EGF-TM7 receptors: A diverse and still evolving family of receptors on the leukocyte surface
Matmati, M.

Citation for published version (APA):

General rights
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations
If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: http://uba.uva.nl/en/contact, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.
Scope
SCOPE

Research on the EGF-TM7 family of receptors started in 1995 with the cloning of the human EMR1 and CD97 family members [1;2]. As all members of the large G-protein-coupled receptor (GPCR) superfamily of integral membrane proteins, EMR1 and CD97 are embedded in the cell membrane with a seven-span transmembrane (TM7) region. What makes them unique is their large extracellular N terminal part with the tandemly repeated epidermal growth factor (EGF)-like domains. Receptor isoforms differ in the number of these EGF-like domains. With the unraveling of the human genome, new members of the EGF-TM7 family have been identified and added to the family: EMR2 in 2000 [3], EMR3 in 2001 [4] and EMR4 in 2003 [5]. At the completion of the human genome project in 2006, it has become clear that this is the complete family and that all the genes were clustered on chromosome 19. The finishing of the mouse genome project in 2002 and the rat genome project in 2004 showed that only EMR1, CD97 and EMR4 have homologs in these widely used experimental animals [6-9].

When the project from which this thesis is a result started in 2002, several EGF-TM7 receptors were still not or poorly characterized. This was especially true at the protein level. Thus, the main goal was to refine the characterization of the EGF-TM7 receptors and to generate the tools for systematic proteomic research on these receptors.

In chapter 1 the present status of our knowledge about the structure, expression, ligands and functions of EGF-TM7 receptors is summarized. In chapter 2 we report the generation of human EMR3 specific monoclonal antibodies and the first analysis of the receptor expression on different leukocyte subtypes. In chapter 3 we describe the differential expression of CD97 on human lymphocyte subsets. In chapter 4 the evolutionary origin of EMR2, which possesses a chimeric structure with a TM7 region most related to EMR3 and an EGF domain region nearly identical to CD97, is sketched. Moreover, different molecular mechanisms that prevent CD55 binding to EMR2 are defined in hominoids. In chapter 5 we tackle the field of NK cells biology. Here, the TNF-receptor family member CD27 is described as a novel marker for the characterization of functionally different NK cell subsets in humans. Finally, in chapter 6 some of the findings of this thesis are discussed in the light of still unanswered questions in the field of EGF-TM7 biology. These questions comprise the mechanisms
underpinning EGF-TM7 receptor function and the initiation of signal transduction by these receptors.

Reference List


