





Press Release

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CELL ENCAPSULATION COULD ENHANCE ANTIVIRAL VACCINES

Immunotherapy techniques developed in oncology to combat cancerous cells have great potential for fighting viruses. A research team from the University Hospitals of Geneva (HUG) and the University of Geneva (UNIGE), in Switzerland, in collaboration with MaxiVAX, a spinoff of both institutions, developed an innovative technology called "cell encapsulation". Originally designed to stimulate immunity to fight cancer, the COVID-19 pandemic motivated the scientists to broaden the scope of their technology to test its effectiveness against viruses. The first results of a pre-clinical study are very encouraging and can be discovered in the journal Vaccines.

The immune system is able to identify cancer cells and fight them, just as it does against a viral or bacterial pathogen. Researchers therefore rely on this to develop vaccines against cancer. "To develop an effective vaccine, two elements are needed: a target recognized by the immune system, such as cells, proteins, DNA or RNA sequences, and an adjuvant able to effectively stimulate the immune response", says Nicolas Mach, an oncologist at the HUG Division of Oncology, and a professor at UNIGE Faculty of Medicine Department of Medicine and Translational Research Centre in Onco-Haematology, and co-author of this study. To this end, Nicolas Mach and his team, in partnership with the company MaxiVAX, developed a novel cell-based cancer vaccination using cell encapsulation technology. With the coronavirus pandemic and the need to develop effective vaccines, they decided to extend the scope of this technology to test its effectiveness against viruses.

Exciting the immune system over the long term

Cell encapsulation consists of filling a semipermeable capsule with engineered cells before implanting it subcutaneously. The cells contained in the capsule are thus kept alive without spreading in the body, unlike their secretion, which is free to diffuse through the capsule wall. This technology therefore allows the stable and sustained long-term production and release of proteins such as cytokines or antibodies.

Loaded with cells modified to secrete a substance capable of stimulating the immune system, the capsule can be used as an adjuvant cargo ship. Since the encapsulated cells survive for days, weeks or even months, they allow for prolonged exposure to the substance they secrete, here the vaccine adjuvant. This is an undeniable advantage compared to standard vaccination strategies that cannot achieve such goal.





Coronavirus as proof of concept

For this study led on mice, the research team first vaccinated healthy mice against SARS-COV-2 by injecting them with the gene coding for the Spike viral protein, which is one of the small parts of the virus recognised by the immune system. Since only a small fraction of the virus is injected, the virus, lacking its machinery, is unable to infect the body and cause COVID-19.

To efficiently boost the immune system, the scientists used the tool they developed over the last two years, a genetically modified muscle cell line secreting GM-CSF, a protein known to promote the growth of white blood cells and able, under certain conditions, to train very effectively the immune system to react against a pathogenic target. "GM-CSF is like a hormone for the white blood cells, which are just as useful for defeating tumours as they are for defeating pathogens," explains the oncologist. In order to use GM-CSF as an adjuvant to enhance the immune response against the SARS-CoV-2 Spike target, the lab-produced cells are encapsulated. The capsule, introduced subcutaneously close to the vaccination site, remains in place for several days before being removed.

Treated mice developed antibodies and lymphocytes against SARS-CoV2. The study shows that their immune response was stronger when using the encapsulation technique to produce the booster protein GM-CSF over several days than when GM-CSF was injected directly with the target. "Our results show that our cell encapsulation approach significantly enhances the excitatory effect of GM-CSF ", Nicolas Mach is pleased to say. Furthermore, when used without any GM-CSF adjuvant, the vaccine triggered an even weaker immune response.

An innovative avenue to fight vaccine-resistant viruses

"In view of the remarkable efficacy of mRNA vaccines against coronavirus, we do not consider it useful to develop clinical trials in humans for this use. However, if the efficacy of this vaccination technology is confirmed in other models of viral diseases, it could be used to fight pathogens against which we are currently lacking efficient vaccines, such as HIV or hepatitis C virus," concludes Nicolas Mach.

The capsules and the cells used in this study are certified for Phase I and II clinical trials in oncology and are produced by the HUG's clinical cell therapy centre.

This study is being conducted by the following teams :

HUG-UNIGE

Nicolas Mach, Head of the Clinical Research Unit Division of Oncology, HUG Associate Professor, Department of Medicine & Translational Research Centre in Onco-Haematology (CRTOH), UNIGE, Faculty of Medicine





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Reference

Vernet R, Charrier E, Cosset E, Fièvre S, Tomasello U, Grogg J, Mach N. Local Sustained GM-CSF Delivery by Genetically Engineered Encapsulated Cells Enhanced Both Cellular and Humoral SARS-CoV-2 Spike-Specific Immune Response in an Experimental Murine Spike DNA Vaccination Model. Vaccines. 2021; 9(5):484. https://doi.org/10.3390/vaccines9050484

Illustration



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The cargo capsule can contain up to one million protein-secreting cells (adjuvant, antibody or other). Placed under the skin, it allows the cells it contains to be nourished by the body and to be active until the implant is removed several days after vaccination.





The HUG: Care, Teaching, and leading-edge research

The Geneva University Hospitals (HUG) comprise eight public hospitals and two health clinics. Their missions include providing health care to the community in all medical specialties, contributing to training physicians and health professionals, and conducting medical research as well as finding treatments. The HUG operate as a national reference centre for influenza and emerging viral infections, as well as for liver disease in children and paediatric liver transplant. They are a WHO Collaborating Centre in five areas. In 2020, with their 13,557 staff, the HUG treated 56,761 hospital cases, 190,825 emergency admissions, and 1,074,645 outpatients, and performed 22,409 surgeries and 4,020 birth deliveries. The HUG ensure the training of 1,093 physicians, 2,760 interns and 200 apprentices. They collaborate closely with the Faculty of Medicine of the University of Geneva, the WHO, CHUV, EPFL, CERN and other actors in the Lemanic Health Valley on a number of training and research projects. The HUG have an annual budget of 2.14 billion Swiss francs.

More information on :

- HUG: <u>www.hug.ch</u> <u>presse-hug@hcuge.ch</u>
- Activity report, HUG at a Glance, and 2015-2020 Strategic Plan: <u>https://panorama.hug.ch/ et publications-hug</u>

About the University of Geneva

The University of Geneva, Switzerland, was founded in 1559 by Jean Calvin and Théodore de Bèze and ranks amongst the top 60 best universities in the world. It enjoys worldwide recognition and develops an ever-strengthening international network. The University of Geneva welcomes about 17'000 students in its nine faculties teaching Sciences, Medicine, Humanities, Economics and Management, Social Sciences, Law, Theology, Psychology and Educational Sciences, as well as Translation and Interpreting. The University of Geneva fulfils three missions: education, research and knowledge-sharing. It is a member of the League of European Research Universities since 2002 and is a founding partner of Campus Biotech, the life science hub for the Geneva Lake region. www.unige.ch