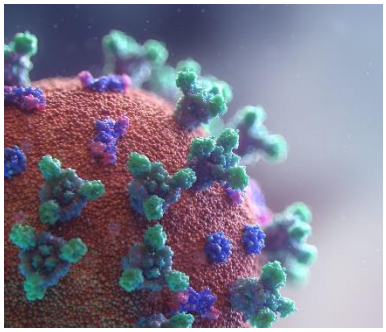
transactiva
MOLECULAR FARMING

Università di Roma Tor Vergata
DIPARTIMENTO DI BIOMEDICINA E PREVENZIONE

A "GREEN" PLATFORM BASED ON PLANT MOLECULAR FARMING FOR THE anti-SARS-CoV-2 VACCINE

BACKGROUND



COVID-19 pandemic is the most severe health and economic emergency since the era of HIV and the crisis of '29. It is due to a human infection from **SARS-CoV-2**, a β-coronavirus for which bat is the natural host. As of May 22, 2020, **over 5 million people have been infected worldwide** with 332.979 deaths. The infection mainly occurs by direct contact and droplet inspiration. At present there are **no specific treatments** (vaccine or anti-virus antibodies) and available therapies are primarily aimed at maintaining respiratory function and reducing inflammation. The recurrence of severe coronavirus epidemics (SARS, MERS) in the last 20 years makes it urgent to develop a platform for **rapid production** of **effective vaccines**. **Plant Molecular Farming** technology is suitable for this problem: plant derived HBV vaccine has been licensed, while influenza vaccine is currently under clinical trial. Moreover, monoclonal antibodies rapidly produced in tobacco leaves were successfully used against Ebola virus.

CRITICAL NEED

The **lack of a human immunological defense** against an **unknown virus**, especially a virus equipped with a highly effective and adaptable cell penetration system, requires a **joint scientific and industrial effort**. The current world population amounts to almost 8 billion people, who are theoretically vulnerable to the virus. No single pharmaceutical company or isolated research program has the means to effectively respond to the pandemic. Only a strategy that combines economic and scientific resources can give an answer to the planetary scale of the crisis. This strategy can be summarized as:

more **companies**
more **projects**
more **variation**

more **vaccines**
more chance of **success**
more **health**

OBJECTIVES

The principal goals of the project are:

- to **build a "green" platform**, based on Plant Molecular Farming, for rapid and effective anti-viral production;
- to **produce** in a reasonably short time (18 months) an **anti-COVID-19 vaccine**, based on immunologically reactive peptide sequences identified by specific immunoglobulins from plasma of infected patients.

SYNERGY BETWEEN THE RESEARCH GROUPS

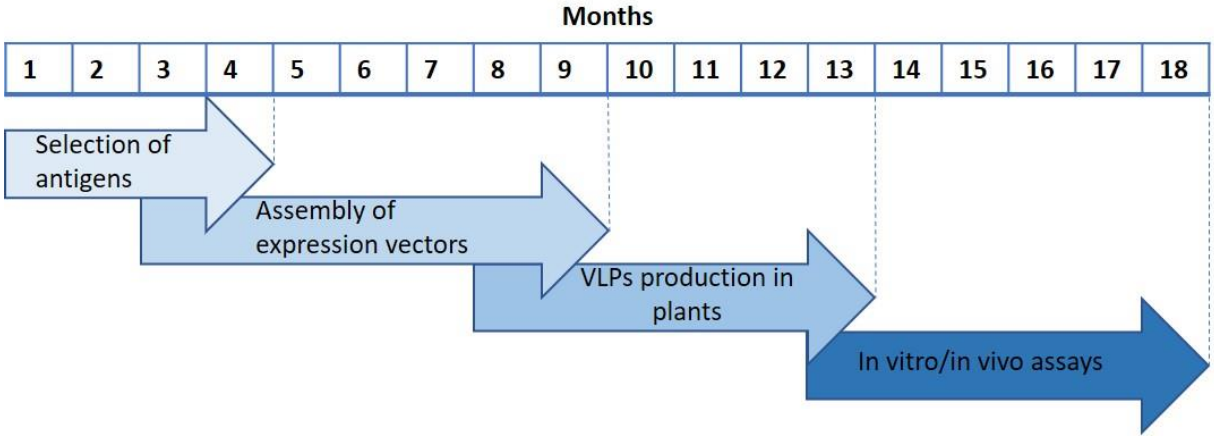
The Department of Biomedicine and Prevention of Tor Vergata University (**UNITOV**) and **Transactiva** Srl have the scientific and technological skills to positively tackle the challenges of this project. The **UNITOV** has the **genetic and immunological competences** to identify and test *in vitro* the candidate peptides to be used in building the appropriate vaccine. At the same time, **Transactiva** Srl has a **long-standing experience in developing "green" platforms** to produce human drugs (enzymes and monoclonal antibodies). It has recently adopted a platform based on a special tobacco species, particularly suitable for recombinant vaccine production. The **synergy of the two teams** will thus lead to the development of an **anti-COVID-19 vaccine** based on epitopes that have already been shown to induce an appropriate immune response in patients who have recovered from COVID-19.

PRELIMINARY DATA

Plants have already been extensively used as bioreactors to produce complex therapeutic molecules due to numerous advantages, such as the **low operating costs**, the ease of **industrial upscaling** and, above all, both the **high quality** and **bioequivalence** of the drug, and the remarkable level of **biosecurity** (absence of microorganism residues and human pathogenic viruses). The plant-based manufacturing system that will be established within this project will allow for the delivery of any new heterologous protein in a matter of a **few weeks**, a very favorable time scale for the development of a potential vaccine to face a global pandemic.

BRIEF DESCRIPTION AND TIME FRAME

The **immuno-informatics** expertise of the UNITOV group will be exploited to identify and characterize a series of **potential epitopes** present on the spike protein. Their **immunological reactivity** will be computationally predicted on the basis of their sequence and structure (mo. 1-4).
Each of these peptides will then be produced in the high-efficiency **plant expression system** set up by Transactiva as part of a **recombinant Virus-Like Particle (VLP) vaccine** (mo. 3-13). Eventually, ***in vitro and in vivo* assays** will be performed to assess the immunological effectiveness of the putative anti-SARS-CoV-2 vaccines (mo. 13-18).



INDUSTRIAL SCALE UP

The number of **doses** that can be delivered by a plant facility depends on many factors, all of which can vary substantially: protein yield per surface unit, amount of protein in a dose, use of adjuvants in the formulation among others, but it is possible to make an **estimate** based on the average parameters, as reported in the literature:

- **Protein yield**: 200 mg/kg of fresh leaf tissue
- **VLP amount**: 30 µg/dose
- **Biomass yield**: 2 kg/m^2/6 weeks

Considering a facility with only a 2500 m^2 surface entirely dedicated to the production of a single vaccine, it is theoretically possible to deliver **67 million doses every three months**.

CONTACTS

Department of Biomedicine and Prevention
University of Tor Vergata, Roma
Prof. Giuseppe Novelli
gnovelli@me.com

Transactiva Srl
"Luigi Danieli" Science and Technology Park, Udine
Dr. Bruno Bembi
bbembi@transactiva.it