RegaVax(Corona)

a potent COVID-19 vaccine candidate

Our COVID-19 vaccine candidate is a self-replicating vector vaccine:

- Live-attenuated vectored vaccine (LAV)
- YF17D based, a well-studied vaccine vector
- Aim: single dose administration
- Likely long-lasting protection
- Simple needle administration (i.m., s.c.)
- Cell-culture based standard production process

The problem and our approach

An emergency response to the rapidly evolving COVID-19 pandemic urges the development of potent and fast-acting vaccines to contain SARS-CoV-2 (2019-nCoV), stop transmission and alleviate human suffering. Generally, live-attenuated vaccines (**LAV**), such as the yellow fever virus vaccine YF17D, display a high potency (>95% seroconversion in vaccinated individuals, meaning the presence of detectable antibodies in the blood against the virus, normally giving life-long protection). This protection is reached within a very short time to benefit (5-10 days).
However, empirically derived (classical) LAVs do not lend themselves for rapid and **rational development of novel vaccines on demand**, e.g. in case of sudden (re-)emergence of pathogens such as Ebola, Zika and recently SARS-CoV-2. Hence, novel **vaccine platform technologies**, ideally providing the same potency as LAVs, and allowing for a rapid vaccine design against newly arising pathogens, are urgently awaited for current and future outbreak control.

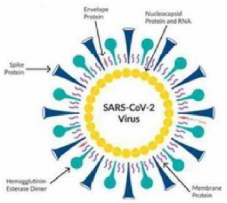
Vaccine platform technology

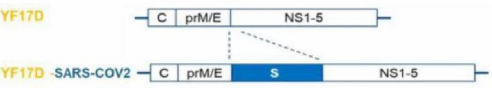
At the KU Leuven, the team of Prof [redacted] (Virology, Antiviral Drug & Vaccine Research), developed a platform technology to design and produce live-attenuated recombinant vaccines vectored by the original yellow fever (YF17D) vaccine. As such the YF vaccine serves as a vehicle (i.e. vector) for the foreign antigen (i.e. part to which immune response/antibodies are developed) to bring it inside the vaccinated individual and trigger an immune response towards this antigen. Our plug-and-play technology has been validated using a series of targets and model antigens such as **rabies** [PMID: 32089431], **Zika, Ebola and Lassa** (inserted in the YF backbone). All constructs proved highly immunogenic (triggering antibodies towards the respective pathogen) and safe in several animal models (mice, hamsters). The rabies vaccine candidate efficiently protects mice against lethal challenge with both the rabies and yellow fever virus *(still to be explored for the Ebola and Lassa vaccine candidates)*. The Zika virus vaccine candidate fully protects against lethal Zika and yellow fever infection in a mouse model [PMID: 32116148]. Moreover, it completely prevented congenital malformations in mice following direct intraplacental challenge of pregnant mothers [PMID: 30564463]. It also results rapidly in high titers of neutralizing antibodies in non-human primates and protection from Zika virus challenge.

This platform is now employed to develop a vaccine candidate against SARS-CoV-2.

RegaVax(Corona): YF17D/SARS-CoV-2

The examples above illustrate that our platform technology allows to **engineer vaccine candidates against viruses within weeks** following identification of a new antigen. This claim was put to the test with the emergence of SARS-CoV-2 as causative agent of COVID-19. Soon after the genetic code of this novel pathogen was available, we cloned (variants of) the Spike protein (S) of the SARS-CoV-2 into the YF17D backbone following a pre-established procedure.

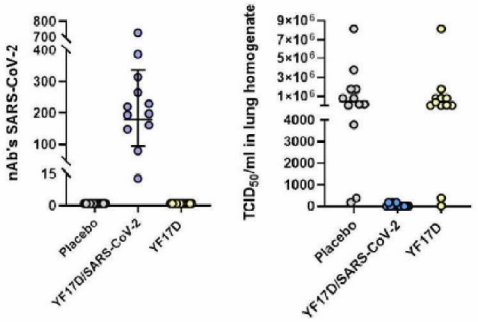




The genetic sequence of the spike (S) protein (blue) of SARS-CoV-2 is inserted in the genetic sequence of the yellow fever vaccine YF17D.

Several constructs were engineered that replicate in cell cultures and that produce the SARS-CoV-2 Spike (S). From the 7 vaccine candidates engineered, two proved most efficient in inducing an immune response in mice. Next, the efficacy of the vaccine candidate against virus infection had to be studied. Since mice did not appear to be a good infection model, we established a robust hamster infection model.

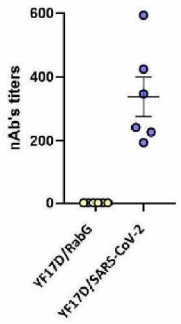
Intranasal infection of hamsters with SARS-CoV-2 results in high viral loads in lungs and severe lung pathology. Disease evolution is monitored by µCT of the lungs under high biosafety level 3+ (BSL3+) conditions. This model allows to evaluate immunogenicity (triggering of an immune response) and efficacy (protection from viral infection) of the vaccine candidates.



Efficient protection from SARS-CoV-2 infection by RegaVax(Corona) in hamsters. (A) Neutralizing antibodies in hamsters at d21 post vaccination (blue) in comparison to Placebo (grey) vaccinated animals and YF17D (commercial YF vaccine); (B) No detection of infectious virus in vaccinated hamsters after aggressive intranasal SARS-CoV-2 challenge.

Our vaccine candidate induces consistently SARS-CoV-2 specific IgG as well as neutralizing Ab (nAb) in vaccinated hamsters. Moreover, it confers spectacular protection against aggressive infection. No virus (RT-qPCR, virus titration) could be detected in the lungs (~500.000 fold reduction). The lungs of vaccinated hamsters that had been infected were near to normal, this in marked contrast to the control vaccinated animals (two independent experiments).

A vaccine-challenge study in a non-human primate model is currently (June 2020) ongoing (at www.bprc.nl). Two doses (10^5 PFU each) of RegaVax(Corona) are given (n=6) at day 0 and day 7 via subcutaneous injection. Interim data reveal that high titers neutralizing antibodies are already observed 14 days after the first dose. A control vaccine candidate, carrying non SARS-CoV-2 sequences, but those of the rabies virus (YF17D/RabG), does not result in antibody titers.



nAb titers against SARS-CoV-2 in non-human primates at day 14 after vaccination.

Our vaccine candidate outperforms other vaccine candidates studied in this model, i.e. the Sinovax candidate (titers ~50), the Oxford vaccine (titers ~20) and the Harvard vaccine (titers ~70) (*Gao et al. Science 2020; Van Doremalen et al. bioRxiv 2020.05.13.093195; Yu et al., Science 10.1126*).

The way forward

Our vaccine candidate holds great promise to contribute to the global effort to combat the pandemic. We have stipulated the path forward to (pre-)clinical development (manufacturing, regulatory, etc) with the aim to fast track for Phase 1/2a clinical testing in human volunteers as early as in Q4/2020-Q1/2021 in UZ Leuven. We identified a competent CDMO (contract development and manufacturing organization) for the manufacturing of our LAV vaccine at high scale. Such CDMO will develop high-quality (GMP) material for pre-clinical safety and toxicity studies and phase I clinical trials. We are in contact with the regulatory authorities (FAGG and PEI).
We are now scouting for additional funding to enable the further fast-track development of this promising candidate.

WHO WE ARE

Our laboratory at the **Rega Institute for Medical Research**, **KU Leuven**, Belgium, has a long-stancing expertise in virology.

- We developed a unique proprietary **vaccine platform technology** [WO/2014/174078A1].
- We collaborate intensively with the **University Hospital** on **COVID-19**, including for access to patients' material.
- Leading **immunology background and vaccine profiling** pipeline.
- **In-house bioanalytical service facility TPVC** (Translational Platform Virology & Chemotherapy).
- Unique state-of-the-art facilities to manipulate **BSL3+ pathogens.**
- **Relevant animal models** available in state of the art high-containment BSL3+ laboratories).
- **In-house expert with >30 years expertise** in vaccine development at GSK and Pfizer.
- Extensive **network of experts and consultants**, including through **KU Leuven Research & Development**
- Contact with relevant authorities and regulatory agencies **FAGG and others.**
- **Proven track record** in **antiviral drug development**, including several molecules discovered by our team and brought to clinical phase in collaboration with the pharmaceutical industry.

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