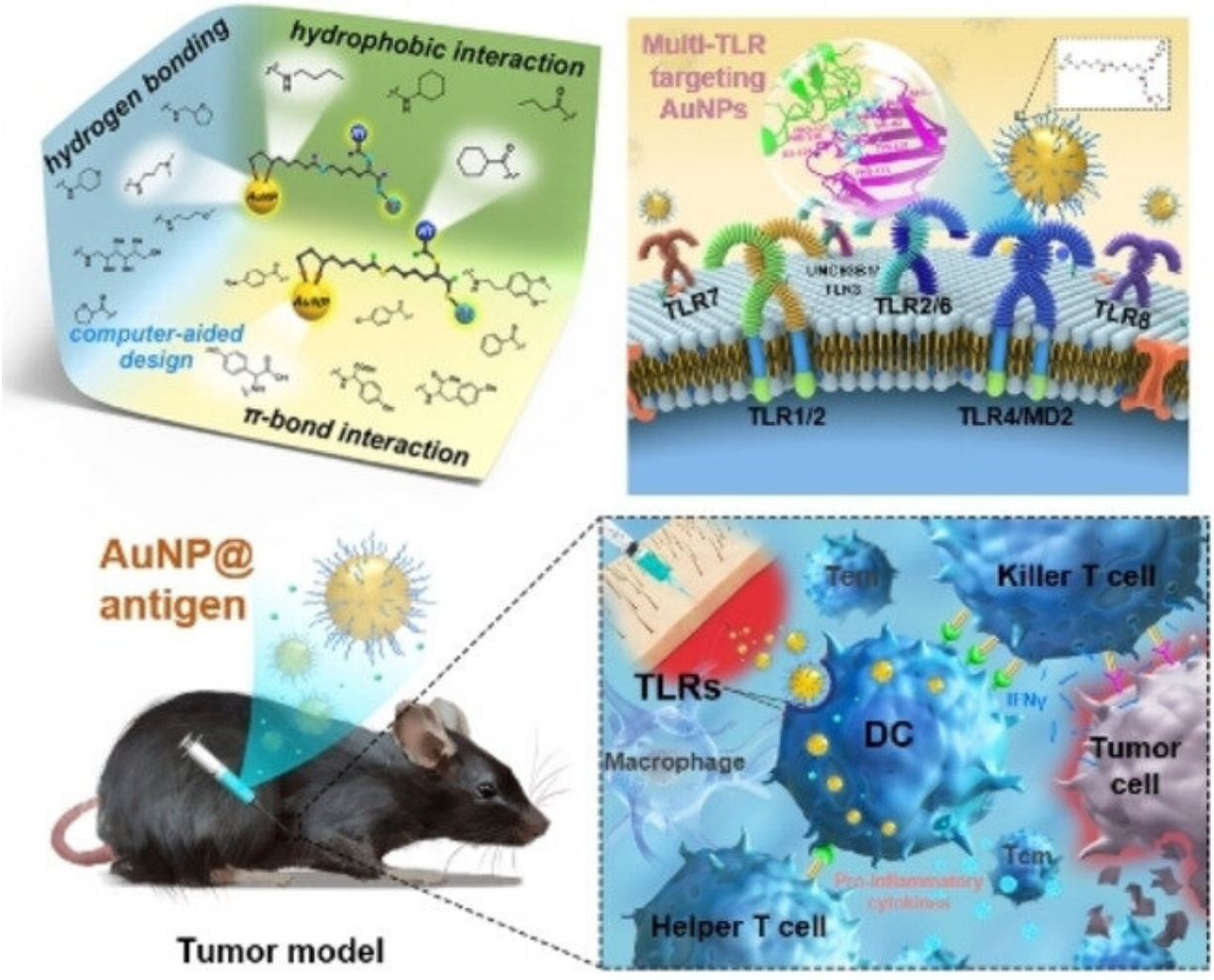
Making immunizations more effective: Exploring how adjuvants developed using computers boost vaccines

March 27 2023, by Sijin Liu



Graphical Abstract. New Au nanoparticle (AuNP) adjuvants are prepared through computer-aided molecule design and machine learning to discover agonist ligands, and sulfur-Au coordination chemistry guided well-ordered

presentation of ligands on AuNP surface. These AuNP adjuvants show advantages in multi-toll like receptor (TLR) targeting and application as broad-spectrum adjuvants to boost robust multifaceted anti-tumor vaccine responses. Credit: *Angewandte Chemie International Edition* (2023). DOI: 10.1002/anie.202301059

In addition to an antigen, many vaccines also contain substances, called adjuvants, which stimulate the immune system. By using computer-aided molecular design and machine learning, a Chinese research team has now developed two novel broad-spectrum adjuvants that can significantly amplify the immune response to vaccines. As reported in the journal *Angewandte Chemie*, they were able to enhance the effectiveness of immunization against certain forms of cancer in animal models.

Adjuvants amplify and prolong the effect of vaccine immunizations. Aluminum salts have been successfully used as adjuvants for many decades. Alternatively, there are oil-in-water emulsions that target pattern recognition receptors on immune cells. However, older versions of this type of adjuvant were not effective enough or had troublesome side effects. Newer versions are well-tolerated and effective but need to be tailored for every individual vaccine.

By using computer-aided molecular design and machine learning, Bing Yan, Sijin Liu, and their team at the Research Center for Eco-Environmental Sciences and the Capital Medical University in Beijing, as well as the University of Chinese Academy of Sciences in Beijing and Hangzhou, the Shandong First Medical University & Shandong Academy of Medical Sciences, and the Guangzhou University, have now developed two novel adjuvants with broad-spectrum effectiveness that can significantly boost the immune response to vaccines.

The new adjuvants are designed to bind to toll-like receptors (TLR), a class of proteins used by dendritic cells to detect the characteristic molecular patterns of pathogens. If an "enemy" is recognized, the dendritic cell moves into a lymph node and "presents" its find to the T-cells. These activated T-cells then multiply and enlist further immune cells in the fight.

The team identified structural characteristics of the binding sites on human TLR and developed a collection, a substance library, with 46 different ligands that are compatible with the binding site. The special twist in this case is that these ligands are anchored to the surfaces of biocompatible gold nanoparticles.

This causes them to be bound more easily by the TLR. Two of the ligands were found to be especially effective. Comprehensive in vitro, ex vivo, and in vivo studies demonstrated that they bind to several different TLR and increase the activation of dendritic cells, presentation of antigens to T-cells, and their activation.

Mice treated with tumor-specific antigens plus one of these new adjuvants demonstrated strong immune responses that suppressed tumor growth and lung metastases after implantation of specific cancer cells.

Adjuvants further optimized through this method could reduce the problem of decreasing immunity for current vaccines and perhaps make booster vaccines unnecessary. Their use in immunotherapy to treat cancer is also highly promising.

More information: Juan Ma et al, Computer-Aided Discovery of Potent Broad-Spectrum Vaccine Adjuvants, *Angewandte Chemie International Edition* (2023). DOI: 10.1002/anie.202301059

Provided by Wiley