Grant agreement Start dete: 01/04/20 End Date: 31/03/22	
Project Title	OPENCORONA
WP number, deliverable number, and Title	WP1, D1.1, All vaccine candidates, proteins and produced and delivered
Responsible partner name and contact	Partner number: 1 Organisation: KI Name: Matti Sällberg Email: matti.sallberg@ki.se
Nature R-Report P-Prototype D-Demonstrator =-Other	R
Dissemination level **PU**-public **PP**-restricted to otherprogramme participants RE-restricted to a group of partners **CO**-only for consortium members	PU
Delivery Month Planned	M3-July 2020
Actual delivery date (dd/mm/yy)	July 10, 2020

Description of deliverable

- **COMPLETED**

- Twelve of the designed genes have now been synthetically generated by Genescript and delivered to us. All genes and have been cloned into pVAX. We are still waiting for five out of six proteins to be produced in E. Coli. We have received the N protein and this has been extensively used in setting up COVID-19 serology and in research. Larger batches of 100 mg have beed ordered. The N plasmid and N protein has already been evaluated for immunogenicity in rabbits and mice. This has now been accepted for publication in the Journal of Virology. Large studies in mice have now been initiated using the DNA vaccines. We have initiated a collaboration with Professor Sophia Hober at the Royal Institute of Technology, Stockholm to obtain eucariotically expressed Spike and RBD proteins to be used in detection of antibodies and T cells in animals and humans. The genes gave all been sent to partner 3 for analysis of activation of innate responses.

- **STILL ONGOING**

- We are still waiting for delivery of five E. coli expressed proteins.

- **PUBLICATIONS**

- **Ahlén G, Frelin L, Nekoyan N, Weber F, Höglund U, Larsson O, Westman M, Tuvesson O, Gidlund EK, Cadossi M, Appelberg S, Mirazimi A, and Sallberg M.** 2020. The SARS-CoV-2 N protein is a good component in a vaccine. J Virol (Accepted)

- **Varnaite R, García M, Glans H , Maleki KT, Sandberg JT, Tynell J, Christ W, Lagerqvist N, Asgeirsson H, Ljunggren HG, Ahlén G, Frelin L, Sällberg M, Blom K, Klingström J, Gredmark-Russ S**. 2020. Expansion of SARS-CoV-2-specific Antibody-secreting Cells 1 and Generation of Neutralizing Antibodies in Hospitalized COVID-19 Patients (Submitted to J Immunol).

Grant agreement **Start date: 01/04/20** **End Date: 31/03/22**	
Project Title	OPENCORONA
WP number, deliverable number, and Title	WP1, deliverable 1.2. Evaluation of immunogenicity of vaccine candidates
Responsible partner name and contact	Partner number: 1 Organisation: KI Name: Matti Sällberg Email: matti.sallberg@ki.se
Nature R-Report P-Prototype D-Demonstrator O=-Other	Report
Dissemination level **PU**-public **PP**-restricted to otherprogramme participants RE-restricted to a group of partners **CO**-only for consortium members	PU
Delivery Month Planned	M6, September 2020
Actual delivery date (dd/mm/yy)	13 November 2020

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101003666

Description of deliverable

- **COMPLETED**

- The vaccine candidates from D1.1 have all been produced in house in quantities and of purity sufficient for immunization of rabbits and mice. Both C57BL/6 and BALB/c mice have been used. Of the original candidates, several were found to induce strong T cell response, in particular OC2 that contains the RBD, the M and the N protein. However, no detectable neutralizing antibodies were induced by OC2 whereby two modified genes were generated based on OC2, termed OC2.2 and OC2.3. The OC2.3 was found to induce both T cells to all proteins in the construct as well as high levels of antibodies to S and RBD that could neutralise SARS-CoV-2 in vitro. The OC2.3 was therefore selected as the vaccine candidate and has been forwarded to Cobra Biologics for production according to GMP.

- **STILL ONGOING**

- Challenge studies in hACE2 mice and ferrets has been initiated and ongoing. SA macaque study is in the planning stage. Preliminary data from the ferret study show that the OC2 and OC12 (N) constructs induce T cell responses that can limit virus replication. This suggests that T cells alone can limit SARS-CoV-2 replication. The ferret and the hACE2 mouse studies will be completed around January 2021. The macaque study is planned to be completed in January or February 2021.

- **PUBLICATIONS**

- **Ahlén G, Frelin L, Nekoyan N, Weber F, Höglund U, Larsson O, Westman M, Tuvesson O, Gidlund EK, Cadossi M, Appelberg S, Mirazimi A, and Sallberg M.** 2020. The SARS-CoV-2 N protein is a good component in a vaccine. J Virology 94(18):e01279-20.

- **Varnaite R, García M, Glans H , Maleki KT, Sandberg JT, Tynell J, Christ W, Lagerqvist N, Asgeirsson H, Ljunggren HG, Ahlén G, Frelin L, Sällberg M, Blom K, Klingström J, Gredmark-Russ S**. 2020. Expansion of SARS-CoV-2-specific Antibody-secreting Cells 1 and Generation of Neutralizing Antibodies in Hospitalized COVID-19 Patients. J Immunology 205(9):2437-2446.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101003666

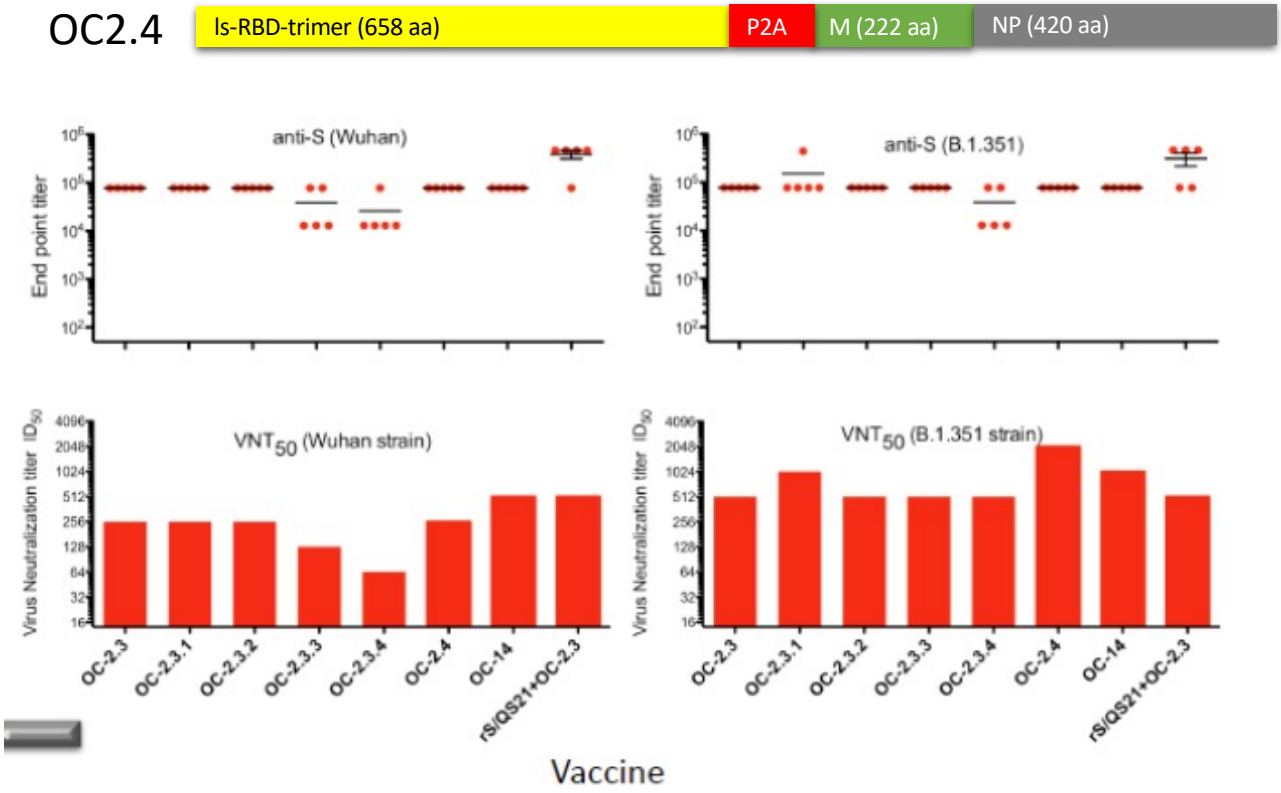
GA 101003666 Start date: 01/04/20 End Date: 31/03/22	
Project Title	OPENCORONA
WP number, deliverable number, and Title	WP 1 D1.3 : Selection of the best vaccine candidate for GMP and tox studies
Responsible partner name and contact	Partner number: 1 Organisation: KI Name: Matti Sällberg Email: matti.sallberg@ki.se
Nature R-Report P-Prototype D-Demonstrator O=-Other	**R**
Dissemination level **PU**-public **PP**-restricted to otherprogramme participants RE-restricted to a group of partners **CO**-only for consortium members	**PU**
Delivery Month Planned	9 (31/12/20)
Actual delivery date (dd/mm/yy)	29/5/2021

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101003666

Description of deliverable

- **COMPLETED**

During the first year of the project a total of 24 different vaccine candidates has been generated, produced and evaluated both *in vitro* and *in vivo*. Studies performed by KI, FoHM, JLU, IGEA and Adlego identified already in October 2020 one potential vaccine candidate that induced strong antibody, T cell responses as determined in mice, rabbits and ferrets. The studies revealed leading up to the vaccine showed that although T cells alone can help to control the SARS-CoV-2 replication, the simultaneous presence of neutralizing antibodies (NAbs) are vital for an optimal protection. This gene consists of a highly modified version of the receptor binding domain (RBD) of Spike, the Nucleoprotein (N) and the Membrane (M) protein. The selected plasmid (OC2.3) was produced by Cobra (HQ DNA) for toxicological evaluation. In parallel with this work mutant strains of SARS-CoV-2 started to appear and we realized that this might impact on the spread of the virus and efficacy of the vaccines. The project therefore decided to adapt the vaccine to the most prominent mutations. This revealed a clear benefit with our vaccine design which is that we can include several unique repeats of the RBD sequence and thereby include multiple mutant RBD sequences in the same vaccine construct. This updated vaccine construct (OC2.4) has now been evaluated *in vivo* and to induce very high levels of neutralizing antibodies against both Wuhan and the B.1.351 strains. On May 7, 2021 the C2.4 plasmid was delivered to Cobra and HQ plasmid production was initiated.



OC vaccine candidates immunogenicity in BALB/c mice. Antibody responses (upper) after three immunizations determined using S proteins from the Wuhan and B.1.351 strains. Neutralizing antibody responses (lower) were determined using Wuhan and B.1.351 strain virus.

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