nature immunology
volume 2 no 2 february 2001

Celebrating chemokines

They permeate every nook and cranny: immunology is now replete with chemokines, those cytokines that cause the directed migration of leukocytes. Immunologists were almost caught unawares. Years ago, only those interested in inflammation seemed concerned with the travelings of leukocytes and the molecules that directed their journeys. But the realization that a major coreceptor for HIV was a chemokine receptor catapulted the study of chemokines into the mainstream. Suddenly those who had been analyzing chemokines all along seemed prescient.

And chemokines have continued to surprise us. Their numbers keep mounting, with more than 40 identified so far, many of which share specificity for the numerous receptors. Together, the chemokine network seems to supply the needed subtlety and necessary nuance in the effort to stave off infections and infiltrations. Although their primary roles can be thought of as traffic coordinators for an organism's defense system, they are also responsible for orchestrating and carefully balancing just when and which cell or protein chimes in.

In this issue of *Nature Immunology* we celebrate the contributions that these proteins, and those who have investigated them, have made to our understanding of the development of both the immune system and immune responses. Half of the journal this month is devoted to chemokines, from Reviews and Correspondence to a collection of Round-ups that summarize the most interesting recent papers on chemokines in other journals.

Our special online Focus on Chemokines (http://immunol.nature.com/special_focus/chemokine) is free to all who register. With the generous help of our advisors in the scientific community (we are most indebted to the authors of our Review articles and to M. Baggiolini and A. Lanzavecchia), we have compiled and present on the site an annotated list of important papers that we consider "selected classics". To further aid those curious about "all things chemokine", one can also find on our site a compilation of links for free access to the major papers on chemokines published in *Nature* and the other monthly publications of the Nature Publishing Group, such as *Nature Medicine* or *Nature Biotechnology*. Our Chemokine Focus website will be available free-of-charge for 3 months, during which time we will update the Round-ups on a monthly basis. After 1 May 2001, however, the site will be available to our subscribers only.

For the reader who needs to get his or her bearings, be sure to look at Mackay's overview of the multifaceted roles of chemokines in the normal regulation and movement of immune system cells and their involvement in its dysregulation. Focusing on lymphocytes in their review, Moser and Loetscher delve into how chemokines affect lymphopoiesis and recirculation and their role in moving lymphocytes to the site of an infection or inflammation.

Chemokines and cytokines do more than just tell white blood cells where to go. Luther and Cyster describe how chemokines can also affect the differentiation of T cells by influencing the quality and the quantity of their responses. The presence or absence of certain chemokines can determine whether helper T cells become polarized as type 1 or type 2 responders. The chemokines' ability to influence cytokine production and a T cell's response to various other environmental stimuli begs the next question. How do the chemokine receptors transmit such complex signals? Thelen reviews the trimeric G protein–linked and other signaling pathways that emanate from chemokine binding. Although our understanding of these processes is in its infancy, the field seems on the brink of major breakthroughs in "receptor cross-talk" and unraveling the intertwined threads that initiate and carry through directed movement.

With the myriad of chemokines and receptors, how can one hope to harness this system to manipulate immunity? Redundancies, backup factors and safety nets abound. One way to find therapeutic direction is to take our cues from viruses. As discussed in a review by Murphy, some virus families—such as herpesvirus, poxvirus and retroviruses—have already determined the most useful chemokines and receptors to thwart, subvert or mimic. Thus out of the multitude, a few key components can be exploited to further a different program.

These clues may be helpful in the search for chemokine agonists or antagonists that may aid in the treatment of multiple human disease conditions. In their review, Gerard and Rollins discuss a number of conditions in which the expression of chemokines is altered or chemokine receptors are inappropriately expressed. Multiple sclerosis, HIV/AIDS, arthritis, cancer and heart disease are just some of the pathological settings in which chemokines could potentially yield treatments.

We hope to provide for you a snapshot of how chemokine research is presently impacting immunology. These are exciting times, with much to be learned and new opportunities to move basic research to the clinic. Enjoy the issue and our Chemokine Focus website—and let us know what you think.