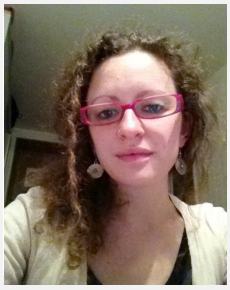
ImmunoTools *special* Award 2015



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Study of the immune modulant properties of the protein HP1454 produced by *Helicobacter pylori*

Helicobacter pylori (Hp) is a Gram negative bacterium that specifically colonizes the gastric mucosa of about half of the world's population, thus being the most common bacterial infection worldwide.

Typically acquired during childhood, the infection can persist in the gastric ecosystem throughout the life span of the host, if untreated. Colonization of the stomach by Hp causes chronic gastritis that can evolve into more severe diseases, such as atrophic gastritis, peptic ulcer, lymphoma of the mucosa-associated lymphoid tissue (MALT) or gastric adenocarcinoma.

In spite of about 30 years of active research (since 1983, when Hp has been identified and its causative role in gastric diseases demonstrated), many key questions are still opened about the molecular mechanisms by which the bacterium interact with the host cells of the human gastric mucosa subverting their functions so as to allow the bacterium to achieve its paramount goal of a successful and persistent colonization.

The proteins on the surface of the external membrane and the secreted proteins exert a crucial role in Hp infection; indeed they are the first to be involved in the host-pathogen interaction processes. Those proteins seem to play a pivotal role in the modulation of host immune response and represent potential good candidates for a vaccine.
Detailed analysis of *H. pylori* secretome revealed the presence, among other proteins already deeply characterized such as VacA and the flagella proteins, of proteins with unknown functions. Among them, there is the protein HP1454, a 303 amino acids protein, which resulted to be abundant in the supernatant of *H. pylori* liquid culture and, moreover, it was present in high proportion in the Hp outer membrane vesicles (OMV). The OMV were demonstrated to be involved in biofilm formation and to participate in immune system evasion through the antigen removal from bacterial surface. Considering that OMV contain various virulent factors, such as VacA, CagA, SabA e BabA, it is possible that these vesicles could be also implicated in the pathogenesis of the H. pylori-associated diseases.

The gene encoding for the protein HP1454 is part of a cluster of genes containing two lipoproteins; one of these is Lpp20, a highly immunogenic lipoprotein anchored to the bacterial external membrane; moreover, HP1454 shows a high homology with the protein Lpp20. On the basis of these premises, and considering that HP1454 is highly represented in the OMV, in order to obtain information about the role and the function of the protein HP1454, it will be evaluated the gene expression and the production, in human monocytes and in human monocytes-derived macrophages (hMDM) exposed to OMV wt and OMV derived from a bacterial strain lacking the hp1454 gene, of those cytokines which are most relevant in the inflammatory processes such as TNF-α, IL-1β, IL-6, IL-12 and IL-23.

Preliminary data, suggest that the presence of HP1454 induces in both monocytes and hMDM the production of cytokines, which drive the differentiation of T lymphocytes toward a Th17 phenotype, one of the T cell subset highly represented in the Hp infection.

In order to deeper investigate this aspect, we will evaluate the effect of HP1454 on T cells directly exposed to OMV wt or ΔHP1454, or exposed to the culture supernatants derived from activated monocytes. The phenotype of T lymphocytes will be evaluated both in terms of transcription factors gene expression (RORγt, Tbet and GATA3) and in term of cytokines production by FACS analysis.

The data obtained, will shed light on the Hp protein HP1454 function and its possible role and involvement in *H. pylori*-associated diseases.