

Translational Medicine and its Perspectives in Poland

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Abstract

This article presents Translational Medicine (TM), one of today's 'buzz words'. Moreover, it seeks to identify the factors which stimulate or impede TM's development in Poland, based on desk research and a series of expert interviews conducted in four countries. TM is a new trend in research and clinical practice. It stems from two sources: observation of how ineffective the traditional drug development process is, and from the public need for innovative therapies. Strategies developed within the translational approach optimize medical innovation development so that the chasm between impressive scientific discoveries and poor pharma productivity is filled. Our diagnosis shows that Poland is a minor player on the market of new technologies, particularly drugs. However, Polish scientists and industry do have a potential that will enable them to play major roles in international research teams that work on innovative, global projects.

Key words: translational medicine, pharmaceutical industry, R&D, innovations, SWOT, project SPIN

Słowa kluczowe: medycyna translacyjna, sektor farmaceutyczny, B+R, innowacje, SWOT, projekt SPIN



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Introduction

Translational Medicine (TM) is a new trend in biomedical research and clinical practice, which has been gaining growing international popularity for several years. The aim of this article is to assess whether the idea and practice of translational medicine is likely to take root in Poland, thus supporting medical innovations based on Polish companies and R&D staff. The following paragraphs provide a detailed description of the concept of translational medicine in its many meanings typical of the different groups participating in the development of new medical technologies. We refer mainly to the major assumptions and postulates made by practitioners of translational medicine. Next, we present results of the SWOT (strengths, weaknesses, opportunities, threats) analysis in order to assess the prospects for the development of translational medicine in Poland. The presented facts, opinions

and conclusions are based on the results of a study carried out as part of the project titled 'SPIN – Model of Innovation Transfer in Malopolska'. The study included the analysis of existing data (review of scientific literature, own calculations based on publicly available data) and a series of in-depth interviews. All respondents are professionally involved in the development of new medical technologies (at its different stages), or in their implementation in clinical practice. The pool of sixteen interviews included six interviews with scientists, five with representatives of the pharmaceutical industry (or persons conducting clinical trials on behalf of private companies), and another five with representatives of the institutions supporting the development of medical technologies, including one American, one Swiss and one German company. All interviews were conducted in the second half of 2012.

Poland is a peripheral player on the market of innovative therapies, and so we think that it is not possible

to realize all stages of drug development – from their discovery to implementation in clinical practice – using national (financial, technological and human) resources. However, based on the conducted analysis, we believe that Polish scientists, universities and companies *can* be an important partner to international consortia working on drug development.

What is translational medicine?

Translational medicine is a relatively new field of knowledge and medical practice, which aims to bridge the gap between impressive results of basic research (especially in the field of biotechnology and genetic research) and a modest number of new medical technologies that are available to patients. This is to be made possible by ‘translation’, usually understood as a transfer of basic medical research results to direct use in clinical practice. Translational medicine demands that basic medical research be inspired by real clinical problems and targeted practical solution. The process of translational medicine, understood as the implementation of innovative medical technology in clinical practice, may be applied to any medical technology, e.g. a drug or therapy, vaccine, medical device, surgical technique, or diagnostic method. In practice, however, translational medicine is most frequently mentioned in the context of drug development, and it is so also in this article.

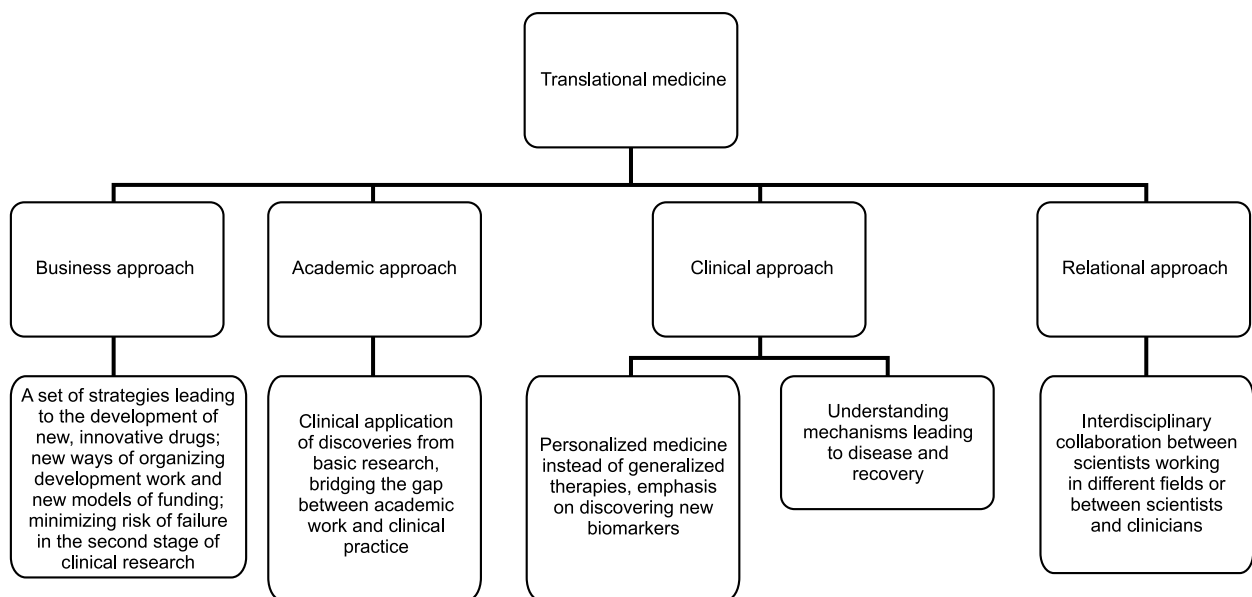
Translational research, rather than competing with basic or clinical sciences, bridges the two by leading to

the development of new, more effective or safer therapies, broadens the spectrum of diagnostic and preventive possibilities, and improves the comfort of treatment [1]. Exemplary translation responds to the real need of patients and helps to reduce the clinical problem; is efficacious and safe (which has been confirmed in thoroughly conducted and documented clinical trials) and is not only legally available but also practically accessible to patients e.g. reimbursed and/or adequately propagated in the medical community.

This young discipline has already gained both recognition and criticism. The critics evaluate this new approach primarily as a fad or a new label for the long-running development research. The best example of a successful translation is the discovery of penicillin, a side effect of Louis Pasteur’s other research. The cynically predisposed also point to the incredible effectiveness of research projects bearing the translational tag in obtaining public funding [2], suggesting that the main task of ‘translational medicine’ is simply gaining public support, which will launch new financial streams for further research and development [3]. Interestingly, these critical voices can be heard mostly in the corridors or in popular science press. An open, systemically argued scientific criticism has so far been lacking.

Figure 1 is a graphic summary of the most important ways of understanding translational medicine, typical of different groups of stakeholders. The key points presented in this figure will be developed later in the article.

Figure 1. *Translational medicine – academic, business, clinical and relational perspectives*



Source: Own elaboration.

Translational medicine gives hope of overcoming the pharmaceutical crisis

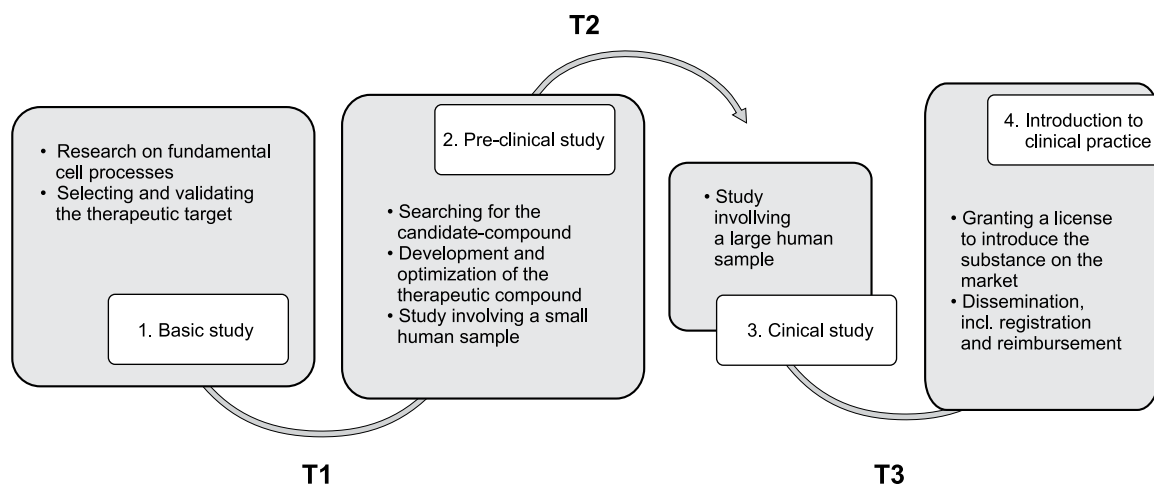
To understand the need for and popularity of the new ‘translational’ narrative in life sciences, one has to refer to the crisis of the pharmaceutical sector, announced a few years ago. Despite increased spending on research and development in this field, the annual number of new medicinal compounds registration² (in other words, therapeutic active substances which may be marketed as drugs) has remained relatively constant since the 1950s [4]. The exception was the 1995–1996 period, the time of a significant increase in the number of new registrations [5]. Therefore, it is often erroneously stated in the literature that the crisis of innovation in the pharmaceutical sector is due to the ever-decreasing number of new registrations. In fact, the essence of the crisis is increasing the cost of introducing new medical compounds on the market [5]. The crisis is believed to have been caused also by the fundamentally flawed cycle of innovation.

Four stages can generally be distinguished in the process of developing a new drug³ (see **Figure 2**). The purpose of the first stage, known as basic research, is to define the therapeutic target – the protein located in the human body whose activity is associated with the disease. In the second stage scientists develop a therapeutic compound which is able to interfere with the functioning of that protein (either by blocking or stimulating the protein’s activity) [6]. The search for such a compound is a difficult task, which involves selecting the most promising molecule among thousands of others. For this purpose, laboratory studies on isolated cells or computer simulations, as well as medical experiments on animals

are conducted. In the third step large-scale observations are carried out in order to observe the effect of the therapeutic compound on the human body, in particular its safety and efficacy. This traditional, linear model of developing new drugs does not lead to broadening the spectrum of therapeutic possibilities, at least not on the scale that would be expected, given the increasing expenditure on research and development in this field [7]. An especially critical stage in the development cycle of a new drug is the second phase of clinical trials [8] (3rd stage shown in Figure 1). It is time-consuming, costly, and typically involves hundreds of patients – an insurmountable barrier in the case of as many as 9 out of 10 carefully selected molecules [9], e.g. in oncology [10].

In a sense, the pharmaceutical industry and the scientists involved in the development of new drugs became a victim of their own success. The starting point for most of drug development projects are advanced biomolecular studies. In recent years, this domain of science has made an unprecedented progress, which resulted in an impressive number of potentially efficacious therapeutic targets and their corresponding drug molecules [7]. The number of such molecules is too high to allow for testing them all in clinical, or advanced pre-clinical studies. Even if that were possible from the organizational and financial points of view, it would take hundreds, if not thousands of years, while medication is needed here and now. Therefore, it is important to be able to make an accurate and early assessment of the safety and efficacy of thousands of potentially therapeutic molecules. For several years it has been indicated that ‘easy therapeutic objectives’ have become exhausted, which led to the increasing complexity of drug development [11]. In

Figure 2. Translational stages (T1, T2, T3) and a new drug cycle



Source: Own elaboration.

addition to that, the most popular methods of early drug validation – studies in cell cultures and in animal models – are proving to be increasingly unreliable in the case of very complex pathophysiological mechanisms occurring in the human body [12]. The second reason given to explain the rising cost of launching new molecules emphasises the aggressive strategy of large pharmaceutical companies, investing in costly and high-risk projects, with the hope of high returns in the case of an exclusive development of a niche [4, 7].

In summary, the poor productivity of new drug development is determined by its three characteristics – high (and continually growing) cost, and the time and risk involved. Some estimate that the introduction of one new drug to the market costs an average of \$ 1.8 billion [13]. The whole process, starting with the first laboratory test and ending with the registration, takes at least several years. At the same time the risk that the compound developed in the course of basic and pre-therapeutic research does not show sufficient or any therapeutic efficacy in clinical trials involving patients as a result of insufficiently accurate pre-clinical selection of molecules, is very high [14]. The chasm between progress in basic research, increasing spending on research and development in the pharmaceutical industry and the small number of innovative drugs has given rise to the aforementioned discussion of a fundamentally flawed development cycle of medical innovation. Translational medicine, in particular the new way of organizing research and development that reduces the risk of failure during the second phase of clinical trials, is considered to be the answer to the failure of the traditional linear development cycle of new drugs.

Early validation using biomarkers

A unique role in a translational research project is played by the earliest possible pre-clinical validation of potentially therapeutic compounds, which usually takes place with the use of biomarkers. Biomarkers – objective, measurable indicators of the physiological state of the body [8] – bridge the tangible, concrete, measurable laboratory work with a multi-dimensional reality of the disease, experienced by the patient, and the clinician. From the point of view of the academic world, the considerable importance of biomarkers is not only to facilitate the introduction of a given substance on the market. A key benefit of exploring and discovering new biomarkers is to better understand the mechanisms controlling the disease in question, which in turn creates the opportunity for a more effective and safer therapy.

A completely new field for the diagnosis and treatment was opened with the mapping of the human genome (the particularly important part of the DNA) [9], preparing the ground for the so-called ‘personalized medicine’ that uses genetic biomarkers to determine e.g. the kind of disease the patient is most susceptible to or drugs that they will best react to [15]. This enables e.g. the stratification of cancer patients to those who can be effectively subjected to traditional low cost-therapies and those who will need to undergo an extremely costly treatment with

innovative drugs. The interest in biomarkers is shared by personalized medicine and translational medicine, making the latter sometimes (wrongly) identified with genomics. It is far too narrow an understanding of this broad and largely vaguely defined term.

Early validation in human studies

The use of biomarkers for early, pre-clinical validation requires that the first tests in humans take place earlier than it would traditionally be the case. This approach and the denial of linearity of the medical innovation process are common features of many translational projects. If one were to indicate the most recognizable slogan accompanying translational medicine, it would surely be: ‘from the bench to the bedside’ (i.e. ‘from the laboratory to the bedside’), reflecting the emphasis on the practical application of new discoveries. The essence of translational medicine is better expressed using another slogan: ‘from the laboratory to the bedside and back’ [16] which takes into account the two-way flow of knowledge in translational projects – on the one hand, scientific discoveries are developing clinical capabilities, and – in return – the clinical observations provide scientists working in labs with important insights and data for further work. In this sense, the process of discovery and implementation of new medical technology into clinical practice is neither one-way, nor linear. It does not need to start with the discovery in the field of basic sciences, and is characterized by multiple feedback loops at the interfaces between the subsequent stages of new drug development. Interestingly, such approach towards creating a medical invention is typical also of the general modern concept of innovation generation. The constituent feature of this modern concept is the transition from a supply model, where the science sector plays a major role, to the demand model, assuming the earliest possible involvement of practitioners/users in the process of creating new solutions [17].

Interdisciplinary communication

Good communication between scientists and clinicians know the problems and needs of patients is a key to success of a non-linear and two-directional translational project. Ideally, the same staff are involved at different stages of the translational – both scientific and clinical – process. However, this postulate is made very difficult by the vast amount of knowledge one person needs to have to fulfil these two roles well [12]. The development and specialization of science separates not only scientists working in basic fields, theoretical doctors and medical practitioners. Also within the researchers working in related areas – such as, genomics, molecular biology, neuroscience, bioengineering and bioinformatics, cell culture, biotechnology, biophysics, pharmacology and pharmacokinetics – a common language and good communication are often lacking. Translation is therefore often understood also as an interdisciplinary agreement of representatives of a wide spectrum of basic scientific

fields, and translational medicine becomes the banner under which they work jointly with clinicians, pharmaceutical industry, and finally the patients themselves to generate new quality in health care [18].

New models of financing the development of new drugs

The traditional model of new drug development involves a large commitment of public resources for early, preclinical stages of the development cycle. One of the instruments of this funding is – among other things – supporting basic research in life sciences. The cost of later stages of this process i.e. research on the proper dosage of the drug substance, the best form of administration, general safety and efficacy, are typically borne entirely by the pharmaceutical companies. Between the early and late stages of drug development extends the so-called ‘valley of death’, where potentially effective substances become halted. The high cost of conducting further work on them and the huge risk of failure in the clinical trials stage causes a lot of potentially successful projects to be abandoned⁴ [19]. Meanwhile, there is enormous demand of aging European societies and the rapidly developing Asian and African societies for new pharmaceuticals. There is also immense public pressure for greater translational efforts, resulting in new funding sources coming from different areas, e.g. governments and supranational organizations, charities [9] or public collections. For example, the Wellcome Trust has earmarked 91 million pounds for the Seeding Drug Discovery project subsidizing various stages of developing pharmaceuticals. The development of new drugs is also sponsored by other charities, for example The Bill & Melinda Gates Foundation which supports the fight against malaria and tuberculosis in developing countries. Another new model of financing the development of new drugs is the public-private partnerships, for example the Innovative Medicines Initiative, with a total budget of 2 billion euros, covered in equal parts by the European Union and the EFPIA, the European Federation of Pharmaceutical Industries and Associations.

It is important to realize to what extent the development of new drugs is financed (though not always directly) from public budgets – in the first place by funding basic research in life sciences, and later through targeted grants for science and business partnerships and by training scientific personnel and finally through the massive purchase of new medicinal products. This means that governments and societies providing funding for research and development may demand that new discoveries in life sciences be carried out with a practical clinical application in mind and then made available in open models. An ‘open innovation model’ implies openness in sharing research results between commercial and non-commercial research teams. This approach assumes that the increase in the number of people trying to solve the same R&D problem will result in a prompter success [20]. Open innovation is likely to be effective in developing new solutions, but poses a major challenge for the business model of pharmaceutical companies, most

of which have the tendency to restrict knowledge rather than to open it. From their point of view, only a patent guarantees returns of the development investment. Very few companies see open innovation not only as the noble aim to improve public health, but also an opportunity to break the deadlock of the pharmaceutical sector. Hence, for example, Eli Lilly took the initiative to share their research results as part of the Open Innovation in Drug Discovery project.

New organizational models

New translational projects are no longer conducted in a centralized way, in research departments of large pharmaceutical companies. The increasingly common business partnership with the academic world can produce synergies since the two communities will focus on what they know best [16].

The scientific component of the project is now mainly realized within the walls of the university and to a large extent it is the scientists who play the role of the project leaders [9]. Often a few scientific research teams work within one project and each of them focuses on the selected aspect of the research problem [14]. Joint research programmes contribute to creating a network of researchers and build the competencies of the people involved. With time, this can lead to the creation of purely academic units aiming at new drug development, such as the Institute for Cancer Research, Centre for Cancer Therapeutics in London (England); Imperial College Drug Discovery Centre, London (England); Texas Therapeutics Initiative of Houston (USA) and the Centre for Drug Research and Development in Vancouver (Canada).

In turn, the industry generates a business model and coordinates the entry of the product into the market. It also provides management solutions and ensures that the scientists’ work meets stringent quality requirements. These organisational enhancements can truly improve some phases of the process of discovery, testing, and deployment of pharmaceuticals; however, whenever the results depend primarily on the discovery, the serendipity factor is crucial.

Translational medicine and public health

Translational strategies go far beyond the laboratory, and far beyond the process of discovering new drugs. An integral element of the translational process is its implementation into clinical practice, often made possible only through reimbursement and promotion. This has led to the emergence of the idea that a molecule in the development stages should be optimized for economic evaluation which it needs to undergo before being launched. Obviously, reimbursement of new therapies brings serious consequences not only for the budgets of the ministries of health and insurance companies, but also for public health. However, the relationship between translational medicine and public health is more complex. For example, Ogilvie [21] proposes a comprehensive model indicating a multidirectional relationship between life scienc-

es, social health sciences, pro-health behaviours, health status and public policies. On the other hand, Kardas [22] points to the consequences of the implementation of new technology, especially bio-informatics, into the practice of family physicians and epidemiological research.

Prospects for the development of translational medicine in Poland

The interest in translational medicine has reached also Poland. In 2011 Warsaw hosted a Polish-German seminar titled ‘Translational research in diseases of the cardiovascular system’ [23, 24]. In 2012, a new consortium was established – the Centre of Chemistry, Biology and Translational Medicine Poland, working in cooperation with the prestigious American centre engaged in oncology research, MD Anderson Cancer Center, University of Texas. Last but not least, OMICRON – the first modern genetic testing laboratory was set up at the Faculty of Medicine of the Jagiellonian University, followed by the Malopolska Centre for Translational Medicine. The latter initiative was funded by the Malopolska Voivodeship, whose authorities chose life sciences to be one their ‘intelligent specializations’ (i.e. strategic areas) [25]. In addition, a number of highly advanced research projects are being conducted in Poland and although they do not bear the translational label, they are part of this research trend. A good example is the EU-funded study of epilepsy and tuberous sclerosis. The aim of this project, run under the

name EPISTOP by the ‘The Children’s Memorial Health Institute’, is to understand the mechanisms of these diseases through the identification of diagnostic biomarkers. The results of these studies can be used in the future to develop new targeted therapies.

There is no doubt that high-quality research projects in the field of life sciences can be successfully implemented in Poland. The question is whether we are able to successfully carry out the translational work from the beginning to the end, which is to actually apply new solutions in the clinical setting. Table I contains a summary of the most important decisive factors. Following the SWOT methodology, these factors have been divided into four categories. The internal factors that have a positive effect are listed in the upper left corner (relating to the characteristics and resources of Poland) – these are the strengths. The internal factors impacting negatively are listed in the upper right corner – these are the weaknesses. In the bottom half of the table external factors related to global rather than local conditions of translational medicine are presented – these are the opportunities and threats for the development of translational medicine in Poland (Table I).

The factors listed in the table are arranged in several thematic issues, which are discussed below in four sections – Clinical trials in Poland, Innovation efforts at Polish pharmaceutical and biotechnological companies, Polish scientists and innovation and the Functioning of universities.

Table I. SWOT analysis for the development of translational medicine in Poland

<p>Strengths</p> <ul style="list-style-type: none"> ✓ very good pool of patients for clinical trials because of the large absolute number of population, and prevalence often higher than the European average ^{w adz} ✓ very good academic background, well-equipped laboratories ^w ✓ many good specialists working in narrow fields ^{w*} ✓ stream of government funding for innovation in medicine ^{w adz} 	<p>Weaknesses</p> <ul style="list-style-type: none"> ✗ high rate of patient resignation from participation in the study ✗ very low innovation of Polish pharmaceutical companies ^{w adz} ✗ a relatively small market for innovative therapies (dominating market of generic drugs, little chance for reimbursement) ^{adz} ✗ lack of experience in the development of new drugs ^w ✗ lack of appropriate regulations for the conduct of clinical trials, or imprecise regulations ^{w adz} ✗ scant tradition of cooperation between science and business (both in medicine and in other fields) ^w ✗ lack of curricula adapted to the needs of translational projects ^{adz} ✗ low innovation of researchers (poor knowledge of the industry, lack of interest in the implementation, copying foreign research) ^w ✗ little interest of university, little interest of professors in applied research, erroneous understanding of basic research ^w
<p>Opportunities</p> <ul style="list-style-type: none"> ✓ compared to Poland, much higher labour costs, even specialized, in the most technologically advanced countries 	<p>Threats</p> <ul style="list-style-type: none"> ✗ global oligopolistic nature of the very competitive pharmaceutical market ^{w adz} ✗ cost of the process – no possibility of financing it entirely from its own business resources or grants ^{w adz} ✗ insufficient availability of funds covering <i>proof of concept</i> ^w ✗ decreasing role of venture capital funds in the life science industry ^w

The ‘w’ index indicates the factors that have been identified in the course of in-depth interviews. The ‘adz’ index means the factor emerged in the course of existing data analysis. The asterisk * indicates the factors for which there were conflicting opinions in a series of interviews.

Source: Own elaboration.

Clinical trials in Poland

Due to the ease of patient recruitment, Poland is one of the most attractive markets for conducting clinical trials in Europe. A large absolute size of the population, and a suboptimal health status of the population, allows a relatively prompt collection of the necessary pool of patients. The patients agree to participate in research on experimental drugs relatively willingly as new, innovative therapies are seldom funded by the National Health Fund [26]. However, the benefit of the rapid recruitment for a clinical trial is to some extent undermined by a large percentage of those who drop out of participation in the course of the project. This factor is crucial because maintaining the highest possible proportion of patients correctly using the new therapy during the clinical study is essential for results credibility. Losing data on the progress of the disease for more than 5% of patients jeopardizes the entire time- and cost-consuming project involving hundreds (and sometimes thousands) of participants [27]. One of the experts, who otherwise speaks very positively about Polish doctors, suggested that they often lack soft skills which would facilitate convincing the patient to continue treatment and participation in a clinical trial. The fear of losing patients involved in the study is discouraging the pharmaceutical industry from recruiting participants to experiments based in Polish clinical centres. At the same time, imprecise regulations on clinical trials impede or prolong the negotiations between clinical centres and pharmaceutical companies (called sponsors). The former are often afraid of being accused of double funding of medical procedures, especially because the precise separation of components of the procedure paid for by the National Health Fund and those covered by the sponsor, is difficult and tedious. Pharmaceutical companies interested in conducting clinical trials in Poland become discouraged by the long duration of the bureaucratic procedures required to run the study, and often transfer their trials over our eastern and southern borders to countries, such as Ukraine or Hungary.

Innovation efforts at Polish pharmaceutical and biotechnological companies

A good patient base for clinical research could be useful for the pharmaceutical companies in Poland. According to INFARMA estimates – the Employers' Association of Innovative Pharmaceutical Companies – as many as 450 pharmaceutical companies [28] operate on the Polish market, and there are countless companies offering medical devices and services. According to INFARMA, sixty-two are innovative companies which conduct research on new therapeutic compounds. However, the vast majority of companies operating on the Polish market, including almost all native Polish companies, produce only generic drugs, whose chemical formula has been developed by foreign research centres.

It should be realized that the Polish market for generic drugs is extremely absorptive and has been increasing since 2004 [26]. The National Health Fund is willing

to buy and reimburse drugs that are cost-effective but is very reluctant to finance innovative therapies. Polish companies showing interest in the production of new drugs must therefore expect to compete on the international, oligopolistic market of giants, who have mastered the process of managing the development of new drugs. For many companies, the entry barrier may be too high. According to information received from our respondents the pioneers and key players in the domestic innovative pharmaceutical market are two Warsaw-based companies: Adamed and Polpharma, as well as a biotechnological company Bioton. These few cases of independent, extensive work on new therapeutic substances require a large mobilization of resources and rapid training of the involved personnel. Quick learning, however, is not sufficient as the search for new drugs, the so-called drug-hunting, requires many years of experience. According to our expert, people with such experience and competence are simply not to be found in Poland. It is for this and other reasons that the venture towards the discovery of a new molecule must be supported by external, foreign consultants.

(We lack a person) who would be able to plan the project, choose a variety of options, and then to interpret the results and to see if (the molecule – editor's note) meets the criteria, whether it is the right one or not, and so on (...). We need to combine these blocks, that is what we are missing, because we have never worked towards a common goal so far, have we?

Scientist working on the discovery of new therapeutic molecules

In recent years, one of the Polish pharmaceutical companies actually reached an advanced stage of new drug development, a precedent on a national scale. The molecule, obtained in a Polish laboratory, underwent the pre-clinical phase and was qualified for the first phase of clinical trials. These studies, however, were not performed in Poland but abroad. According to an expert we interviewed, this decision was rational in the light of the partnership with a foreign organization that had already had the know-how and experience in first-phase clinical trials. The second important factor in favour of the continuation of research in another country was probably the shorter path to potential registration of the drug by the American FDA (Food and Drug Administration). This situation is hardly surprising. The innovative drugs market is a global one, and new discoveries are created in a global context. Even if an institution manages to develop a medicinal product based on their own internal resources, the process leading from the laboratory through clinical trials to market entry may not be possible without international financial support. The above-mentioned molecule developed by Polish scientists passed the first phase of clinical trials, but work on its further development was suspended because of the enormous cost, the long duration of the process and the high risk of failure. In other projects, conducted perhaps with less momentum, the financial barrier is sometimes too high. At the initial stage of innovative work, a com-

mon barrier is insufficient funding sources of the so-called *proof of concept*, or prototype. As indicated by an expert, the prototype is a necessary element of communication at the stage of establishing science-business partnerships. It allows, for example, to clearly present to an interested party the features and capabilities of the technology developed by scientists. However, prototypes are not easily funded – they cannot be covered by grants from the National Science Centre, and at the early stage they are not interesting for the industry, also the universities themselves cannot provide the funding, at least not on the scale which is required, according to the expert. In addition to that, funds from capital funds allocated to life sciences projects are shrinking. Some investors, discouraged by the very high risk which the innovative drugs market is burdened with, direct their interest to the flourishing IT sector. Some help is presented by the new streams of funding cooperation between science and business, launched by the National Centre for Research and Development, such as the INNOMED programme.

Polish scientists and innovation

However, not all respondents indicate the financial difficulties to be the main barrier to innovation in pharmaceutical and related industries. Some of them argue that the biggest challenge is the low innovation predisposition of Polish scientists, who do not have a good insight in their fields, do not follow the latest discoveries, and are instead satisfied with small successes on a local scale. According to the expert (employed in one of the institutions supporting the transfer of knowledge), scientists do not understand patent law and cannot use patent databases. Sometimes praising their new discovery, they are not even aware that a similar one has already been patented. The issue of the quality of work of Polish scientists was described differently by other respondents, who indicated their excellent preparation for work in a narrow field, and relatively low remuneration compared to the scientists from the international market.

Perhaps it is true, then, that Polish science has a group of great professionals who are, however, unable to work together, making it very difficult to achieve common, complex goals, which the development and introduction of new technology on the market always is. Here is another remark by the already-quoted expert:

And this [the creation of a new drug – editor's note] may therefore be unsuccessful, because our transplant specialists are great, our behaviourists are great, our oncologists are great, but the drug is a very complicated thing, even a 'drug candidate' because the drug is so much more than that. Meanwhile we are missing reviewers, consultants, good project leaders, but we're not lacking specialists, and equipment not in the least.

Scientist working on the discovery of new therapeutic molecules

The same issue is indicated by Guzik [12] and other Polish scientists. Prof. Jerzy Naskalski [29] called upon the members of the College of Translational Medicine in 2010:

(...) teaching new people who take on jobs in different departments of laboratory medicine is done in a way that preserves the traditional divisions into specializations described using specific names of university Chairs and Departments. This happens despite the fact that in practice there are no technical nor intellectual premises for these divisions.

So the question arises, why medical schools maintain outdated teaching methods that do not meet our rapidly changing reality, in the world of science, and also in the quickly evolving clinical practice? With all certainty, policymakers *are* aware of the shortcomings of the current curriculum, but there is probably no academic consensus as to the desired direction of change, needed to start radical reforms. According to one respondent, exceptionally good results of translation could occur if the system supported a way of frequent interaction of different research teams and design – including interaction unconnected with science. Others, however, do not attach to the issue any importance. There is also a group of distinguished professors who are opposing the ever-increasing pressure that science be useful and that implementation efforts be undertaken. This is one of them speaking:

We are primarily interested in scientific research, because we believe that this is the fundamental vocation of any scientist: to discover the truth, to attempt to explain the functioning of the systems that we deal with. But since we deal with, for example, a field [field name] where some application may arise ... may, but may not, and so it is not our main objective.

A prominent scientist in the field of life sciences

The functioning of universities

From the point of view of university authorities, innovative research projects in partnership with entrepreneurs bring a certain prestige and acclaim. Some university authorities look favourably on innovative and implementation work, and even support them. However, this dimension of university activity is not considered a priority by many decision-makers and influential professors. Despite the fact that for several years there have been ongoing attempts to try to open up the possibility of cooperation with industry, Polish universities are still a very difficult partner. As indicated by one of the respondents and the experience gathered during the running of the SPIN project, the wording of the consortium agreement between the university and the company is a very difficult task, requiring patience, willingness for concessions, and time. Our respondents indicate that universities have to face the challenge of the excessive ambition of their scientists who do not allow their research project to be too strongly intervened. On the other hand, entrepreneurs do not understand the specifics of university work and demand a corporate mode and pace of work which universities find unattainable and often undesirable. These difficulties in science-business cooperation probably result from the limited experience of Polish universities and businesses in this arena. It should be expected that with time a path will

be paved for subsequent research teams to follow. So far, two solutions to this impasse can be seen in Poland. The first is the creation of Centres of Technology Transfer, in which employees are familiar with the nuances of the commercialization process and rules for the distribution of intellectual property rights, the so-called brokers, aiming to combine the two often incompatible worlds of business and science. The second solution, commonly used, is to extend collaboration with the university beyond its walls, e.g. through 'brain drain' or employment of academic specialists in research and development departments of private companies, using civil law contracts.

According to one respondent, the faculty is to some extent interested in the prestige associated with conducting cutting-edge research; however, this approach is discorded by the fear that the researchers involved in innovation activities along with their business partners, will neglect their academic work. Meanwhile, the amount of ministerial subsidies financing statutory activities of academic units is dependent on the assessment of scientific achievements – above all publishing – affiliated with individual researchers. According to our respondent, the authorities of university units are very much afraid that this output be reduced, their fear strengthened by the fact that commercialization or application activities are not treated as a purely scientific achievement and that in the current assessment system of scientific institutions and scientists, they do not generate sufficient profits.

Whatever the reason, there are very few truly innovative translational actions that would indeed be directed to the implementation of new discoveries into clinical practice. One of the respondents involved in a major translational project, summarizes this issue:

[Such projects] are rare because people do not believe that they can achieve something, they do not invest because they are afraid that it is a very risky business. Nor do we know if we will achieve something, in fact, we have a greater chance of failing than succeeding. 'The attrition rate', i.e. the percentage of candidate-compounds that are rejected, is huge, so why invest in something like this? People are afraid; they prefer to [invest] in generic drugs. [...] If you make a lot of them, you can earn quite a bit of money, you can live on it somehow, it's predictable, manageable, and the process is repetitive. I'm not saying that it is not difficult: the market is very aggressive, prices erode in connection with reimbursement activities, and so on, but the level of the complexity of the process is incomparably [lower]. And companies they just don't want to do that, they don't believe it will work. And if this approach continues, it won't work, because they won't do it.

*Scientist working on the discovery
of new therapeutic molecules*

Discussion

Poland is a peripheral player in the field of developing innovative medical technologies, including medication. The key decisive factors are the global nature of the pharmaceutical market and the huge time and cost requirements of the drug discovery process, combined with an extremely high risk. Polish companies and researchers

usually lack cooperation experience and the competence to independently carry out a very complex project of a multidisciplinary and implementation nature. Highly complex undertakings require technical and financial support of many partners, and drug development is generally a global process and business. The need for such collaboration, however, is actually in accordance with the general objectives of translational medicine. Therefore, instead of asking questions about whether in Poland we can independently conduct complex translation projects, we should ask whether we are able to participate in these international endeavours as equal partners. We are convinced that, thanks to well-educated staff and good technological facilities, our scientists *are* attractive partners. In turn, Polish pharmaceutical companies have high competence and efficiency of production and distribution of generic drugs. These experiences can be their capital also on the innovative drugs market. In Poland, life sciences are regarded as a priority and strategic area for innovation, as it is the case in the Malopolska Voivodeship. This will lead to a growing public pressure on achieving and promoting the social benefits of investment in the area of life sciences. Our SWOT analysis shows that the new policy to encourage innovation in medicine should be aimed at facilitating the efforts of Polish entrepreneurs and scientists to build various international partnerships. In the early stages of development of new medical technologies it is worthwhile to promote scientific and business partnerships and finance prototypes, for example within start-ups. Providing subsidies for Polish pharmaceutical companies, e.g. by the National Centre for Research and Development, should be associated with realistic expectations as to the outcome of their work – although new drugs cannot be introduced on the market using state subsidies, certain stages in the development cycle of new drugs can be finalized and can form the basis of negotiations with investors. It should be expected that the most attractive projects, including those financed with public money, will be introduced on the international market. The advantage of entering the global markets will be increased know-how in the field of drug discovery, clinical testing, and process management, as well as developing a network of international business contacts. However, the vision of the independent development of new drugs we find unrealistic.

An important factor in the formation and development of translational medicine are the global trends in the international scientific community. The concept that science be open to cooperation with institutions operating in its environment: businesses, regional authorities and non-governmental organizations, is currently gaining popularity [30]. These are not easy partnerships to establish and maintain; therefore, there is need to introduce institutional arrangements that will intensify cooperation between science and stakeholders interested in practical application of the research results.

An example of such a solution is the Malopolska Centre for Translational Medicine which operates at the interface of science, business and public administration. One of the elements of its strategy is focusing on personnel training so that they will be able to support the

processes of translational medicine and life sciences. It is open to projects that generate small costs (compared to those incurred by the search of new drugs) and at the same time have implementation potential. In our view, initiatives such as the search for new diagnostic and preventive measures, construction of medical appliances, planning new therapeutic regimens – can be of great importance from the point of view of public health, and at the same time it is indeed feasible to implement them based entirely on internal, Polish resources. A similar strategy is assumed by some prestigious world universities. For example, University College London (Wolfson Institute for Biomedical Research) is primarily involved in screening and medical chemistry [9], while Stanford University operates the SPARK programme, bringing together scientists, entrepreneurs and other experts to monitor and support medical projects developed there.

Summary

Translational medicine, understood as a new trend in research and clinical practice has grown out of – on the one hand – the observation of how inefficient the traditional development cycle of new drugs is, and – on the other – from the social expectations that the scientific community and the pharmaceutical industry provide new life-saving and health-promoting solutions [31]. The very concept of translational medicine is not precisely defined, and its general understanding as “the process of implementing new medical achievements in clinical practice” gives rise to many interpretations. A very narrow business understanding of the term is that it is a set of strategies used to increase the chance of success of a new drug in the second phase of clinical trials. A slightly wider academic approach puts greatest emphasis on the clinical use of discoveries from basic research, reducing the enormous gap between the rapidly increasing number of promising results of basic research in life sciences and the very small number of new therapies [12]. The optimization of research and development efforts, in this sense, is to also lead to the reduction of the period from the first observations in the laboratory to the registration of new therapies and bringing them into general use, which may even take 30 years. From the point of view of clinicians, the definitional element of ‘translational medicine’ is its interest in bio-markers (primarily genetic), whose discovery facilitates the exploration and understanding of complex disease processes. In effect, it leads to a better diagnosis and personalized therapy (e.g. by means of targeted therapies). In the broadest sense, the translational approach emphasizes the need to join forces in a number of specialized teams to make a new medical technology possible. Translational medicine is to be an approach that will unify the goals and means of communication of these diverse groups, which will enable the optimization of the innovation process and a faster implementation of new technology in a clinical setting.

To our knowledge, there has not been any systematic analysis serving to decide whether the philosophy and tools offered by translational medicine actually accelerate

the discovery of new drugs and their introduction into clinical practice. However, in the face of the pharmaceutical crisis and high social expectations, it is necessary to search for new solutions to meet the growing demand of the increasingly informed and demanding patients. Poland should participate in this process, and not just as a donor of patients for clinical trials.

In our opinion, the financial requirements, and technological and organizational challenges of new drugs are too demanding to enable a full cycle of translating new drugs based on only indigenous resources. Nevertheless, Poland can still be an attractive place to conduct specialized research. The high level of competence of at least a part of Polish scientists and the vast experience of Polish companies in the production of generic pharmaceuticals make them valuable members of international research consortia. This is how we imagine the future of translational medicine in Poland.

Notes

¹ The authors were involved in the foundation of the Malopolska Centre for Translational Medicine, funded by the SPIN Project (www.spin.malopolska.pl).

² NME (*New Molecular Entities*) and *biologicals*.

³ Reference to the so-called target-based approach, a modern technique based on the understanding of physiological mechanisms, typical of the projects developed since about 1990 [15].

⁴ This is problematic especially in the case of potential drugs for rare or tropical diseases.

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