

Ketol-Acid Reductoisomerase as a Novel Nanoparticle

Researchers at the La Jolla Institute for Immunology have designed a novel nanoparticle using an archaeal ketol-acid reductoisomerase (KARI). KARI oligomerizes into a 12-mer nanoparticle, and antigens of interest can be tagged in the C- or N-terminal using the SpyCatcher/SpyTag system.

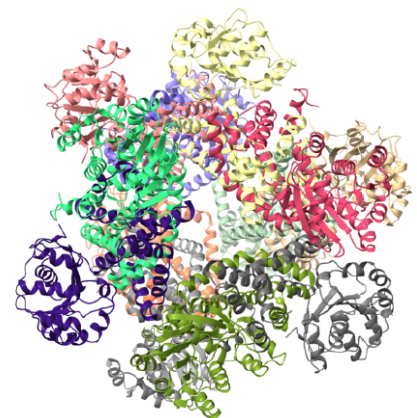
Nanoparticle platforms involve the attachment of antigen to the surface of a particle to promote an immune response through enhanced trafficking and recognition by cellular receptors. Protein-based platforms are highly biocompatible, can assemble homogeneously, and can be effectively tailored to suit any antigen. Furthermore, protein-based platforms enable antigen attachment through genetic fusion or affinity tag complexes which allow for a homogeneous decoration of antigens on the platform. Two characteristics of nanoparticle platforms contribute to generating the B-cell IgG response: (1) the attachment of the antigen to a larger scaffold which improves APC uptake and retention in lymph follicles and (2) the repetitive array of antigens which enables efficient binding and activation through efficient crosslinking with multiple BCRs. This evidence has been largely demonstrated in side-by-side experiments of the same antigen delivered as sub-unit ectodomain or bearded on different size self-assembling nanoparticles in viral diseases such as HIV, influenza, and SARS-CoV-2.

As such, researchers at LJI have designed a KARI nanoparticle. Compared to ferritin nanoparticles, the most used protein self-assembling nanoparticles used for the delivery of 8 antigens on each molecule, the 12-meric nanoparticle KARI will display 12 antigens on the surface, presumably increasing the trafficking of the antigens to the lymph nodes and the APC presenting, increasing the immunogenicity and the affinity maturation of the elicited B cells.

ADVANTAGES:

- Can display up to 12 heterologous antigens of interest
- Highly biocompatible
- Able to self-assemble homogeneously
- Increases immunogenicity of elicited B cells

Novel Self-Assembling Multivalent Protein Nanoparticle Useful for the Development of Universal Vaccine Candidates



Atomic model of the 2.4Å KARI nanoparticle where each monomer is colored differently