

Letter to the editor

We refer to data published by Rigby et al. (1), mapping the epitope of the anti-FcεRIα mAb 15/1 to peptide εRI 11.

There are indications that mAb 15/1 recognizes a conformational epitope:

- 1) 15/1 does not detect denatured FcεRIα in Western blots
- 2) its epitope cannot be mapped with a bacterial random peptide library – in contrast to the anti-FcεRIα mAb 5H5F8 – demonstrating the system validity (2)
- 3) 15/1 *does not* immunoprecipitate denatured FcεRIα (3).

IgE binding is mediated via domain D2 of FcεRIα, including the FG-loop. The binding site is thought to contain four tryptophans (Trp^{87,110,113,156}) forming a flat hydrophobic ridge next to the FG-loop, which itself was postulated to determine partially the specificity of FcεRIα interaction (4).

The FG-loop residue Trp¹⁵⁶ contributes to the 15/1 epitope (2). Peptide εRI-11 (containing Trp¹¹⁰ and

Trp¹¹³) covers the BC-loop close to the FG-loop, and inhibited 15/1 binding by about 60%. Partial inhibition of 15/1 binding (20%) and IgE binding (10%) was also observed for the Trp¹⁵⁶-containing peptides εRI-15 and εRI-16. This indicated that the 15/1 epitope is discontinuous and that different FcεRIα peptides are recognized by 15/1.

The specificity of the inhibition of IgE/FcεRIα binding by peptide εRI-11 has yet to be demonstrated since it has significant homologies with known receptors, such as FcγRIII.1 (4). In contrast, the amino acids surrounding Trp¹⁵⁶ are unique to FcεRIα (2) and may contribute to the specificity of the IgE/FcεRIα interaction.

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References

1. RIGBY LJ, TRIST H, SNIDER J, HULETT MD, HOGARTH PM, EPA VC. Monoclonal antibodies and synthetic peptides define the active site of FcεRI and a potential receptor antagonist. *Allergy* 2000;**55**:609–619.
2. NECHANSKY A, ASCHAUER H, KRICEK F. The membrane-proximal part of FcεRIα contributes to human IgE and antibody binding – implications for a general structural element in Fc receptors. *FEBS Lett* 1998;**441**:225–230.
3. LETOURNEUR O, SECHI S, WILLETTE-BROWN J, ROBERTSON MW, KINET JP. Glycosylation of human truncated Fc epsilon RI alpha chain is necessary for efficient folding in the endoplasmic reticulum. *J Biol Chem* 1995;**270**:8249–8256.
4. GARMAN SC, KINET JP, JARDETSKY TS. Crystal structure of the human high-affinity IgE receptor. *Cell* 1998;**95**:951–961.