Why immunology is important for MDs

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There are a number of critical reasons why Immunology is today a major subject in medical education, and I am astonished that the discipline often occupies only some 50 hours or so in a semester of the medical curricula.

Historically, Immunology has emerged as a branch of Microbiology, having contributed to establish, early in the XX Century, the theory of "specific causes of disease". We all know the grand statement "one disease, one microbe, one vaccine". Yet, as N.K. Jerne used to say, it made little sense to teach Immunology in Microbiology courses, as bacteria do not produce antibodies. Immunology was to remain a subsidiary discipline for another 100 years, largely because of the misleading concepts introduced by the very influential Ehrlich, who continues, nevertheless, to be given wide recognition. Ehrlich contended that all cells in the body produced antibodies, and it took another 50 years for Gowans to demonstrate that lymphocytes mediate specific immunity, and for Fagraeus to discover that antibodies are made by plasma cells. Another Ehrlich's serious mistake, in spite of much contrary evidence from Metchnikoff's laboratory, was the notion of "horror autotoxicus": autoreactivity was "disteleological" and could, thus, not exist. Again, it took over 50 years for Doniach & Roitt, and Rose, to demonstrate autoimmune diseases, and nearly another 50 for the notion of "physiological autoreactivity" to be established. By the 1970's, many medical schools had "transferred" Immunology to Pathology departments, but it was the tremendous progress on the molecular and cellular basis of adaptive immunity, together with the genetic solution for the generation of antibody diversity, that brought Immunology to maturity, and made it an autonomous discipline.

It is to be noted that Immunology represents the first branch of Molecular Medicine, having used immune antibodies as "biopharmaceuticals" in the treatment of infectious diseases already in the XIX Century, and being responsible for the greatest contribution to public health in the past 100 years: vaccines have essentially doubled life-expectancy at birth. Furthermore, once Jerne introduced the Darwinian principles that provided for the foundation of modern Immunology, immunologists lead the progress in life sciences and medicine, producing monoclonal antibodies used daily in diagnostic and therapy, "engineering" molecules and receptors, and, for the first time

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in history, completely solving inheritable diseases (from the genetic, molecular and cellular basis, to effective gene therapy of primary immunodeficiencies).

Immunology has thus matured at the leading edge of life sciences, and the immune system remains a most useful subject in basic cell and molecular biology, having critically contributed to general questions such as, cell fate and commitment, stem cells, apoptosis, cell cycle and signaling pathways. Lymphocytes became the E. coli of eukaryotes. The fact that immunologists have cultivated notions and approaches of cooperation between molecular pathways, cell types and organs, together with their attempts to integrate multiple levels of organization in a context of physiological significance, has naturally brought the field to "systems biology" that is thus far absent in most other areas of life sciences. It is not by chance that, perhaps more than in any other field, immunologists speak of "homeostasis", and I would not be surprised if the solution of immunological "recognition" and "memory" will serve in the approaches to other cognitive systems. With the description of the system's components close to completion, Immunology is, in a way, post-mature, but also the best model system for the "new biology" of integration. Moreover, as the "evolutionary strategy" of the immune system transfers "variation & selection" to the somatic lifetime, individual immune systems represent fractals of biological evolution itself, and Immunology should perhaps be, together with evolutionary biology, the first topic in teaching life sciences.

The extraordinary relevance of Immunology in basic biology is matched, however, by its importance in medical practice. Thus, immunological dysfunctions are increasingly frequent in modern societies: autoimmune diseases strike to 5-10% of the general population, while the prevalence of allergies reaches up to 50% in some age groups of "clean societies". Furthermore, transplantation of tissues and organs is increasingly relevant, and it will be more so if the promises of stem cell transplantation will be confirmed. Moreover, many immunologists believe that therapeutic vaccines will be the "final solution" in cancer. In other words, it is to be expected that many of the patients seen by doctors in the economically developed world, will suffer from some kind of immune disorder, or else, can benefit of some type of immune intervention. Finally, we have today no effective vaccines to chronic infectious diseases (HIV, malaria, tuberculosis) that continue to take millions of lifes. In other words, the need for MDs who know Immunology has never been so clear, as there are many "windows of opportunity" for ambitious professionals to produce novel contributions of extraordinary importance for human kind.

Perhaps the argument for the medical relevance of Immunology should be constructed as a dichotomy in our world of profound economic differences: for the poor world, immunology is needed to develop vaccines against chronic infections; for the rich world, immunology is necessary to treat allergies and autoimmune diseases, produce cancer vaccines and tolerate graft recipients. Either way, Immunology cares for the most prevalent and serious health problems.

Yet, this is not all. Scientists who think "organism-centered" are increasingly necessary to "make sense" of modern life sciences, to make the step from component analysis to system's biology. Clearly, the best education for "organism integration" is a good medical curriculum. In other words, MDs with a solid education in Immunology will be instrumental, I believe, in the solution of basic biological problems, as well as, for the long-expected success in translational medicine of immune disorders.

Finally, as I have speculated years ago, the diversity of molecular shapes produced in the immune system, together with its unique dynamics, capable to vary concentrations of each antibody by over a million fold in a week, should make it possible to "regulate" or "compensate" any other biological system in the body, just by manipulating production of specific (auto)antibodies to mediators and receptors. In other words, "immunosomatics", as I coined this notion, will be the last frontier of Immunology, and recent observations on the role of "natural antibodies" in regulating physiological levels of oxidized LDLs, goes very much in this direction. This hypothesis does not propose to treat the immune system as a general panacea, but it underlines the value of purposeless diversity for the solution of the unknown.