Modeling and Analysis of Ag:IgE Interface of House Dust Mite Allergens of Group 1

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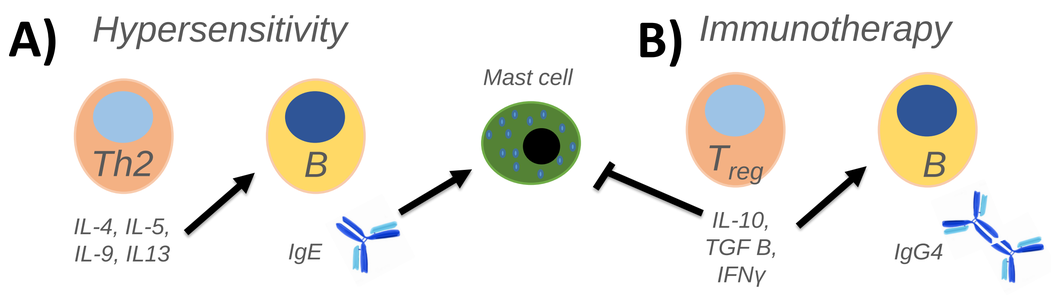
INTRODUCTION

In Peru, 20 - 28 % of people has hypersensitivity to allergens; of these 80 % are sensible to at least one house dust mite. Immunotherapy is based on the regular administration of increasing doses of allergens extracts or purified allergens. This procedure allows that the patients immune systems changes is Th2 cell response and IgE humoral response induced by the allergens (Hypersensitivity (Fig. 1A)) to a Threg cell response and IgG4 humoral response avoiding the appearance of symptoms of hypersensitivity (Fig. 1B).



At the moment, there are not available treatments for allergies caused by the majority of house dust mites described so far. For this reason we are investigating at the structural levels several group 1 allergens of house dust mites with the main goal of producing a immunovaccine against all this group. For this we plan to produce *in silico* structural models of group 1 allergens (Fig. 2A) to perform several analysis aimed to identify commons epitopes (conserved peptides) (Fig. 2B). After this, we intend to rationally modify the peptides producing less immunogenic variants better for immunotherapy (Fig. 2C).

Here we present the description of 4 conserved motifs that could be used to design immunovaccines against house dust mite group 1 allergens

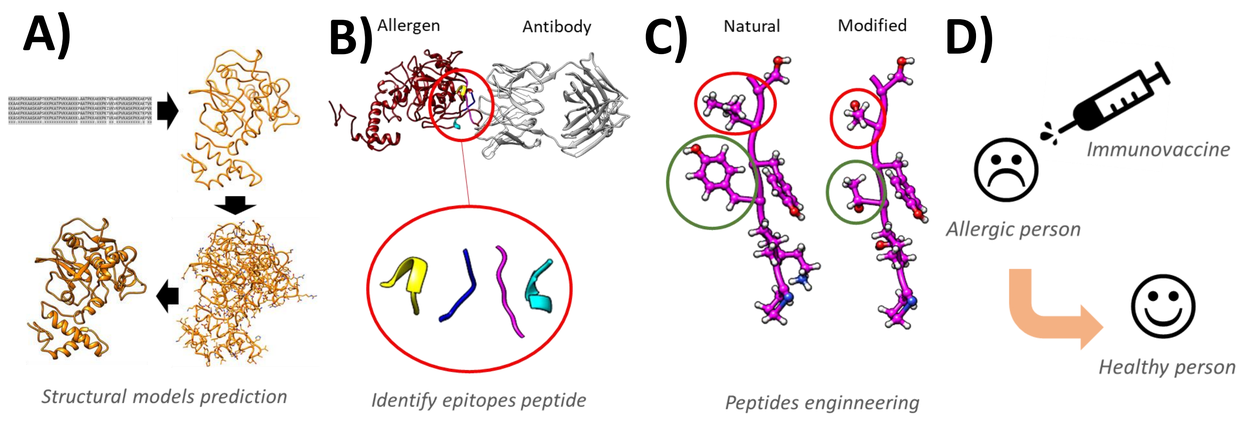
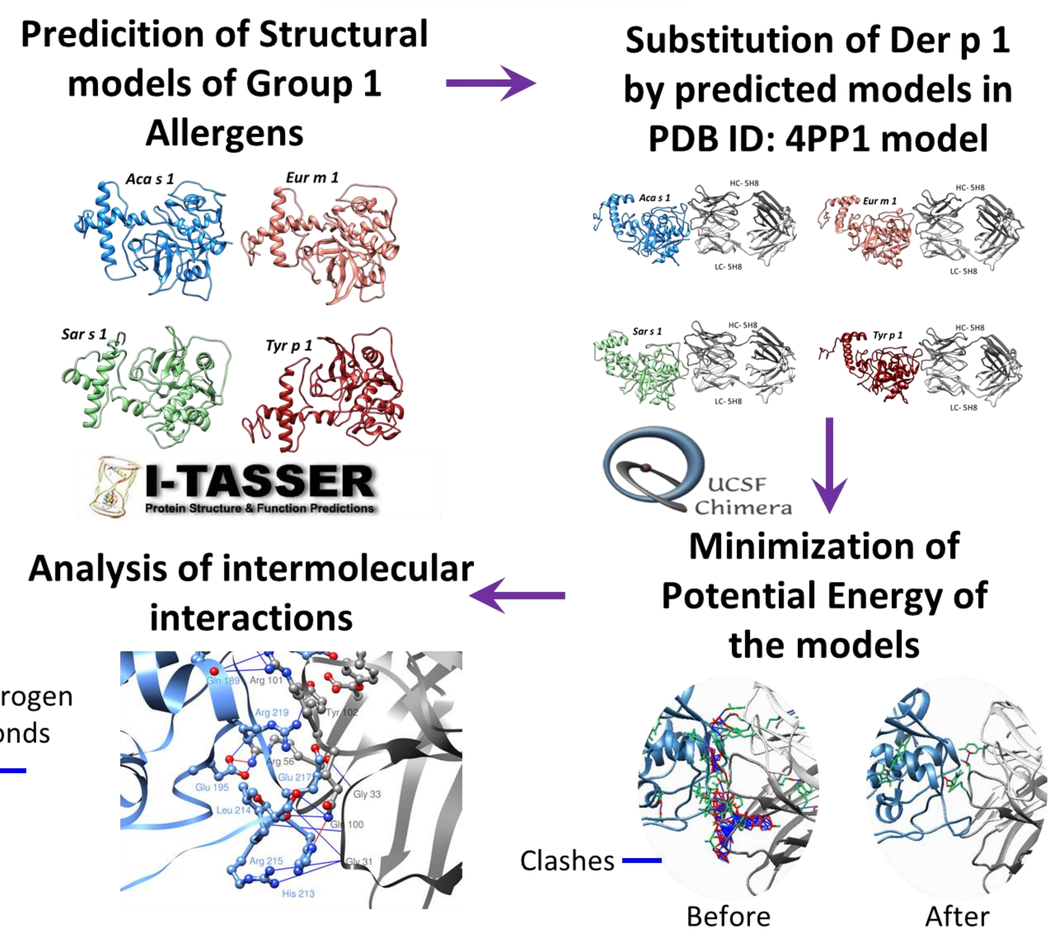
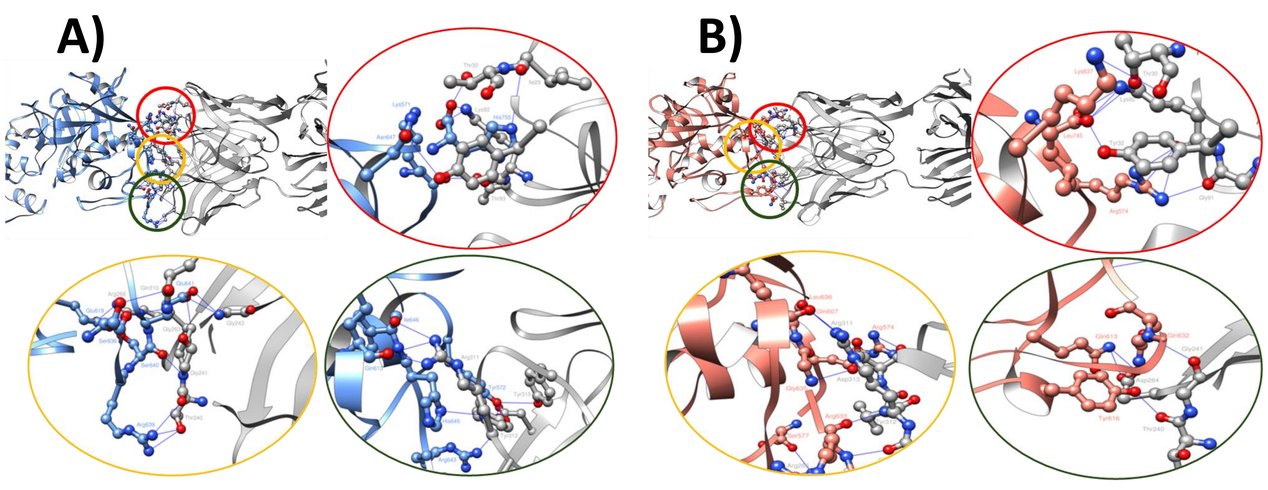


Figura 2: General idea to rationally design a immunovaccine against house dust mite group 1 allergens. Structural models will be produced (A) to identify possible epiotpes peptides by antibody interaction analysis (B). These identified peptides will be engineered trying to reduce its immunogenicity (C). Finally, the efficacy of these peptides will be tested (D).

METHODOLOGY



RESULTS



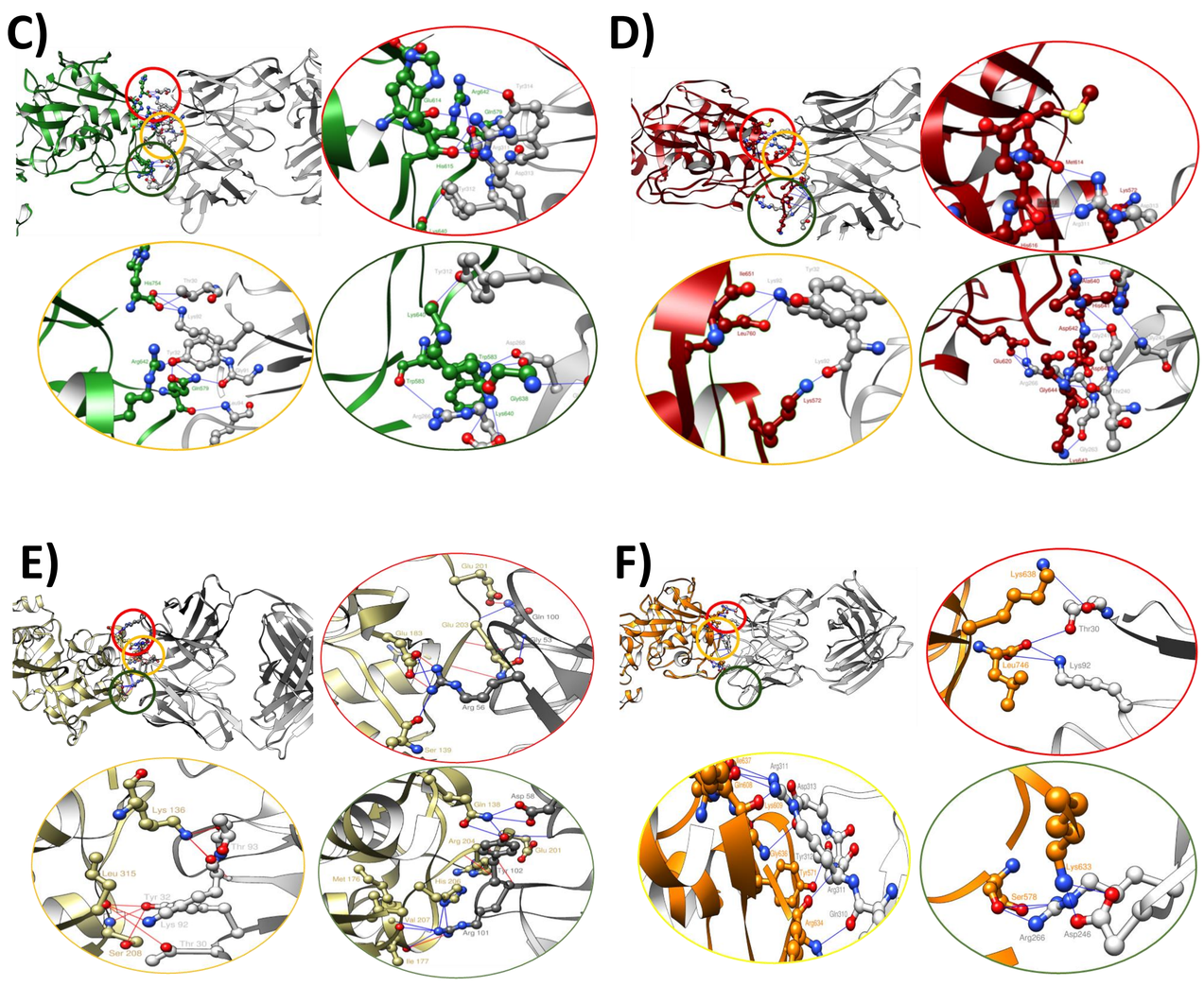
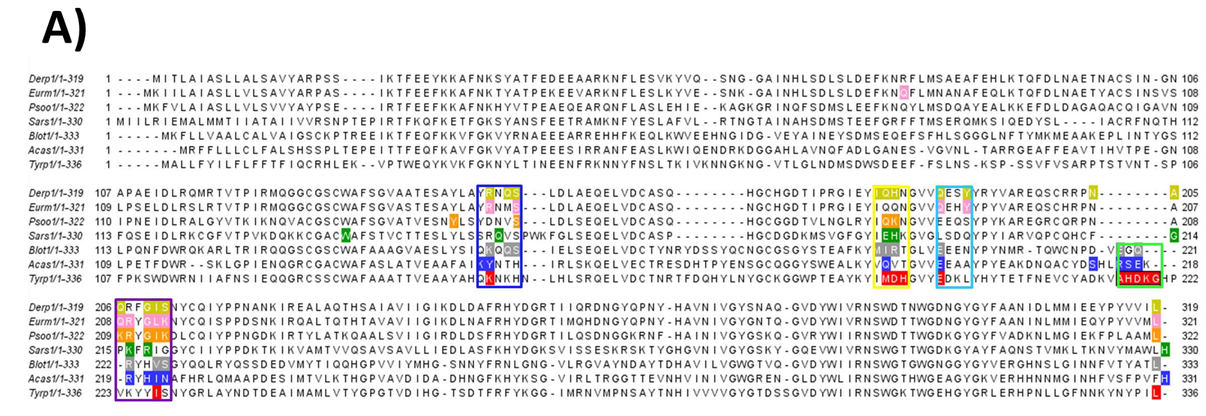


Figura 3: Hydrogen bonds between mAb 5H8 antibody and group 1 allergens of house dust mites. **A)** Aca s 1-mAb 5H8, **B)** Eur m 1-mAb 5H8, **C)** Sar s 1-mAb 5H8, **D)** Tyr p 1-mAb 5H8, **E)** Blo t 1-mAb 5H8, **F)** Pso o 1-mAB 5H8. Hydrogen bonds are represented as blue lines between acceptor and donor atoms.



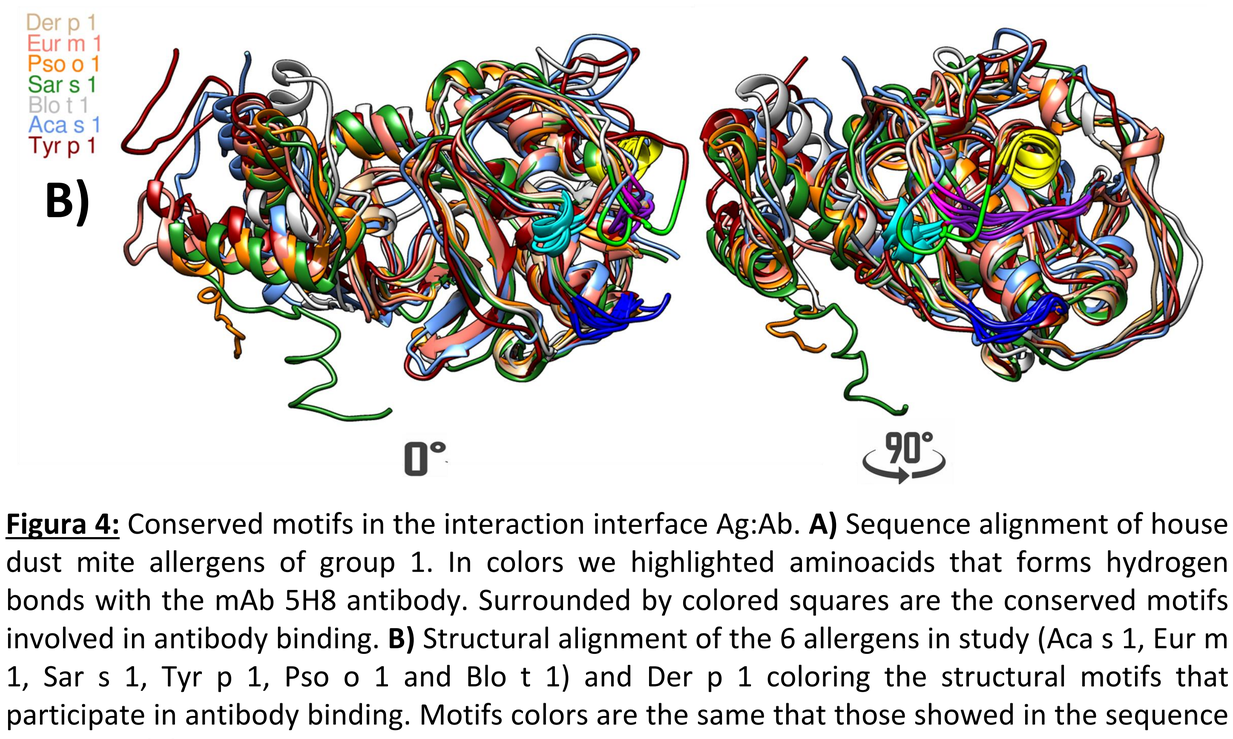


Figura 4: Conserved motifs in the interaction interface Ag:Ab. **A)** Sequence alignment of house dust mite allergens of group 1. In colors we highlighted aminoacids that forms hydrogen bonds with the mAb 5H8 antibody. Surrounded by colored squares are the conserved motifs involved in antibody binding. **B)** Structural alignment of the 6 allergens in study (Aca s 1, Eur m 1, Sar s 1, Tyr p 1, Pso o 1 and Blo t 1) and Der p 1 coloring the structural motifs that participate in antibody binding. Motifs colors are the same that those showed in the sequence alignment (B).

CONCLUSIONS

- We were able to identify 4 conserved motifs that interacts by hydrogen bonds with atoms of 5H8 antibody (Fig. 4).
- These conserved motifs showed the following sequences: blue motif D/Dc/Dn/x/D, yellow motif H/A/x/D, cyan motif A/A/x/x, purple motif Dc/Ar/x/H/D. Where D = donor residue, Dc = Charged donor, Dn = Neutral donor, H = Hydrophobic residue, A = Aceptor, Ar = Aromatic residue and x = Any aminoacid.
- Three allergens (Aca s 1, Tyr p 1 and Blo t 1) showed and insertion with aminoacids involved in antibody interactions (green) (Fig. 4).
- Finally, in this work we described 4 very well conserved motifs that could be used to design immunovaccines against house dust mite allergens of group 1.

REFERENCES

Chruszcz M, Pomés A, Glesner J, Vailes L, Osinki T, Porebski P, Majorek K, Heymann P, Platts T, Minor and Chapman M. 2012. Molecular determinants for antibody binding on group 1 house dust mite allergens. The Journal of Biological Chemistry. Volume 287, No. 10, pp. 7388 –7398.

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