

The human genes for the α and γ subunits of the mast cell receptor for immunoglobulin E are located on human chromosome band 1q23

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Abstract. The receptor with high affinity for immunoglobulin E (Fc ϵ RI) is a key molecule in triggering the allergic reaction. It is a tetrameric complex of one α subunit, one β subunit, and two disulfide-linked γ subunits. This receptor is present exclusively on mast cells and basophils. Molecules identical to the γ subunit of Fc ϵ RI also form a cell surface complex with other Fc receptors such as mouse Fc γ RIIa in macrophages and most probably with human Fc γ RIII (CD16) in natural killer (NK) cells. Here we show by in situ hybridization that the human genes for the α (*FCER1A*) and γ subunits (*FCER1G*) of Fc ϵ RI and the gene for Fc γ RIII (*FCGR3*, *CD16*) are located on human chromosome band 1q23.

Introduction

Receptors for the Fc fragment of immunoglobulins (FcRs) are essential components of the immune system. They link the humoral system to various cellular responses such as antibody-dependent cytotoxicity, processing of immune complexes, release of important mediators, and secretion of cytokines. Molecular cloning of many of these FcRs has shown that, with one exception (Fc ϵ RII, *CD23*), their genes are members of the immunoglobulin superfamily (reviewed in Kinet 1989). Three distinct classes of human FcRs specific for IgG have been identified: one high-affinity receptor (Fc γ RI) and two low-affinity receptors (Fc γ RII and Fc γ RIII). The genes for the low-affinity receptors (*FCGR2*, *CD32* and *FCGR3*, *CD16*) have been mapped to chromosome 1q (Grundy et al. 1989). *FCGR2* has been further localized to band 1q23–q24 (Sammartino et al. 1988). The gene for the human α chain of Fc ϵ RI has been mapped in the same region of chromosome 1, on bands 1q21–q23 (Tepler et al. 1989).

With the exception of the tetrameric Fc ϵ RI (Blank et al. 1989), FcRs were thought until recently to consist of single polypeptide chains. It is now clear that this is not the case. For example, mouse Fc γ RIIa forms a surface complex with γ chains identical to those from Fc ϵ RI (Ra et al. 1989). Similarly, human Fc γ RIII in natural killer (NK) cells associates with ζ chains identical to those found in the T-cell receptor (Lanier et al. 1989). Human Fc γ RIII probably associates also with γ chains from Fc ϵ RI (Hibbs et al. 1990).

Recently, the gene for the γ subunit of these FcRs was located at the distal end of mouse chromosome 1 and was linked to the gene for the α subunit of Fc ϵ RI and to the gene for Fc γ RIIa (Huppi et al. 1989). In this article we localize by in situ hybridization the human genes for the α and γ subunits of Fc ϵ RI and the human gene for Fc γ RIII.

Materials and methods

Chromosome spread. High-resolution preparations of human chromosomes were obtained from phytohemagglutinin-stimulated blood cell cultures of healthy males after methotrexate synchronization (Yunis et al. 1978). Slides were stored at room temperature for at least 1 week before use.

cDNA probes. The cDNA probe for the human Fc ϵ RI α chain is a 1.2 kilobase *Eco* RI–*Eco* RI insert excised from the pGEM-3Z vector (Kochan et al. 1988). The cDNA probe for the human Fc ϵ RI γ chain is a 710 base pair (bp) insert excised by *Xba* I–*Bam* HI from a fragment subcloned into *Xba* I–*Sma* I of the pSVL vector (Küster et al. 1990). The cDNA probe for human Fc γ RIII-2 in NK cells is a 887 bp insert excised by *Eco* RI–*Bam* HI from a fragment subcloned in pUC9 (Ravetch and Perussia 1989). The three cDNA inserts were labeled by the multiprime DNA labeling system (Amersham, Amersham, UK) as described by Feinberg and Volgenstein (1983). Specific activities of 3×10^7 to 7.5×10^7 cpm/ μ g were obtained by using 8 μ Ci (^{3} H)dCTP and 50 ng DNA.

In situ hybridization on metaphase chromosomes. The technique of in situ hybridization was followed as described by Harper and Saunders (1981), with slight modifications (Caubet et al. 1985). The probes

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FcεRIα, FcεRIγ, and FcγRIII-2 were used at concentrations of 20, 50, and 80 ng/ml, respectively. The slides were treated with Kodak NTB2 emulsion and autoradiograms developed after 1–2 weeks' exposure. G-bands were obtained using Wright's staining.

Results

Localization of the human gene for the α subunit of FcεRI (*FCERIA*). Out of a total of 159 metaphases hybridized with the FcεRIα probe, 222 autoradiographic silver grains were localized on chromosomes. Seventy-four grains (33.3% of the total) were localized to chromosome 1. Thirty grains (13.5% of the total and 40.5% of those on chromosome 1) were located at band 1q23. The distribution of these grains is recorded on a diagram of the karyotype (Fig. 1).

Localization of the human gene for the γ subunit of FcεRI (*FCER1G*). A total of 203 silver grains were counted from 126 metaphases. Analysis of their distribution (Fig. 2) showed that 55 grains (27% of the total) were on chromosome 1, 21 of which (10.3% of the total and 38% of those on chromosome 1) were found on band 1q23.

Localization of the human gene for FcγRIII (*FCGR3*, *CD16*). The distribution of 187 silver grains from 89 metaphases (Fig. 3) was analyzed to localize the gene for CD16. Eighty-eight (47% of the total) were on chromo-

some 1, 51 of which (27.3% of the total and 58% of those located on chromosome 1) were on band 1q23.

Discussion

In situ hybridization on metaphase chromosomes indicates that the human genes for the α (*FCERIA*) and γ subunits (*FCER1G*) of FcεRI and the human gene for FcγRIII (*FCGR3*) are localized on the same band 1q23 of the human chromosome 1. These results are consistent with the previously reported mapping of *FCERIA* on 1q21–1q23 (Tepler et al. 1989). In addition, the localization of *FCGR3* fits very well with two other previous observations: *FCGR2* was localized on bands 1q23–q24 (Sammartino et al. 1988) and shown to be physically linked to *FCGR3* (Peltz et al. 1989).

It is worth mentioning that two associated polypeptides, the α and γ subunits of FcεRI, have genes localized on the same chromosomal band. This is unexpected because their respective DNA and amino acid sequences are completely unrelated. These two genes were also found closely localized in mice (Huppi et al. 1989). It may be possible to evaluate by pulsed-field electrophoresis the distance between these genes in mice and humans; if they are found to be very closely situated, one could argue that they have been maintained together for the purpose of regulation.

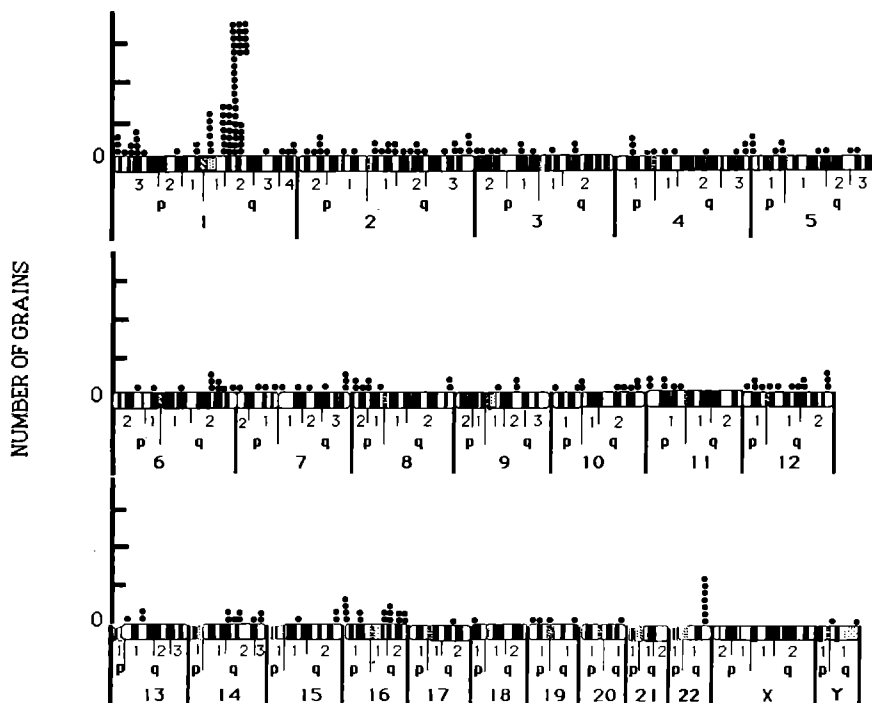


Fig. 1. Diagram showing grain distribution in 159 metaphases hybridized with the ³H-labeled FcεRI α subunit (*FCERIA*) probe.

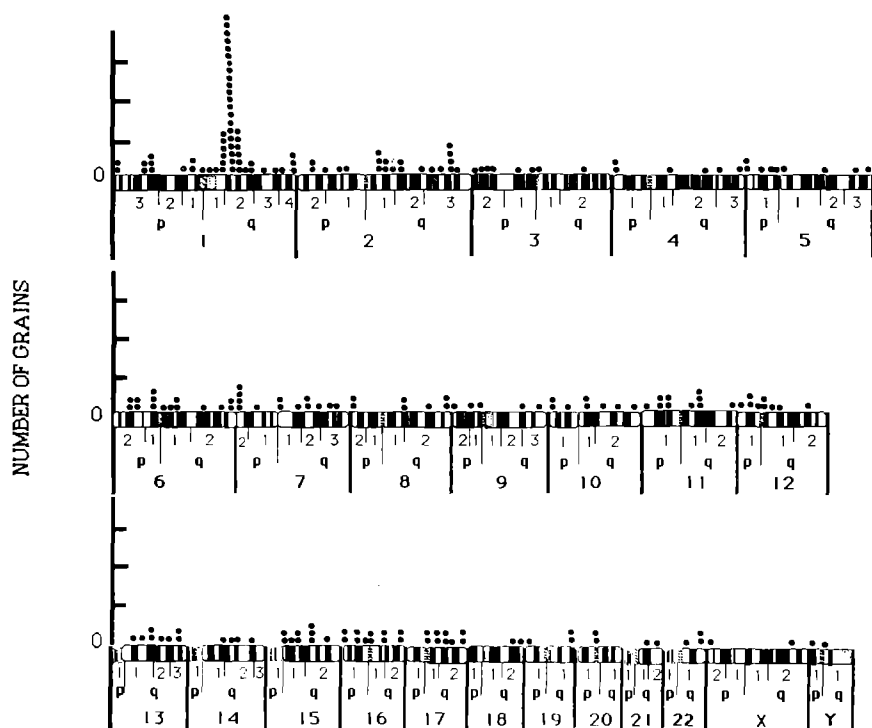


Fig. 2. Diagram of grain distribution in 126 metaphases hybridized with the FcεRI γ subunit (*FCER1G*) probe.

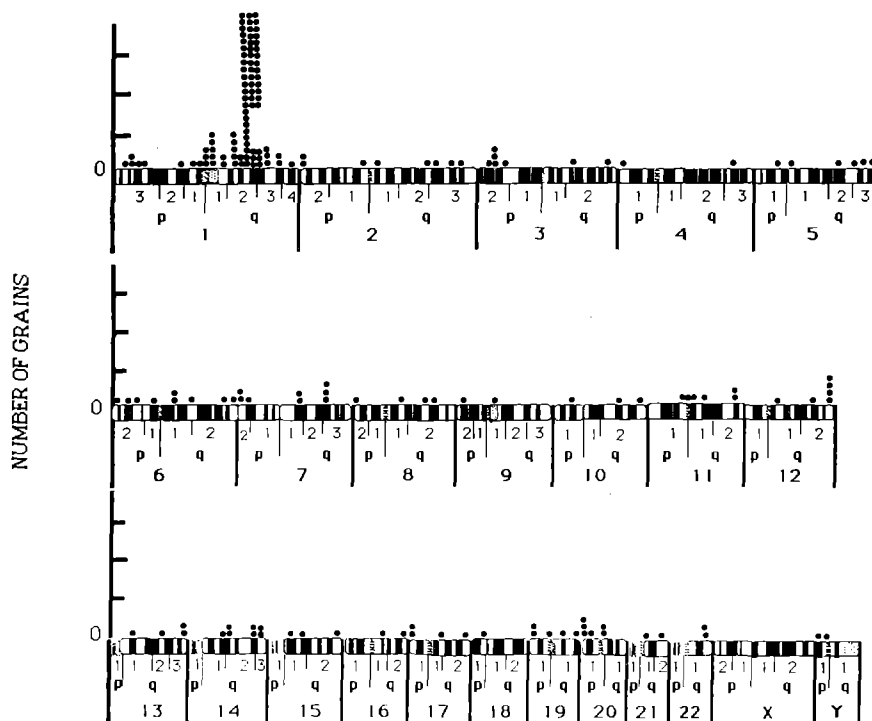


Fig. 3. Diagram of grain distribution in 89 metaphases hybridized with the Fc γ RIII (*FCGR3*, *CD16*) probe.

Recently, we established that the gene for the γ subunit of FcεRI and the gene for the ζ chain originally found in the T-cell receptor are homologous and most likely have evolved by gene duplication (Küster et al. 1990) to form

a new gene family. Both genes have been localized on mouse chromosome 1, although not in close association (Huppi et al. 1989). This study, together with the previous chromosomal localization of the gene for the ζ chain

(Weissman et al. 1989), now demonstrates that both genes are also on human chromosome 1. It is therefore possible that other members of this gene family, such as the gene for the η chain of the T-cell receptor, will also be localized on mouse and human chromosome 1.

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