) are listed, according to key tasks that have to be accomplished. Main roadblocks are indicated (a–f), that have to be overcome to reach the main goal.

guidelines to increase the effectiveness by which clinical testing can be applied to novel drugs with early go/no go decisions. Translational medicine integrates innovative pharmacologic tools, putative biomarker identification, testing and validation, clinical methods and study design to better understand disease biology, asses therapeutic index, select drug targets with greater confidence, and facilitate decision making process, and all to enhance the success of phase II and III trials. Translational research supports predictions about potential drug activity across species and novel compounds are brought to humans for the first time.[2] At the same time, translational research, while performing scientific and clinical tasks, acts as a supportive "coach" and promotes cooperation among various institutions to justify excessive investment in biomedical research, providing transparency to the public and encouraging health care education and understanding of its goals.

Setting goals and plans The main goals of translational research encompass several areas[2-8]:

1 the establishment of guidelines for drug development or for the identification and validation of clinically relevant biomarkers

2 experimental nonhuman and nonclinical studies with the intent to develop principles for the discovery of new therapeutic strategies

3 clinical investigations providing the biological foundation for the development of improved therapies

4 any clinical trial initiated in accordance with the above goals

5 basic science studies which define the biological effects of therapeutics in humans.

As biomedical research has become progressively more complex and specialized, a need emerged for researchers with different skills and expertise to work in concert as a team.

In addition to the general goal to discover new clinically relevant concepts or invent new clinically useful technologies, shared by all biomedical researchers, translational medicine tests swiftly the relevance of novel therapeutics with a promise in experimental setting within the realms of human reality. Thus, the primary goals of biomedical research may be considered as a substrate for the catalytic activity of translational research, considered as the "enzyme".[2] The efficacy of the process will be enhanced by translational medicine efforts, while the process itself is not modified. To foster the catalytic reactions of integrated disciplines, open dialogue is needed among stake holders with attention to clinical realities but also utilization of animal models that may frame the pharmacology and pharmacodynamics of therapeutics, the mechanisms of action on predicted targets, and the variable biology of disease in response to treatment biomarkers from these animal models to predict pharmacology in humans.[9-12]

Translational research: work to be done Translational research aims at reaching an accurate diagnosis and designing an appropriate treatment by following a systematic pathway of consecutive steps from specimen sampling, patient data collection, laboratory investigations, data analysis, preclinical testing, clinical trials, monitoring of treatment efficacy, as well as evaluation of immediate and, most importantly, long-term therapeutic results. Various studies summarized the steps along the translational pipeline, highlighting the most essential elements and possible difficulties that influence the chances of success.[1,13-15] Only properly applied clinical research can help to develop prospective care and personalized health planning based on rationally processed research discoveries. In addition, translational research, while increasing the efficiency with which the usefulness of novel biological discoveries is tested in the clinic following the bench-to-bedside direction, it can follow the bedside-to-bench direction, and through detailed human observation provide new alternative hypotheses relevant to human disease.[16,17]

The new vision of translational research calls for a multidisciplinary teamwork model that allows continuous and bidirectional exchange of knowledge and information between basic researchers, clinicians, laboratory scientists, and manufactures following an adhocracy system.[1] This, however, is not an easy task and often difficulties arise in the communication between the two main disciplines of basic and clinical research.[16] While scientific requirements for good and rigorous science should be better understood by clinicians, difficulties of dealing with human subjects should be better understood by scientists.

From accurate diagnosis to appropriate treatment In the application of translational research, understanding of human subjects through direct study of clinical samples can provide a bottom-up view of biology based on direct observations.[18] This has recently been well-demonstrated by a modular analysis of immune pathologies described by Chaussabel et al.[19] This discovery-driven, inductive, hypothesis-generating approach well complements deductive studies in which system biology is approached with a top-down attitude, and the convergence of the two strategies may strongly enhance the effectiveness of discovery by providing a framework of information relevant to human pathology (bottom-up approach), in which speculative analyses based on mechanistic information can be congregated through the power of present bioinformatic tools. This will ultimately enhance the accuracy of diagnosis and effectiveness of future treatments. A comparative approach should be considered which looks at diseases according to their biological principles rather than a discipline in which they are studied. A good example is human immunology which for too many years has been subclassified according to a discipline (cancer, infectious disease, autoimmunity, transplantation) rather than the mechanisms that may be shared by the various conditions to lead to similar results.[20] We recently suggested that immune-mediated tissue destruction follows common pathways in all these cases, which we defined as the immunologic constant of rejection.[21] This concept is being increasingly appreciated as illustrated by the newly formed Center for Human Immunology at the National Institute of Health (NIH), which is an inter-institutional effort to study immunology across disciplines (http://www.lassie.nhlbi.nih.gov/resources/chi/index.htm). By integrating molecularly-based technologies, systematic tissue procurement and medical informatics it is now possible to identify clinically applicable "genotype-phenotype" associations across cohorts of patients, which can be translated into useful diagnostic and therapeutic strategies.[13,22,23] Yet, the collection of human material is hampered in the translational medicine pipeline by several roadblocks of practical and ethical nature. Collection of materials needs to be standardized and assays require validation; extensive work is being done in this regard but certain issues still remain unresolved. Much has been achieved in the immune monitoring studies[22,24-27] or by the cancer network consortia[28-33]. At the same time, critical ethical issues covered by Institutional Review Boards such as the Health Insurance Portability and Accountability Act (HIPAA), as well as issues related to potential conflicts of interest, strategies for data standardization and sharing of information have proven difficult to overcome in an efficient manner.[1,13,34]

The parallel drawn between translational research and a marathon run intends to emphasize trivial and outstanding aspects, all the same essential to achieve success in spite of the sometimes overwhelming challenges ahead. A reasonable plan (an executable basic scientific project testing hypothesis derived from solid clinical observation), a good outfit (necessary infrastructure for high efficiency and quality laboratory and clinical work), support for training (enough financial support in order to obtain all the necessary reagents and medicaments, facilities for best patient care, support of the training of clinical scientists, etc.), a good coach (highly prepared scientific and clinical advisers with combined expertise in the scientific and clinical arenas), available educational resources (established scientific and clinical best practices for the conduct of experimental plans and their translation into clinical trials) are the basic important parameters that determine the success of any project, provided that there are no or not too many obstacles to face which would make the achievement of the goals impossible.

Obstacles and opportunities Obstacles to face, emerging opportunities, as well as their recognition and characterization through expedite publication will ultimately influence the final outcome.

In 2003, the *Journal of Translational Medicine* was launched with the purpose of providing expedite publication of articles relevant to clinical research through a specialized review process consisting of Board and reviewers able to work in the interface between basic and clinical research.[3,16,17,35] The *Journal of Translational Medicine* has rapidly grown and others followed the steps with similar initiatives; most recently the American Association for the Advancement of Science started a publication dedicated to science translational medicine. The hope is that these specialized journals will improve dissemination of concepts that are broadly relevant to the field of biomedical research independent of the specialized area of basic or clinical research. In particular the Open Access format of the *Journal of Translational Medicine* allows a rapid and worldwide access to any scientist with an otherwise limited access to resources. Thus, this forum may ultimately identify the several barriers that delay the process as well as work out solutions.

Basic processes sponsored by government institutions that target specific funding for translational research The NIH addressed the need to accelerate translational research by launching the NIH Roadmap (http://www.nihroadmap.nih.gov) in 2004. The main goal of the roadmap is "to identify major opportunities and gaps in biomedical research that no single institute at NIH could track alone". Clinical Research Enterprise specifically addresses translational research, acknowledging the bidirectional nature of discovery (bench to bedside and bedside to bench).[1] First signs of the successful implementation of this strategy are starting to emerge. However, the funding provided by the NIH through the roadmap is quite limited and offers primarily a proof of principle rather than covering the extensive needs of biomedical researchers in the basic/clinical interface, and other funding opportunities will need to be identified.[2]

Searching for new funding opportunities may solve the problem of insufficient funding The health care industry A coalition encompassing scientific, clinical, commercial, and regulatory disciplines might be established with the goal of seeking new sources of funding through patient, public and congressional education. One approach would be to help to support the cost of institutionally approved clinical trials in cases where standard treatments do not offer a greater chance for survival or improved quality of life.[1,36,37]

Academia-industry synergies The funding and infrastructure necessary to move a drug or a new test from the bench through the initial proof of principle to marketability is huge. Most academic institutions do not provide appropriate regulatory support or the facilities necessary to meet the standards for clinical product preparation. A complication of these partnerships is a conflict when research at an academic institution is sponsored by a biotechnology company. Limitations set by material transfer agreements may be in conflict with the scientific and financial interests of the institution that provides resources for other aspects of the same project and may frustrate the dissemination of important research findings by limiting publication and presentation of the research; such issues have been extensively discussed elsewhere.[8] Although potential solutions may be considered and implemented, it is likely that the best way to bypass the tremendous cost of clinical trials beyond the proof of concept will be to rapidly license a potential therapeutic out of academia to the commercial sector were venture capital resources may be applied rather that the governmental ones.[2] Several US institutions are starting to approach this partnership systematically.

The unique challenge of orphan diseases The challenge remains of increasing an interest in and research spending on diseases that are either too rare to support a cost-effective market for drug development, or are prevalent among disadvantaged populations (good examples are anti-viral agents or antibiotics for diseases of high prevalence in Sub-Saharan Africa). These aspects are generally covered by federal funding or by charitable institutions for example public/patient--driven organizations such as the Bill & Melinda Gates Foundation (http://www.gatesfoundation.org), the Personalized Medicine Coalition (http://www.personalizedmedicinecoalition.com), and the National Organization for Rare Disorders (http://www.rarediseases.org/).

Questions related to product development Identifying surrogate biomarkers that can predict the outcome of new therapies is becoming a central topic of translational research. These biomarkers can be applied at an early stage (phase I/II) or at the time of registration (phase III to commercialization) when the greatest costs are incurred.[38] Criteria are needed to identify markers that can be clinically useful, to assess the best methodology for clinical evaluation, and to establish criteria to appraise the incremental value offered over standard prognostic factors.[32] The National Cancer Institute (NIH, Bethesda, USA) sponsored the Program for the Assessment of Clinical Cancer Tests[30,31] in order to assess the likely responders to therapy.[39-41] However, the biological relevance of a biomarker may diverge from its clinical relevance. Thus, although the treatment seems to be effective in reaching its biologic purpose (anti-cancer vaccine inducing consistent cellular immune responses that can recognize cancer cells), additional steps may be necessary to achieve the desired therapeutic goal.[42-45] Unfortunately, a large proportion of translational medicine deals with phase 0 or phase 1 proof of concept studies. Although they are extremely important in testing novel ideas, they

rarely have the power to provide conclusive validation of potential biomarkers or surrogate markers. This problem also results from the difficulty in standardizing the process of protocol design, sample accrual, collection, storage, and analysis.[22,24-26,46,47] For these reasons, guidelines for statistically valid studies, standardization of assays, possibility for evaluating large data sets have to be introduced. Multidisciplinary workshops and consensus conferences that involve scientists, industry and regulatory agencies will be necessary. A good example is the upcoming workshop on biomarker validation sponsored by the International Society for the Biological Therapy of Cancer and the United States Food and Drug Administration.[22] Another important event is the NIH Biomarker Consortium developed to encourage government, academia, and commercial partnership to speed the identification of useful biomarkers relevant to clinical trials (http://www.biomarkersconsortium.org).

Accrual limitations and patient stratification Appropriate patient selection is highly important for phase I/II studies to successfully assess toxicity, identify optimal biological dose, characterize kinetics, and better predict the biological or clinical effectiveness of treatment. Epidemiology of the biomarker in the targeted population and its biological relevance might sometimes be unknown, emphasizing the need for prospective collection of clinical material to identify novel biomarkers with high throughput technology and validate the known ones.[48]

Appropriateness of sample collection Although high throughput technologies enable researchers to study human diseases, accounting for genetic variability of individual patients and the heterogeneity of their diseases, a major limitation remains the ability to link clinical information to high quality sample collection. General rules and ethical considerations have to be taken strictly into account, to continue small- to large-scale human specimen collection. The approved ethical permission application and the patients' informed consent are essential but problems arise when too many limitations delay or hinder this approval even temporarily. Legislative and regulatory limitations such as material transfer restrictions and HIPAA severely limit the utilization, interpretation and correlation of biological data with clinical data.[38] If various biological samples are taken according to guidelines, stored properly and provided with patients' necessary clinical data, the input results may be of much higher value. However, in most cases specimen collection is not carefully supported because of limitations in clinical study design, relationship between surgeons and pathologist, inflexible requirements for the use of samples as diagnostic material, lack of organized tissue banks inclusive not only of the technical expertise but also of the necessary regulatory support that allows eventual use of human material of biomarker discovery[30,31]; all this requirements not only make sample collection burdensome but also exceedingly expensive. Another limitation is the ability to link clinical information to high quality sample collection. Samples obtained by surgery, through venipuncture, fine needle aspiration, through-cut needle biopsies, and cytological smears can be further processed for various cellular and/or molecular investigations. DNA and RNA amplification techniques and high sensitivity proteomic tools are the basis for powerful studies performed, concerning the revealing of disease background. The opportunity to take specific steps to preserve the ex vivo profile is often lost unless researchers identify the sample for use in a particular clinical study a priori.

Samples collected retrospectively are often unusable for analysis since materials degrade quickly after tissues or fluids are removed from the organism. Clinical trials are often designed without knowledge of these limitations and the collection and preservation of clinical samples does not follow the strict guidelines that would optimize their usefulness.[1,48] There are already good examples of great efforts for prospective collections, e.g., the integration of translational research in the European Organization for Research and Treatment of Cancer[28] and the Cooperative Breast Cancer Tissue Resource[29]. These consortia have already collected large libraries of tumor samples, prospectively linked to clinical information, while patient privacy is preserved. Listed below are other important aspects, the solution of which would help to successfully implement the above project.

1 A systematic and comprehensive view of the methods applied and the purposes of the proposed investigations should guide designing an initial stage of the study as well as timing and location of sample collection.

2 High throughput tissue and cell banks provide a great chance for scientists, clinicians and patients: in the case of effective study results (e.g., finding effective patient selection criteria for a new targeted therapy), they could provide direct therapeutic advantage for sample donor patients.

3 An effective tissue bank has to be always up-to-date and an equal access to the modern biobank has to be ensured. Donors of a tissue sample preserved in a modern, fast-frozen biobank have a greater chance for modern diagnostic (and therapeutic) processes.

4 Effective and appropriate sample collection with registration, categorization, and clinical data collection require considerable effort from both clinicians and scientists. Collaboration (communication, common terminology, common interests) between them has to be emphasized. A bridging step (skilled assistant or automated sample collection device) is needed to organize the cooperation of clinicians and scientists.

5 Routine sample collection should focus more on fast-frozen tissue conservation where

the logistic and technical backgrounds (liquid N_2-supply, −80 °C refrigerators, etc.) are commonly established.

Opportunities for developing more effective therapeutics Target identification Developments in whole genome biotechnology and the potentials of modern technology in general have provided huge opportunities for the identification of more effective therapeutics that are tailored for patients who are most likely to benefit.[49] High throughput technologies enable researchers to study human disease in its entirety, accounting for genetic variability of individual patients and epigenetic instability of their diseases. Extensive analysis of individual polymorphism could complement information related to the disease process at the genetic, functional and post-translational levels.[50] Genome-wide analysis is easy and requires only small samples for the preparation of genomic DNA. As these new frontiers in science emerge, a unified science curriculum that fully incorporates mathematics education and quantitative thinking has been proposed to prepare the 21st century scientists to the challenge of the study of system biology.[2,51,52]

The identification of clinically relevant biomarkers for various diseases is associated with unique challenges because biomarkers, whether biochemical, pharmacological or physiological measurements, are obviously likely to be relevant in a disease specific manner. Platforms that may allow the analysis of multiple biomarkers independent of a disease process, may also facilitate the discovery of unknown facets of disease biology that would not have been otherwise discovered.[40] Thus, for financial reasons, a balance needs to be struck between the necessity to limit biomarker analysis to those which are most likely relevant in a particular condition and the desire to globally study human samples with a discovery-driven, hypothesis generating goal.[17,22,53-55]

The advancement of translational medicine is strongly dependent upon novel assay technologies (e.g., microarrays, high throughput microchips, protein microarrays, imaging technologies, miscellaneous assay technologies, etc.) as with them a great field of knowledge might be harvested and new directions developed for the future with high efficiency and no preconceived bias.[17,56]

Study of the therapeutic mechanism In order to understand the reason for therapeutic success or failure and utilize the acquired knowledge to better design successive trials, the analysis of tissues affected by the disease process and targeted by therapy is likely to be most relevant though difficult because it requires repeated biopsies.[44,57] Less invasive methods, such as serial fine needle aspirates followed by high fidelity RNA amplification techniques, allow to analyze pre-treatment samples which are then left in place to assess their response to therapy.[58] Fine needle aspirates or other minimally invasive techniques allow to perform repeated biopsies during therapy, which can shed light on the mechanism of action of the therapeutic.[59,60] Protein analysis completes the picture, since protein function is modulated through post-translational changes and protein-protein interaction. For instance, the introduction of protein arrays dramatically improved our understanding of alterations induced by systemic administration of high-dose interleukin-2 (IL-2) to cancer patients. Prospective collection of serum samples during therapy may help to identify patterns responsible for treatment toxicity and/or effectiveness as we have shown in a number of successive studies in which the mechanisms of action or high-dose IL-2 were evaluated with increasingly higher sophistication[40,58,59,61-63] culminating in a recent discovery of biomarkers potentially predictor of responsiveness to therapy.

Validating surrogate markers Because of high costs in late phase clinical trials it is important to identify relevant biomarkers, predict treatment safety, efficacy and differentiation before investing in large clinical trials. Surrogate biomarkers have the potential to substitute standard clinical endpoints such as X-ray measures of joint damage, functional status, survival, disease-free survival and/or symptom free interval are of increased interest, therefore they can shorten the time necessary for critical go/no go decisions in early phase development. The identification and validation of useful biomarkers will allow researchers to assess whether a novel idea is likely to turn into a useful and profitable product and to obtain treatment approval from regulatory agencies.[2,22,39,41,48,64]

Special issues Last but not least, some unique challenges need to be considered, which in some countries may halt effective implementation of translational research. Like in a marathon run, equal possibilities have to be ensured for all runners, carefully planned rules and some kind of balanced help, for those, in special need. The results of any achievement in medical science are measured on equal footing. However, there is a great difference worldwide regarding the infrastructural background and nation-based possibilities and limitations to make the steps of translational medicine marathon run. A great number of valuable ideas had to be abandoned due to a lack of national or international support mechanisms that could enable a successful implementation of a study design. This situation may improve, however, as through the year long struggle through which the European Commission and other international funding organizations finally gave preferential possibilities to former Eastern European Countries.

Health care institutions all over the world might provide a proper setting for translational research because they host an independent

variable of clinical investigation – the patient around whom clinical research should revolve. However, in practice it is difficult to perform even the simplest study because infrastructure is still imperfect or the gap between clinicians and scientists too difficult to bridge. Therefore, it is vital to educate a new generation of clinical scientists who will have knowledge and competence to address these issues.[1] It is particularly important in developing countries and hence the need for international grant support that could sponsor cross-training at a global level, and provide opportunities and considerable support for international collaborative projects. Organizations such as the Fulbright (http://www.us.fulbrightonline.org/home.html), the NATO Collaborative Linkage Grant (http://www.nato.int/science/nato_funded_activities/grant_mechanisms/clg-nfa.htm) and the Fogarty (http://www.fic.nih.gov/funding/) have been particularly active in ensuring fair possibilities for scientists from all over the world. Particular interest of a proportion of the resources should be directed toward translational studies. As most of the affiliations under discussion are based in the USA, other leading countries should be encouraged to join in the efforts to expand the outreach to less privileged colleagues, thus creating a strong international community of scientists united in pursuing similar goals regardless of geographical background.

Conclusions The goal of translational medicine is to test novel therapeutic strategies developed through experimentation on humans. Its potential is as large as its goal, as it helps to validate the clinical efficacy of novel discoveries, increase the efficiency in which new therapeutic strategies can be tested on human subjects, provide feedback to researchers about the effects of treatment, develop reagents for the characterization of the disease process.

However, we still have to overcome several barriers that slow the progress of translational research, such as insufficient targeted resources, shortage of qualified investigators, or regulatory hurdles. It is necessary to foster close collaboration between clinical and laboratory-based investigators, and to convince health care providers and investors about the need for better opportunities and support. For the translational research project to be successful, it is extremely important to create optimum conditions in which most effective work could be done. All scientists, clinicians, and others involved in the project have to cooperate and focus on the final goal – the effective treatment of diseases affecting women, men and children.[16]

Note On behalf of the colleagues and patients, we dedicate this work to the memory of an outstanding Hungarian clinician in bone marrow transplantation, Dr Robert Denes, PhD, MD.

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Zastosowanie wyników badań podstawowych w leczeniu – cel maratonu, który musi być osiągnięty

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SŁOWA KLUCZOWE

badania translacyjne, medycyna translacyjna, przeszkody, możliwości, terapia

STRESZCZENIE

Misja badań translacyjnych obejmuje trudne zadania, które muszą być zrealizowane dla osiągnięcia ich ostatecznego celu, tj. wprowadzenia do kliniki nowatorskich, skutecznych strategii terapeutycznych w celu zmniejszenia ludzkiego cierpienia i wyleczenia chorób zagrażających życiu. Badania translacyjne (nazywane również medycyną translacyjną) ułatwiają przekształcenie wyników badań biomedycznych w skuteczne metody leczenia. Dotyczy to również postępów w metodach diagnostycznych i terapeutycznych, poprzez udowodnienie ich rzeczywistej skuteczności w dużych badaniach klinicznych, z zastosowaniem zasad *evidence-based medicine*. Z kolei poprzez spostrzeżenia poczynione na ludziach, do laboratoriów badawczych docierają nowe obserwacje na temat chorób, w celu wypracowania nowych strategii postępowania. Ten dwukierunkowy proces („z laboratorium do łóżka chorego i od łóżka chorego do laboratorium") obejmuje: rozwój wytycznych opracowania leków, rozwój zasad dla nowych strategii terapeutycznych, inicjowanie doświadczeń dostarczających biologicznych podstaw nowych metod leczenia oraz powiązanych z nimi badań klinicznych i określanie celów terapeutycznych oraz klinicznych punktów końcowych. To wymaga systematycznego podejścia do kolejnych elementów badań, począwszy od pobierania próbek, zbierania danych pacjenta, wykonywania badań laboratoryjnych, analizy danych, testów przedklinicznych, badań klinicznych, monitorowania skuteczności leczenia i ostatecznie oceny wyników terapeutycznych. Maraton jest dobrym symbolem ogromnego wysiłku włożonego przez klinicystów, naukowców, osoby sprawujące nadzór, etyków, adwokatów pacjentów, firm farmaceutycznych i innych, wspólnie starających się pokonać przeszkody na tej drodze w kierunku ostatecznego celu „maratonu" w medycynie.

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