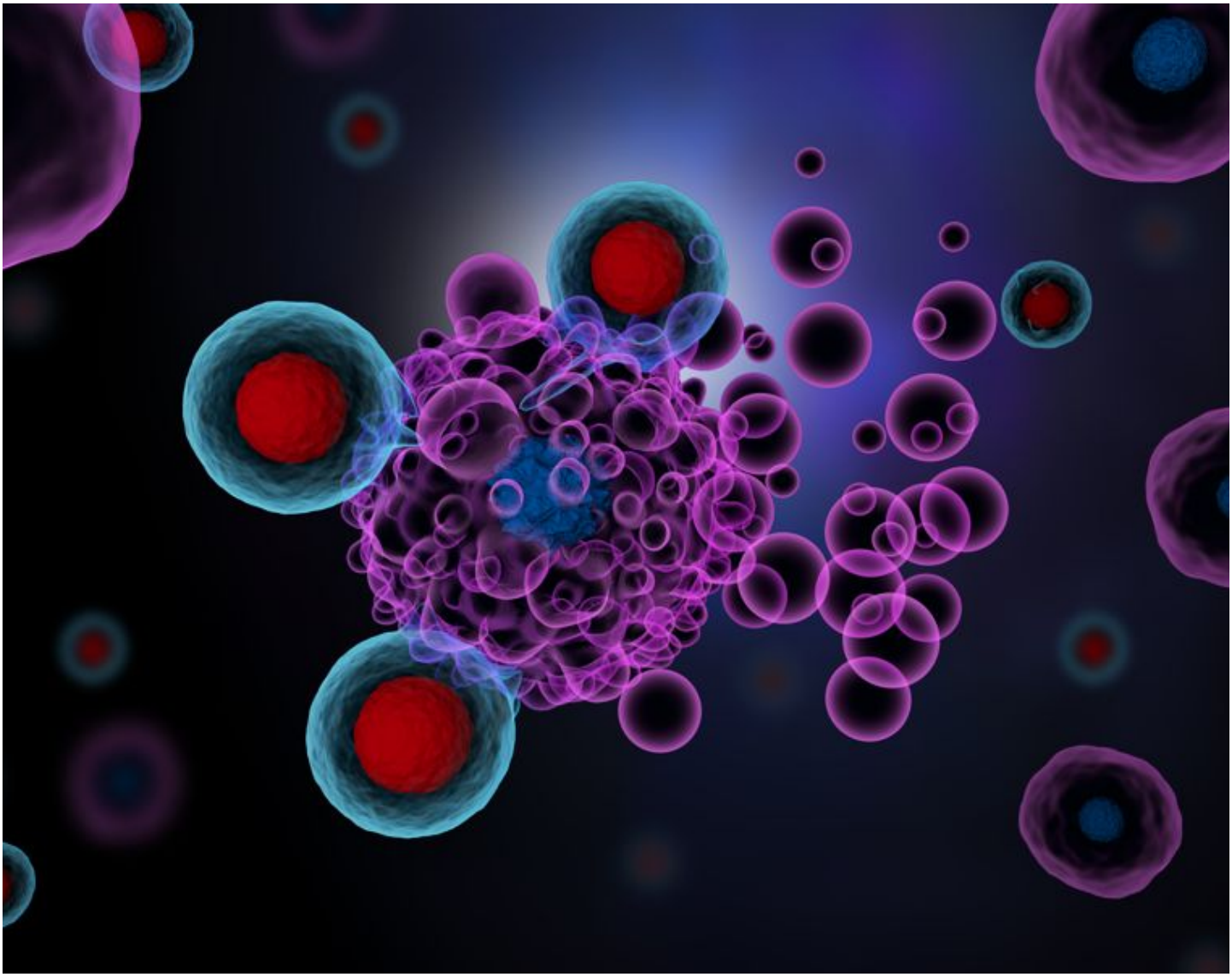
Personalized cancer vaccine prospects improve with self-assembling nanoparticles

Immunologists may have found the secret to manufacturing a personalized vaccine that effectively activates immune cells to target cancer.



T cell cells (blue/red) can be trained to attack tumour cells (purple) but the strength of that response can vary. *Credit: Meletios Verras/Getty Images*

A formula that prompts the self-assembly of consistently sized nanoparticles could contribute to personalized cancer vaccines, say its developers. The findings, which overcome a number of stubborn challenges, were published in the journal *Nature Biotechnology*.

Cancers are genetically unstable. They accumulate unique mutations that lead to the production of mutated proteins, called neoantigens, which can be recognized by the immune system as foreign.

Scientists have been looking for ways to leverage neoantigens to trigger the immune system against cancers. For example, a type of anti-cancer therapy, called checkpoint inhibitors, helps the immune system's T cells break free from cancer suppression so they can target tumour neoantigens. But for this to work, the patient's T cells need to already be 'primed' so they can recognize them. Some people don't have these primed T cells, so scientists have been investigating ways to develop vaccines that can generate neoantigen-specific T cells.

In an episode of the First Author Conversations podcast, cellular immunologist, Geoffrey Lynn, CEO of Avidea Technologies explained, "Our goal was to induce T cell responses in a greater number of patients to be able to extend the reach of immunotherapies." Lynn collaborated with colleagues in the USA, France, the Czech Republic, and the UK, to develop a platform that overcomes manufacturing and efficiency limitations in developing personalized cancer vaccines.

Tumour neoantigens can be identified from patient biopsies using DNA sequencing techniques. Scientists can then manufacture synthetic 'peptide antigens' that contain the same amino acid sequences as the original neoantigens.

Peptide antigens injected into mice induce only a minor immune response; adding an ingredient called a vaccine adjuvant to the antigen slightly improves this response.

Lynn and his colleagues developed a formula that led to a 20-fold improvement in T cell response following injection into mice. Their strategy involves making peptide antigen/adjuvant conjugates that can consistently self-assemble into a 20 nanometer-diameter nanoparticle, called SNP-7/8a.

"The benefit is that you have very consistent formulations, irrespective of the underlying peptide antigen characteristics," says Lynn. "This is a major development in particle formulation."

The secret lies in linking a small, charge-modifying peptide to the synthesized peptide neoantigen. This is then further joined to a water-repelling 'block' formed from a polymer attached to an adjuvant called toll-like receptor 7/8 agonist (TLR-7/8a). Without the charge-modifying group, the

antigen/adjuvant complexes aggregate into clunky microparticles that can cause problems during manufacturing and don't efficiently trigger immune cells. But with the charge-modifying group, the complexes self-assemble into uniformly sized nanoparticles.

The researchers found that the self-assembled nanoparticles (SNP-7/8a) formed even while using multiple types of peptide antigens in a single formula. Also, all of the peptide antigens they used loaded into nanoparticles, compared to only some in other formulas.

Following injection into mice, the particles successfully accumulated in the lymph nodes, where they were exposed to immune cells that activate T cells that can specifically recognize a tumour's neoantigens. Tests performed in macaque monkeys using different neoantigens also showed a high-quality T cell response.

Dr Lynn says the support of biotech company Genscript was part of the project's success. "We worked closely with Genscript over several years to build thousands of peptide antigens for systematically developing this technology," he says. "We even asked Genscript's peptide chemists to synthesize the most challenging, rare, charged, water-repellent, and water-soluble peptides. This allowed us to prove the versatility of the technology."

The team's promising results have secured funding to move the vaccine into clinical trials towards the end of 2020.

To learn more about this work and the reagents required, listen to the First Author Conversations podcast, with Geoffrey Lin, and explore Genscript's Neoantigen Peptide Services.
