Poster

The molecular chaperone HtpG is a promising antigen against *Mycobacterium tuberculosis*

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Tuberculosis (TB) is the second leading killer pathogen after *Covid -19*. In 2022, WHO declared a total of 1,3 million deaths caused by its etiologic agent, *M. tuberculosis*. The currently available vaccine against TB, BCG, is not totally effective to prevent the disease. The urgency to find a new vaccine against TB due to the high mortality led us to approach structure vaccinology (SV) for vaccine antigen design [1]. HtpG is a large and key dimeric chaperone like protein, that belongs to the highly conserved Hsp90 family proteins, and was shown to induce a strong activation of dendritic cells (DCs) enhancing the protective immune response when fused to other Mtb antigens (e.g. ESAT6). Here, we report the structural characterisation of HtpG in its ATP bound state. Structural data of HtpG helped to better understand the biological role of the protein and its ability to stimulate immune system [2]. The identification of the most immunogenic part of the protein allowed us to design enhanced antigens through conjugation of identified epitopes with ESAT6, a well-known T cell activator. The conjugated antigen was confirmed to possess an enhanced immunogenicity and anti-mycobacterial activity [4]. HtpG is a part of a well-orchestrated and complex which includes the chaperone DnaK, its cofactors DnaJ1/J2, the release factor GrpE, and the protein disaggrease ClpB [3]. We provide an overall picture of the contribution of structural studies to the understanding of the complex molecular machinery devoted to the protein refolding in *M. tuberculosis* and to the role of HtpG in this scenario.

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