

CanVirex AG

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Two sides of the same coin: Measles-vectored drugs for cancer immunotherapy and vaccines

The CanVirex platform deploys the oncolytic properties of recombinant measles vectors for innovative cancer treatments. In addition it has now provided a novel COVID-19 vaccine candidate that is approaching clinical trials.

CanVirex was founded in 2017, based on the research of medical oncologist Guy Ungerechts from the Heidelberg University Hospital and the German Cancer Research Center (<https://www.dkfz.de/en/virotherapie/index.php>) who is a pioneer in developing oncolytic measles viruses.

Historically, numerous case reports have described 'spontaneous' tumor regressions after a natural virus infection or immunization. This discovery led to the development of so-called oncolytic viruses for cancer therapy, which are today emerging as a promising treatment option in oncology. The first oncolytic virus therapeutic was approved to treat advanced melanoma patients in 2015.

Although oncolytic viruses can infect and kill cancer cells, often this is not sufficient to eradicate a tumor. "To mount a clinically relevant anti-tumor response, CanVirex 'arms' the virus with immunomodulatory payloads (transgenes) that activate the patients' immune system," said Ungerechts. 'Arming' means that CanVirex's measles viruses are engineered to encode for different immunotherapeutics (Fig. 1). Such engineered vectors can be considered a combination therapy of oncolytic viruses with immunotherapeutics. The approach has the advantage of direct delivery of immunotherapeutics to the tumor site and concomitant immune activation, both of which are essential for safety and efficacy.

CanVirex established from a partnership between Ungerechts and Werner Tschollar, an executive with more than 25 years of experience in the pharmaceutical, biotechnology and finance industries and CanVirex's chairman of the board of directors. The company developed as a spin-off from Heidelberg University Hospital with which it has a strategic collaboration agreement for research and development. "This offers us a very rich and unique infrastructure for swift clinical translation of our most promising drug candidates," Ungerechts explained.

So far CanVirex has created measles viruses encoding four different classes of immune modulators that recruit and activate immune effector cells: (1) tumor-associated antigens, (2) cytokines, such as interleukin-12, (3) immune checkpoint inhibitors, and (4) bispecific T cell engagers. The oncolytic virus approach can be tissue agnostic, although the company's oncology pipeline is focused on advanced gastrointestinal tumors without surgical options.

The CanVirex platform is based on the Schwarz strain, commonly used in measles vaccines since the 1970s. It has been administered to billions of people and is one of the safest and most protective vaccines, producing long-lasting anti-measles immunity. In collaboration with the Paul-Ehrlich-Institute

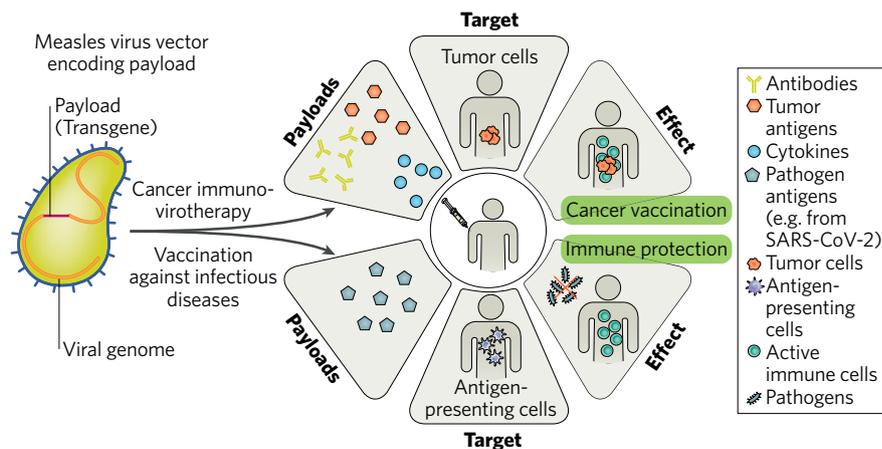


Fig. 1 | CanVirex's platform as a replicating delivery tool. The measles vectors are 'armed' with different immunomodulatory payloads (transgenes) that activate the immune system. For cancer therapy, the transgenes encode immunotherapeutics such as immune checkpoint inhibitors. For vaccination against infectious diseases, the transgenes encode pathogen-specific antigens. Administered vectors infect target cells and induce immunological mechanisms that lead to anti-tumor or pathogen-specific immune responses.

and the German Center for Infection Research, the company is now using its immuno-oncology technology to develop a measles-vectored COVID-19 vaccine by encoding a SARS-CoV-2 surface protein instead of an immunotherapeutic.

Targeting COVID-19

"If we can vaccinate against cancer, we can also vaccinate against other diseases like COVID-19," said Ungerechts. The measles-vectored COVID-19 vaccine induces robust immunity in relevant animal models. Induction of long-lasting immunity requires proper activation of both B cells and T cells, that generate protective humoral and cellular immunity and immunological memory. "You need to have a specific and balanced multifunctional immune response, which is a sequential combination of Th1-mediated cellular response in the early phase of infection and a shift towards a humoral response in the recovering phase," explained Ungerechts, "and this is what our vaccine platform can provide". Preclinical validation of the measles-vectored COVID-19 vaccine has been completed and has shown to induce the desired immune response in animals after immunization.

Many vaccines currently in use contain inactivated 'killed' pathogens or pathogen subunits which are unable to replicate inside cells, leading to suboptimal immune activation. Replicating viral vaccines generally trigger more immune effector mechanisms that lead to more protective and

longer-lasting immunity. By using measles vectors for its COVID-19 vaccination, CanVirex's approach has the advantage of eliminating the risks associated with a live-attenuated coronavirus, whilst maintaining a similar type of immune activation.

Partnering aspirations

CanVirex is gearing up to begin clinical trials for its COVID-19 vaccine in 2021. The company is still open to additional investments from private investors and/or family offices, in order to accelerate its development programs. In parallel, CanVirex is seeking an industry partner with the necessary marketing, sales and distribution capabilities for a global roll-out to take its pipeline through clinical trials and marketing authorization. The company is currently in negotiations with several international pharma companies with franchises in the oncology and vaccine markets.

"We are excited by the commercial opportunities and the almost unlimited versatility of CanVirex's platform technology and are confident that we can make an impact in fighting both cancer and COVID-19," said Tschollar.

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