

New class of molecular adjuvant



Oxford researchers have identified a family of enzymes that can increase immunogenicity towards a wide range of fused antigens.

The adjuvant advantage

An adjuvant is a substance that is able to enhance or prolong the body's antigen-specific immune response to an administered vaccine. Simple inorganic aluminium salts, such as aluminium hydroxide or aluminium phosphate, have been commonly used as adjuvants since the 1930s. Recently, attention has turned to organic or biological adjuvants to tackle more challenging and complex disease targets.

4-Oxalocrotonate tautomerase (4-OT)

4-OT is an enzyme, which forms part of a key metabolic pathway in bacteria. The monomer unit contains just 62 amino-acid residues, making it one of the smallest known enzyme subunits; however, 4-OT forms a hexamer in solution. Researchers at the University of Oxford have been exploring the use of 4-OT proteins as vaccine adjuvants.

Beating the superbugs

The group at Oxford have successfully fused a member of the 4-OT family (SAR1376) to a range of pathogen antigens from *Staphylococcus aureus* and *Plasmodium falciparum*. Following delivery of these fused complexes by DNA or viral vectors, increased immunogenicity has been observed *in vivo*. The 4-OT tag multimerises in solution and it is the aggregation that is thought to cause the observed increase in immunogenicity. This methodology represents a rare discovery of a non-human multimerisation domain that enhances immunogenicity when fused to a range of antigens.

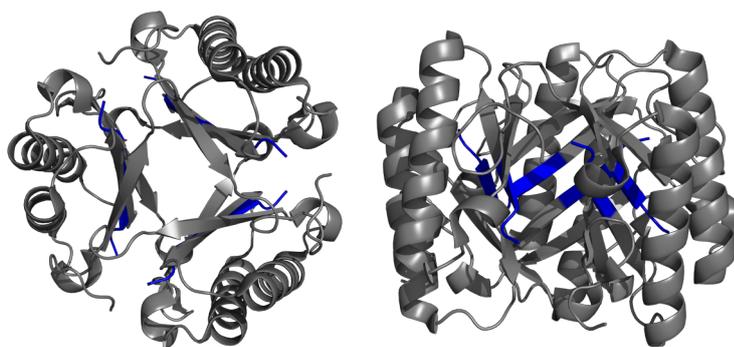
Perhaps most importantly, 4-OTs are widespread in pathogenic bacteria (both Gram positive and Gram negative). Their conserved structure may allow this to be a generalised approach for enhancing antibody responses to vaccine antigens, offering an attractive alternative to virus like particles (VLPs).

We believe that the key advantages of this technology include:

- Adjuvant shows *in vivo* efficacy when fused to antigens from *S. aureus* or *P. falciparum*
- New platform technology for vaccine development
- Hundreds of potential adjuvants identified in diverse bacterial species
- Rare class of multimerisation tags that can enhance immunogenicity
- Fills need for more antigen scaffolding strategies

Commercialisation

Oxford University Innovation Ltd. has filed a patent, which covers this work and is currently seeking a commercial partner to develop the technology.



Above image: Crystal structure of the SAR1376 multimerizing protein, obtained from the Protein Data Bank

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Technology Transfer from the University of Oxford

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