International Union of Pharmacology. XXX. Update on Chemokine Receptor Nomenclature

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Abstract — An update of the International Union of Pharmacology nomenclature for chemokines is outlined, defining one new receptor type, CXCR6, and disqualifying the putative receptor, CCR11.

I. Introduction

In the year 2000, the International Union of Pharmacology Committee on Receptor Nomenclature and Drug Classification (NC-IUPHAR) approved a nomenclature system for chemokine receptors, the major seven transmembrane (7TM) receptors of the immune system, as recommended by the NC-IUPHAR Chemokine Receptor Subcommittee (Murphy et al., 2000). At that time, the chemokine receptor family consisted of 18 7TM proteins in humans, which were divided into four subfamilies based on chemokine subclass specificity. Two additional molecules, named Duffy and D6, which both have 7TM structure and bind chemokines but lack a known signaling function, were excluded from the nomenclature system, as were a group of functional 7TM chemokine receptors encoded by herpesviruses (Rosenkilde et al., 2001). The nomenclature system is logical, noncontroversial, and universally accepted and used (Table 1). Moreover, it has served as a template for the creation of a chemokine ligand nomenclature system (Zlotnik and Yoshie, 2000). Both systems have facilitated communication among immunologists and pharmacologists as these molecules have become important drug targets in immunologically mediated disease and HIV/acquired immunodeficiency syndrome. Since publication of the NC-IUPHAR document reporting the nomenclature system in the year 2000, one new receptor subtype, CXCR6, has been identified (Matloubian et al., 2000; Wilbanks et al., 2001), and one other subtype, CCR11, has been disqualified (Schweickart et al., 2000, 2001). Duffy and D6 remain as binding sites. The aim of the present article is to provide a brief update on these receptors.

A. CXCR6

CXCR6 was originally cloned as an orphan receptor in 1997 by three independent groups who assigned three different names to it: STRL33 (seven transmembrane receptor-like from clone 33), BONZO, and TYMSTR (T lymphocyte-expressed seven-transmembrane domain receptor) (Alkhatib et al., 1997; Deng et al., 1997; Liao et al., 1997; Loetscher et al., 1997). The nomenclature system is logical, noncontroversial, and universally accepted and used (Table 1). Moreover, it has served as a template for the creation of a chemokine ligand nomenclature system (Zlotnik and Yoshie, 2000). Both systems have facilitated communication among immunologists and pharmacologists as these molecules have become important drug targets in...
which defines members of the CXC subclass of chemokines, and a multimodular structure consisting of a transmembrane region and a chemokine domain suspended by a mucin-like stalk previously found only for the CX3C chemokine CX3CL1. The CXCL16 chemokine domain also has characteristics of the CC chemokine subclass. CXCL16 is expressed on the surface of antigen-presenting cells (B cells, macrophages, dendritic cells in lymphoid organ T cell zones) and by cells in the splenic red pulp (Matloubian et al., 2000). Functional CXCL16 is also shed from macrophages (Wilbanks et al., 2001).

CXCR6 is expressed preferentially on memory T cells and on activated Th1 and Tc1 effector T cell subsets (Unutmaz et al., 2000; Kim et al., 2001). The exact biological role of CXCL16/CXCR6 is unknown, but reasonable hypotheses for this role include attraction of activated T lymphocyte subsets during inflammation, facilitation of immune responses via cell-cell contact, and guidance of T cell trafficking in the splenic red pulp. CXCL16 is also expressed in the thymic medulla and in some nonlymphoid tissues, suggesting roles in thymocyte development.

### B. CCR11

The human homolog of the bovine orphan gustatory receptor PPR1 was originally designated CCR11 based on a report by Schweickart et al. (2000) indicating that, when expressed in a transformed mouse B cell line, it functioned as a chemotactic receptor for the monocyte chemoattractant protein family of chemokines (CCL2, CCL8 and CCL13). However, an independent report, published in the same month, found that this same molecule (which was designated by a different name, CCR10) did not bind these chemokines, but instead bound CCL19, CCL21 and CCL25 with high affinity (Gosling et al., 2000). Nevertheless, no signaling function could be identified. On review, the first group confirmed that CCR11 bound CCL19, CCL21 and CCL25 in two independent cell lines and found that the original transfected cell line used in their study expressed RNA for endogenous mouse CCR2, a known receptor for CCL2, CCL8, and CCL13, but lacked detectable RNA for exogenous CCR11 (Schweickart et al., 2001). They concluded that the original data were not due to CCR11 but...
instead may be attributable to up-regulation of endogenous murine CCR2 gene. Since there is now no signaling response ascribed to the receptor, this molecule does not qualify for a CCR# designation and the terms CCR10 or CCR11 should no longer be used to describe it. Moreover, at approximately the same time in 2000, two groups independently identified the receptor for CCL27, which they named CCR10 (Homey et al., 2000; Jarmin et al., 2000). Since this molecule mediates chemotactic signaling, it is a bona fide chemokine receptor and qualifies for this designation.

REFERENCES