Coeliac disease: studying the interaction of HLA-DQ2 molecule with gluten peptides by computational methods - session: Structural Genomics)

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Coeliac disease is the most common food-sensitive enteropathy in humans, caused by a permanent intolerance for the dietary gluten and is considered to be a T cell-mediated multifactorial disease.The large majority of patients express the HLA-DQ2 [DQ(a1*0501,b1*02)] and/or HLA-DQ8 [DQ(a1*03,b1*0302)] molecules. The DQ2 and DQ8 molecules confer susceptibility to celiac disease by presenting gluten-peptides to T-cells in the small intestine. The peptide-binding motifs of DQ2 and DQ8 show a preference for negative charges at anchor positions of the bound peptides. The gluten proteins contain few negative charged residues and are rich of proline and glutamine. Experimentally it has been found that lesion-derived T cells recognize deamidated gluten peptides and that this deamidation can be mediated in situ by the transglutaminase type 2 enzyme.
In our work, we have predicted the three-dimensional structure of HLA-DQ2 molecule by homology modelling and of the complex of HLA-DQ2 with some gluten peptides by superimposition and energy minimization on the basis of the experimental structure of DQ8-insulin B9-23 complex (PDB code: 1JK8). Moreover, we have evaluated the energies of interaction for each peptide/DQ2 complex. We have studied the peptide binding motif for DQ2 and observed that this molecule has the preference for negatively charged residues in the specific anchor positions. Infact, when a single glutamine residue in these anchor positions is exchanged with glutamic acid, the peptide-DQ2 complex appear more stable. This finding is in agreement with the experimental results reported in literature.
We are applying this strategy to evaluate the effects of other peptide modifications as well as the interaction of DQ2 with other peptides. SOLO POSTER