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Modified MHCII associated invariant chain induces increased antibody responses against *Plasmodium falciparum* antigens after adenoviral vaccination

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Adenoviral vectors can be modified to induce both T and B cell immune responses to antigens encoded by the recombined vectors. The MHCII chaperone invariant chain (Ii) has been used as an adjuvant to enhance T cell responses to tethered antigen encoded in adenoviral vectors. Here, we modified this adjuvant by insertion of an intramolecular furin protease recognition site (Ii-fur) to obtain a secreted version of part of the adjuvant in complex with the antigen. To test the capacity of this modified adjuvant to induce immune responses, we recombined vectors to encode *Plasmodium falciparum* virulence factors; two CIDRα1 domains derived from the IT4*var*19 and PFCLIN*var*30 var genes, as a dimeric antigen. These domains are two members of a polymorphic protein family of important host receptor adhesion molecules involved in the vascular sequestration of parasites in severe malaria. The Ii-fur molecule was investigated in vitro and shown to direct secretion of oligomeric antigen as well as functioning as an adjuvant for MHC class I and II restricted antigen presentation, as previously reported with Ii. While Ii-fur shows an unaltered T cell adjuvant effect, it strongly accelerates and enhances the specific antibody response against both targeted CIDR antigens. Mutagenesis studies demonstrated that the combination of an endosomal targeting sequence, secretion and a trimerization domain in the invariant chain C- terminal domain was needed for the full adjuvant effect on antibody responses. As the invariant chain is already a potent T cell adjuvant for vectored vaccines, we conclude that our newly designed adjuvant is an efficient tool for inducing a combination of T cell and antibody responses to plasmodial antigens by adenoviral vaccination.

Biography

Cyrielle Fougeroux has done her Master's in Immunology from UPMC, and is pursuing her PhD from Copenhagen University, Denmark. She has been working on adenovirus based vaccines targeting malaria and mucosal pathogens. She along with her supervisor (Peter J Holst) developed a new adjuvant based on MHCII associate invariant chain inserted with a furin recognition site allowing secretion of a trimerized antigen. This adjuvant was capable of enhancing both T cellular responses as well as humoral specific responses to the encoded antigen, after adenoviral vaccination in mice. This finding has now been patent and we would like to test our adjuvant with different adjuvant and are thus are open to collaborations in the near future.

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