Personalized cancer vaccines: Delivery breakthrough may provide better results

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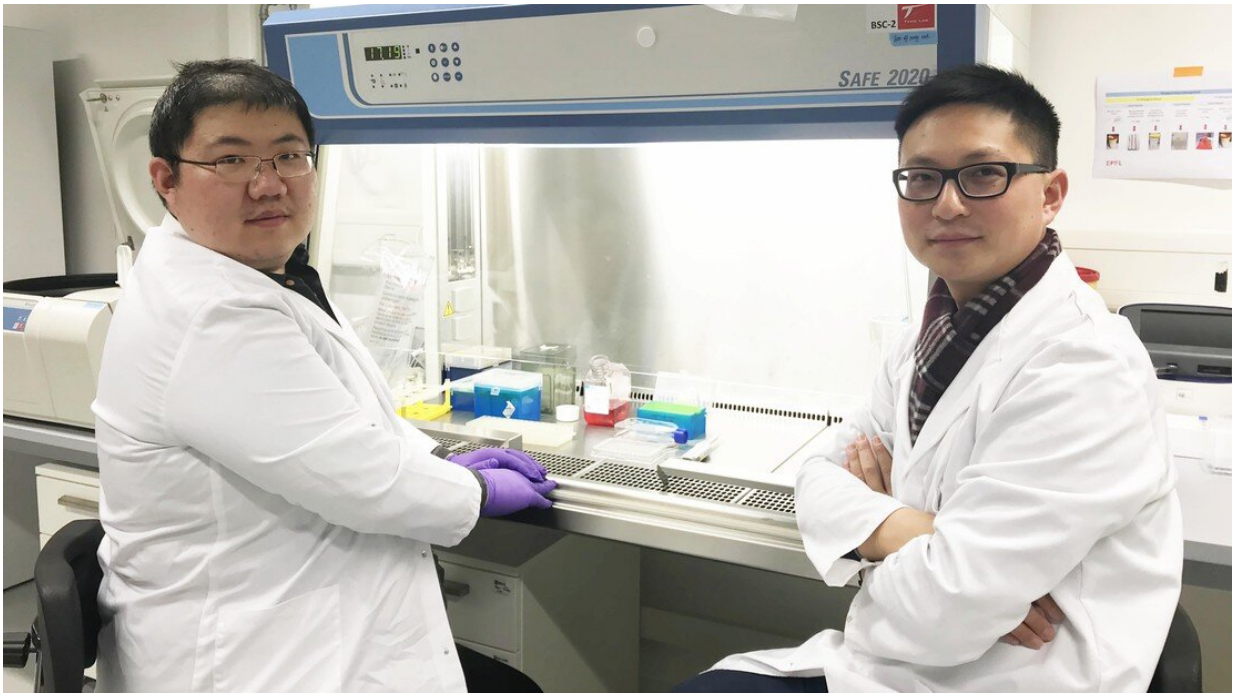


Credit: Ecole Polytechnique Federale de Lausanne

The only therapeutic cancer vaccine available on the market has so far showed very limited efficacy in clinical trials. EPFL researchers are currently working on an alternative. They have developed a platform that allows a cancer vaccine to be delivered to a precise location and stimulate the immune system in a safe way—thereby overcoming one of the two obstacles to creating an effective vaccine.

Therapeutic cancer vaccines were first developed 100 years ago and have remained broadly ineffective to date. Before tangible results can be achieved, two major obstacles must be overcome. Firstly, since tumor mutations are unique to each patient, cancer cell antigens must be targeted extremely precisely, which is very hard to achieve. Secondly, a safe system is needed to deliver the vaccine to the right location and achieve a strong and specific immune response.

Li Tang's team at EPFL's School of Engineering is coming up with a solution to the delivery problem. The researchers have used a polymerization technique called polycondensation to develop a prototype vaccine that can travel automatically to the desired location and activate immune cells there. The patented technique has been successfully tested in mice and is the topic of a paper appearing in *ACS Central Science*. Li Tang has also co-founded a startup called PepGene, with partners that are working on an algorithm for quickly and accurately predicting mutated tumor antigens. Together, the two techniques should result in a new and better cancer vaccine in the next several years.

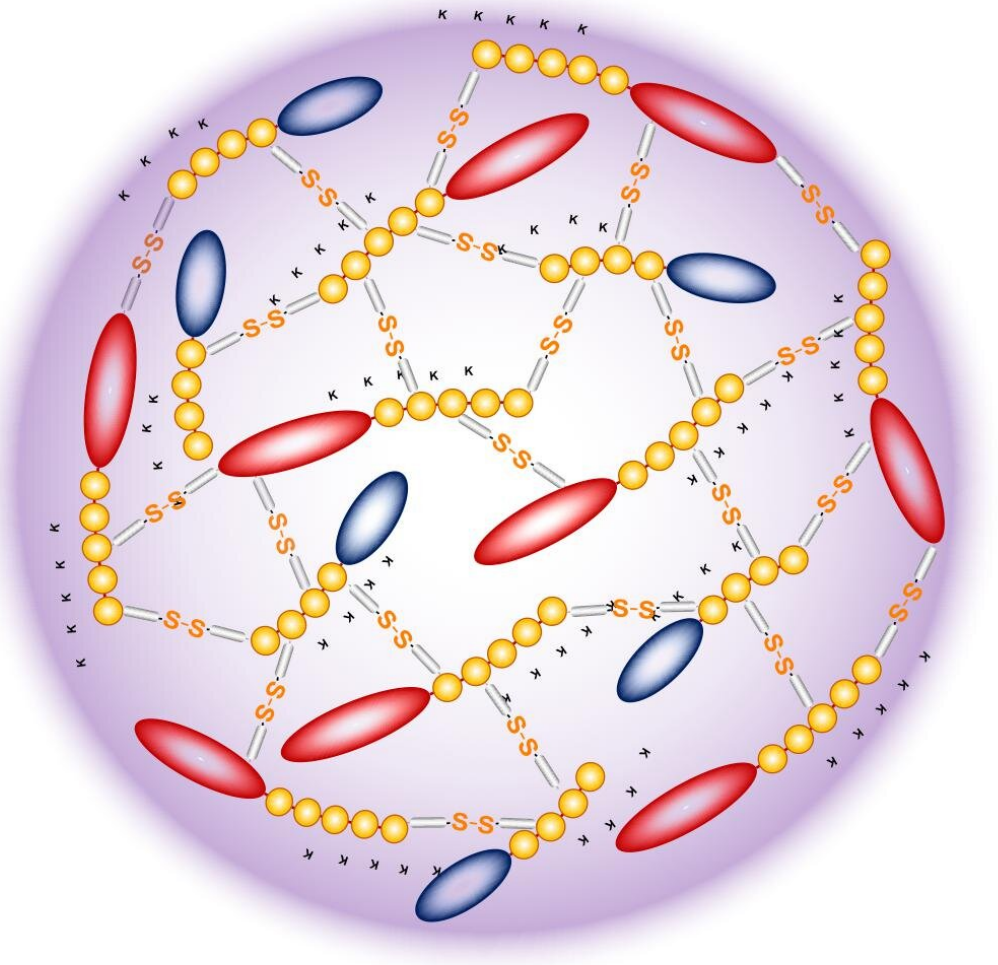
Helping the body to defend itself

Most vaccines—against measles and tetanus for example—are preventive. Healthy individuals are inoculated with weakened or inactivated parts of a virus, which prompt their immune systems to produce antibodies. This prepares the body to defend itself against future infection.

However, the aim of a therapeutic cancer vaccine is not to prevent the disease, but to help the body defend itself against a disease that is already present. "There are various sorts of immunotherapies other than vaccines, but some patients don't respond well to them. The vaccine could be combined with those immunotherapies to obtain the best possible immune response," explains Li Tang. Another advantage is that

vaccines should reduce the risk of relapse.

But how does it all work?



The vaccine is too large to be absorbed by blood vessels: It travels naturally to the lymph nodes. Credit: LBI / EPFL

Avoiding getting lost in the blood stream

Delivering a cancer vaccine to the immune system involves various stages. First, the patient is inoculated with the vaccine subcutaneously. The vaccine will thus travel to the lymph nodes, where there are lots of immune cells. Once there, the vaccine is expected to penetrate dendritic cells, which act as a kind of alert mechanism. If the vaccine stimulates them correctly, the dendritic cells present specific antigens to cancer-fighting T-cells, a process that activates and trains the T-cells to attack them.

The procedure appears simple, but is extremely hard to put into practice. Because they are very small, the components of a vaccine tend to disperse or be absorbed in the blood stream before reaching the lymph nodes.

To overcome that obstacle, Li Tang has developed a system that chemically binds the vaccine's parts together to form a larger entity. The new vaccine, named Polycondensate Neoepitope (PNE), consists of neoantigens (mutated antigens specific to the tumor to be attacked) and an adjuvant. When combined within a solvent, the components naturally bind together, forming an entity that is too large to be absorbed by blood vessels and that travels naturally to the lymph nodes.

Once inside a dendritic cell, the vaccine components separate again. This enables the dendritic cell to present the right antigens to the T-cells, causing a powerful immune response. "This new vaccine, combined with a highly advanced analysis of each patient's neoantigens, should allow cancer patients' immune systems to be activated in a personalized and safe way," says Li Tang.

The team is still perfecting the stage at which the tumor-specific antigens are detected. "This identification stage is just as vital," concludes Li Tang. "Since these neoantigens aren't present in healthy cells, accurate identification will allow us to target tumor cells very

precisely, without any toxicity in healthy tissue."

More information: Lixia Wei et al. Redox-Responsive Polycondensate Neoepitope for Enhanced Personalized Cancer Vaccine, *ACS Central Science* (2020). DOI: 10.1021/acscentsci.9b01174

Provided by Ecole Polytechnique Federale de Lausanne

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