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OPINION ARTICLE

Translational Research in Dermatology

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Ongoing advances in the understanding of skin diseases have transformed dermatology as a specialty.¹ More detailed knowledge of the pathogenic mechanisms involved in the development of various skin disorders has given rise to new conceptual approaches and innovative forms of treatment, revolutionizing everyday dermatological practice. This shift would not have taken place without a constant flow and transfer of information between clinical, biomedical, and pharmacological research. For decades now, steady advances in specialties such as immunology, molecular biology, and genetics, along with exponential progress in technological innovations (microarrays, system automation) have been progressively incorporated into dermatological research.² This is the essence of translational research: the transformation of knowledge of the human body both in health and in illness into relief for those who suffer from a variety of diseases.³ In this opinion article, I would like to share my own experience of translational research in dermatology, and also to express a certain degree of concern about the possible consequences of uncompetitive translational research in Spain.

The rapid development of new knowledge of the pathological mechanisms involved in skin diseases has had a direct impact on the incorporation of new treatment approaches into dermatological practice. Translational research invariably involves greater complexity, and additional effort is required to incorporate new knowledge which is not at present being taught in dermatology training

programs.⁴ Experience with pharmaceutical research and development of new drugs for use in dermatology clearly indicates a growing tendency to improve our knowledge of the intrinsic nature of dermatoses in order to identify potential new drug targets to help us expand the therapeutic arsenal as quickly as possible. As a result, less and less time elapses between the identification of a new drug target and the clinical development of a corresponding drug. In what follows I will mention some examples of the use of this kind of information in the treatment of some of the most prevalent skin diseases.

Psoriasis constitutes an excellent example of the application of translational research to a skin disease.⁵ New treatments for psoriasis are a clear example of this phenomenon, which links together scientists engaged in basic research, specialists in dermatology, and the patients themselves, each making a distinctive contribution to the process. In the past 2 decades, the translational research agenda for psoriasis has been very active and several innovative agents—mainly biologics—have been studied clinically. The identification of immunoinflammatory mechanisms present in psoriasis has made it possible to explore several drug targets: cytokines, cell adhesion molecules, costimulatory molecules, and others. Although the majority of biological therapies initially designed for the treatment of psoriasis have not reached the market (for example, anti-interleukin [IL]-8 antibody, anti-L-selectin antibody, anti-CD5 antibody, recombinant IL-10, anti-CXCR3 antibody), they have given us essential information on the clinical relevance of the target they inhibit selectively.⁶ In addition, various biological therapies that block molecules such as tumor necrosis factor α , or the common p40 subunit of IL-23 and IL-12, have been approved and have been shown to be clinically

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effective. Pharmacogenomic studies carried out on lesions treated with different agents known to be effective against psoriasis have made it possible to identify which pathologic mechanisms in the disease are critical and which are most sensitive to specific treatments.^{7,8} This type of research permits identification of genetic and cellular biomarkers associated with the prediction of clinical effectiveness. Biological therapies, apart from being excellent treatments, should also be considered tools of translational research. Recently it has been possible to determine the relevance of cytokines IL-17 and IL-22 in psoriasis, the first produced by T-helper (Th) 17 cells and the second by Th22 cells that express the cutaneous lymphocyte associated antigen and the chemokine receptor (CCR) 6, CCR10 and CCR4 on their surface.

In recent years there have also been great advances in knowledge of the pathological mechanisms involved in atopic dermatitis. Research on the pathogenesis of several features involved in atopic dermatitis, such as the barrier function, allergic inflammation, and itching has generated information of great relevance for the treatment of this disease. Molecules such as filaggrin, epithelial cytokines (thymic stromal lymphopoietin, IL-33, and IL-25), natural antimicrobial peptides, and IL-31 increase our understanding of this disease,⁹ and they constitute clear pharmacological targets for new therapies. In addition to psoriasis and atopic dermatitis, other skin diseases benefit from translational research. Examples include anti-CD20 antibody (rituximab), a treatment for pemphigus vulgaris that acts on B cells; imiquimod, a toll-like-receptor-7 agonist that modifies the immune response in actinic keratosis; and histone deacetylase inhibitors in the treatment of cutaneous lymphomas.

This dynamism in current scientific knowledge offers us the opportunity to take advantage of this wealth of information in order to continue innovating and improving the scientific quality not only of research but of clinical practice. Competition is fierce and only countries with a strong tradition of multidisciplinary research with infrastructures and personnel dedicated to translational research in dermatology will be able to participate directly in the results and potential benefits of the wealth of resulting information. In countries that lack a consolidated tradition of translational research, the tendency is for research to be limited to advanced-phase clinical trials in which the main priority is to recruit a large number of patients in the shortest time possible.

This distancing has a number of consequences that limit scientific judgment and independence from pharmaceutical corporations with respect to new therapies, entailing stagnation in the training and continuing education of specialists in dermatology, a clearly inferior position with respect to other medical specialties that are better prepared to gain access to new treatments, and a loss of international competitiveness.

Perhaps the most evident need is for interaction between specialties that share interests with dermatology, since this is the basis of translational research. Spain is

one of the few developed countries where this interaction is very weak, and is not reflected in the professional associations representative of Spanish dermatology. This lack of translation, together with a low degree of competitiveness in comparison with other countries, is not good news for the future, for the reasons mentioned above. Knowledge not only transforms research, but has a decisive impact on new therapies and on our understanding of diseases. It is important to note that other medical specialties in Spain have taken on the challenge of bringing themselves up to date. Given this situation, it seems necessary to encourage and support Spanish dermatology research groups producing high-quality work, with the aim of creating a critical mass able to undertake joint projects that enable pooling of knowledge and research technology in dermatology. This will encourage collaborative work with international research groups with proven research traditions; these groups will then be able to share information and knowledge generated by innovations in dermatology taking place outside Spain. In the context of medical education, this is an opportunity to take advantage of new curricula adopted as a result of the Bologna Plan to make our students better able to compete with those from other countries.⁴ Translational research offers the opportunity to familiarize ourselves with new technologies and training methods, thus bringing up to date both practicing dermatologists and those still in training. It can be introduced gradually, ranging from *in vitro* studies of patient cell samples to molecular biology and genetics. The kind of research I am referring to is, in fact, already a reality in fields such as cosmetic dermatology, where these kinds of studies are used with increasing frequency.

Having put on the table some aspects of translational research, I would like to conclude by adding that this article is an invitation to join forces and create synergies among Spanish dermatology research groups. The governing board of the European Society for Dermatological Research (www.esdr.org) is well aware of the situation, and it is hoped that this article will serve to encourage these activities.

Conflict of interest

The author declares no conflicts of interest.

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