A poor view from specialty silos

We live in an era of specialization and, in academic medicine, super-specialization. The super-specialists are, primarily, those engaged in the cutting edge basic and clinical research that drives scientific progress. As a super-specialist in IBD, I often find that I have more in common with rheumatologists than I do with interventional endoscopists. Nevertheless, as institutions and professional societies become increasingly organized towards organ specificity, I tend to communicate most frequently with colleagues in my own specialty. General medical journals that publish articles on a spectrum of specialty topics do so mostly to expand the knowledge base for primary care specialties. Large national societies tend to have a broad purview in relation to health care, and granting agencies (including the National Institute of Health) have in effect become specialized funding agencies. Interdisciplinary funding is more difficult to conceptualize and promote.

A significant downside to super-specialization is that our view from these silos of expertise often misses or even ignores clues that relate to the etiology and pathogenesis of diverse disorders. Organ system specificity, particularly within the realm of autoimmune diseases, is impeding progress toward the application of basic, translational and even pharmacoeconomic principles across specialties.

At a recent multispecialty funding meeting of delegates from “centers of excellence”, who presented topics from diverse medical specialties, I was disheartened at the dearth of genuinely cross-specialty projects—a lack due, primarily, to proprietary funding applications for individual super-specialized programs even though the concept behind such “centers” is to foster integrative research efforts. I was left with the impression that “integration” is predominantly a self-serving term employed to foster the aims of individual centers.

Speaking from the perspective of IBD treatment, I believe that topics ranging from epidemiology and environmental influences to immune mechanisms and therapeutics would derive substantial benefit from truly interdisciplinary research efforts.

Cigarette smoking, for example, has been a favorite topic of mine for several decades and the impact of smoking on autoimmunity has not been appreciated from an investigative standpoint. Cigarette smoking has protective effects against the development of ulcerative colitis, primary sclerosing cholangitis and Hashimoto's thyroiditis, and yet is detrimental to the clinical course of patients with Crohn's disease, Graves disease, rheumatoid arthritis and psoriasis. This simple (probably incomplete)

list indicates that a single environmental factor can drive inflammation in different directions (T_H1 -like versus T_H2 -like responses) despite affecting similar organs. We still don't know why.

Clues to autoimmunity can also be derived from observations in pregnancy, which has a variable effect on the course of IBD, rheumatoid arthritis and systemic lupus erythematosus. In rheumatoid arthritis and IBD, discordance between maternal and fetal human leukocyte antigen (HLA) class I and II loci leads to improvements in disease activity. By contrast, concordance is associated with relapse, which suggests that an endogenous mediator of immune and inflammatory events exists that could potentially be harnessed therapeutically in immune-mediated inflammatory disorders.

The role of vitamin D in numerous autoimmune diseases has also been recently studied and could potentially account for geographical variations in the prevalence of autoimmune diseases; as yet, however, no unifying explanation exists for immune-mediated pathogenesis and no exploration of the potential therapeutic effects of vitamin D has been conducted across organ specialties for potential therapeutic impacts.

We also have a tremendous amount to learn about the immune mechanisms involved in the responses to agents that ‘target’ tumor necrosis factor (TNF). Currently, four such biologic agents are marketed: infliximab and adalimumab are IgG₁ monoclonal antibodies, etanercept is a fusion protein composed of TNF receptor superfamily member 1B linked to the Fc portion of human IgG₁, and certolizumab pegol is a pegylated Fab' fragment of humanized anti-TNF monoclonal antibody. Infliximab, adalimumab and certolizumab pegol are effective treatments for both Crohn's disease and rheumatoid arthritis. Etanercept, although an effective treatment for rheumatoid arthritis, was not efficacious in Crohn's disease trials. Is this discrepancy related to a dosing issue, or to mechanistic difference? Why do some patients initially respond to anti-TNF therapies and then lose response despite adequate circulating blood levels of the therapeutic agent? Are there similarities in the underlying mechanistic explanations and therapeutic algorithms for such patients with different organ system involvement?

Finally, autoimmunity specialists from individual specialties can also learn from other diseases and specialties how to optimize therapies and pharmacoeconomics. In the treatment of patients with IBD, we share biologic therapies with rheumatology and dermatology. We have learned how to deal with the immunogenicity of these agents, but discrepancies still remain in how we manage

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concomitant immunosuppression and dosing. Another major concept that is applicable across diseases relates to the roles of disease modification and early intervention. Rheumatologists have demonstrated that early intervention with disease modifying antirheumatic drugs (including biologic agents) can prevent the progression of rheumatoid arthritis. Across all anti-TNF responsive diseases, the main impediment to increasing use of and early intervention with biologic agents remains their high cost. As we move towards both clinical efficacy and

cost-effectiveness within evolving, worldwide, health-care systems, the ability to balance the benefits of biologic therapies against their costs (both direct and indirect) demands that communication across specialties should become even more important.

These diseases comprise just a few examples where, to improve the harvest from our research efforts across medical fields, we need to move out of our specialty silos.

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