InSilicoVACCINE: a suite of computational models for vaccine design and trial simulation

Chiara Nicolò[1], Fianne Sips[2], Francesco Pappalardo[3,4], Giulia Russo[3,4], Roberta Bursi[2]

[1] InSilicoTrials Technologies S.p.A, Riva Grumula 2, 34123, Trieste, Italy
[2] InSilicoTrials Technologies B.V., Bruistensingel 130, 5232 AC s' Hertogenbosch, The Netherlands
[3] Department of Drug and Health Sciences, University of Catania, Catania, Italy
[4] Mimesis Srl, Catania, Italy

Background

The development of novel vaccines is a technically demanding and expensive process. In recent years, a wide variety of immunoinformatics approaches have been introduced to design effective and stable vectors. However, although these methods are useful to accelerate and reduce costs of vaccine design during the nonclinical development stage, they cannot guide vaccine development throughout the clinical phase.

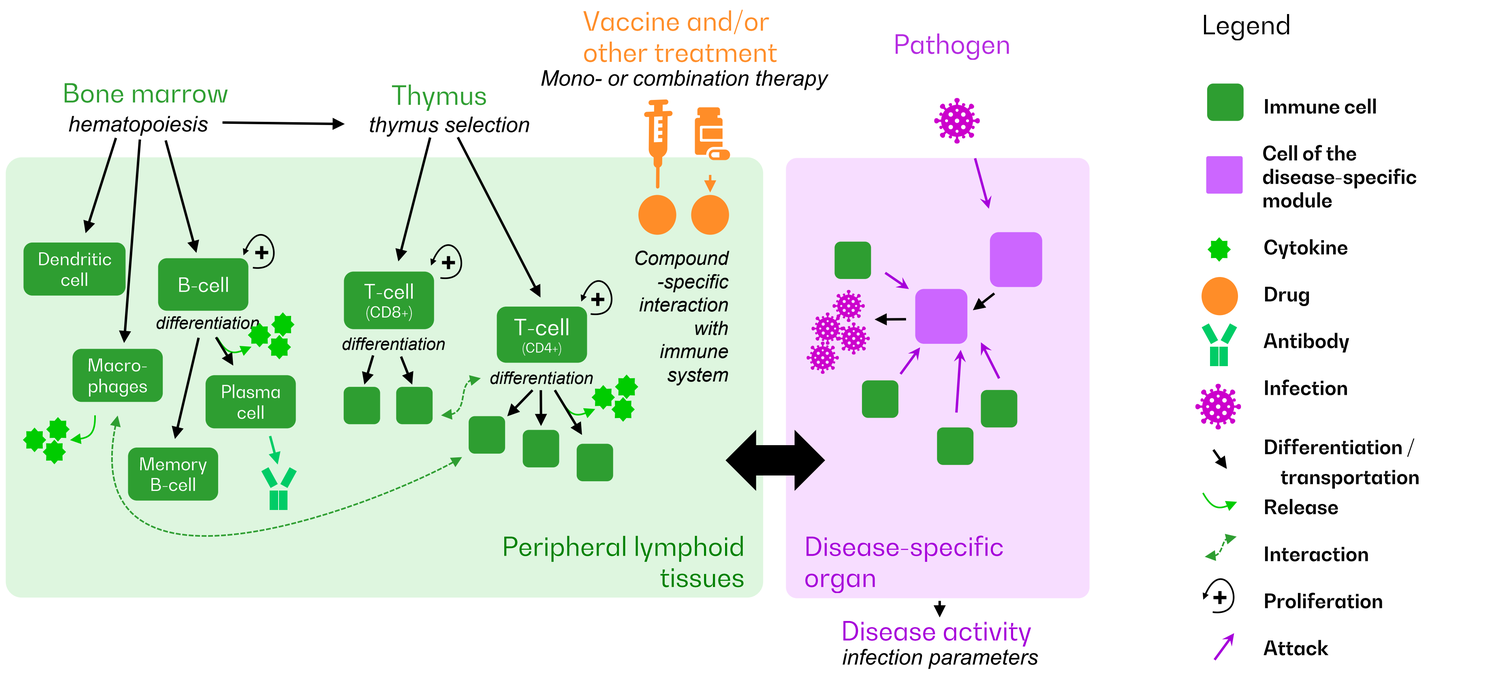
To support (the transition to) the clinical phase, we have combined immunoinformatics tools with a series of mechanistic disease models in the InSilicoVACCINE suite. These mechanistic computational models translate the information gathered from immunoinformatics approaches to clinical level outcomes and in silico clinical trials. Here, we demonstrate the multifaceted utility of the InSilicoVACCINE suite, showing applications in three different infectious diseases and three different vaccine development challenges.

Virtual Patients based on an Agent-Based model

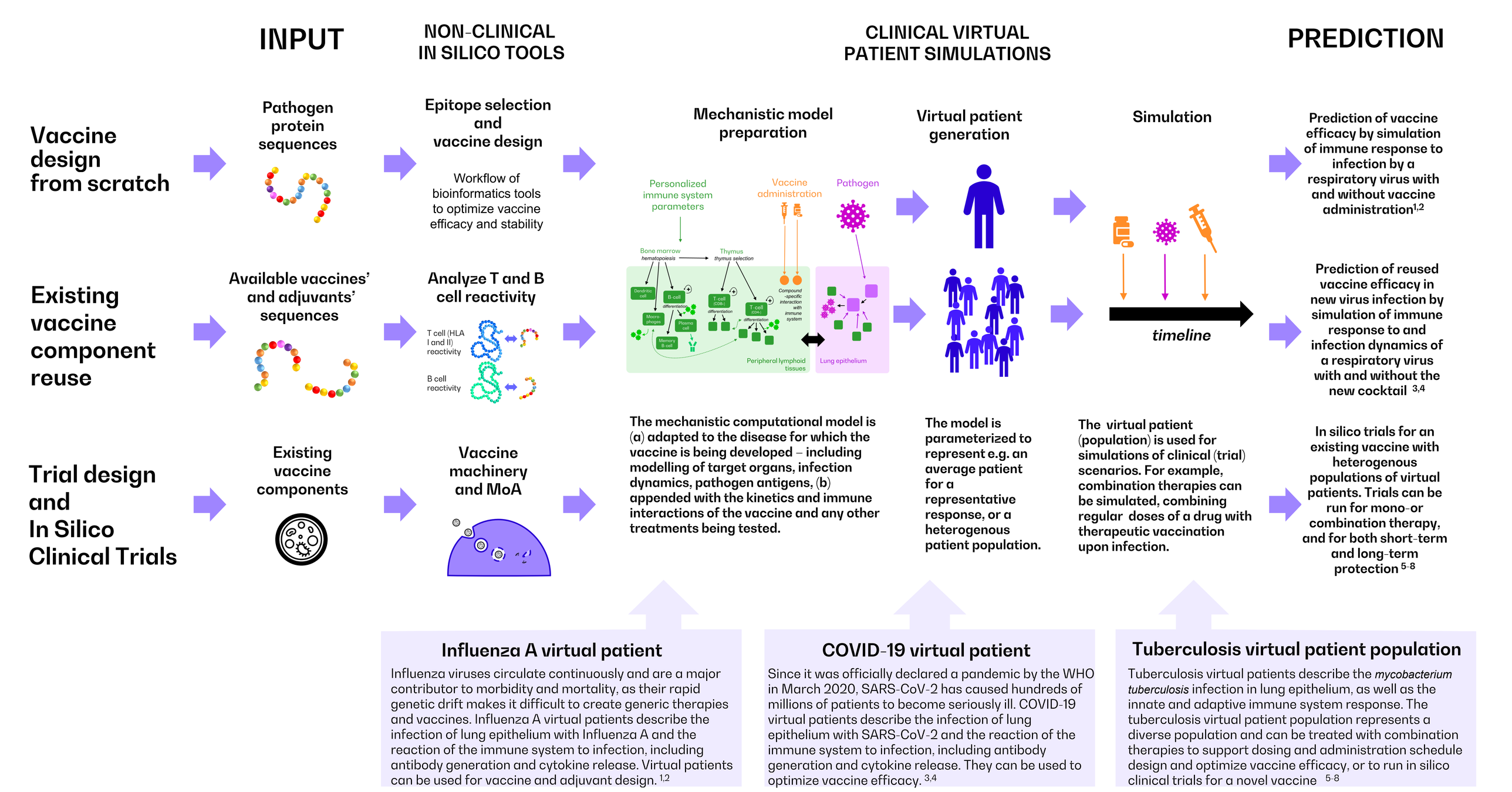
The mechanistic infectious disease models were created by building upon the agent-based universal immune system simulator (UISS) framework (Figure 1).

As a result, each infectious disease simulator is an agent-based model that describes in detail disease mechanisms and their interactions with the immune system. Disease models for influenza A[1,2], COVID-19[3,4] and tuberculosis[5-8] have been developed.

These disease models describe both disease progression and immune system memory, and therefore they are broadly applicable for vaccine development challenges. To represent the range of possible applications, the models have been applied to de novo vaccine design[1], adjuvant identification and optimization[2], vaccine and adjuvant repurposing for a new virus[3,4], and clinical trial simulations[5-8]. In each application, immunoinformatics tools provide important parameters which are then coupled to the dynamic disease model to make predictions of patients' clinical response.



Vaccine Design supported by virtual populations



Influenza A virtual patient

Influenza viruses circulate continuously and are a major contributor to morbidity and mortality, as their rapid genetic drift makes it difficult to create generic therapies and vaccines. Influenza A virtual patients describe the infection of lung epithelium with Influenza A and the reaction of the immune system to infection, including antibody generation and cytokine release. Virtual patients can be used for vaccine and adjuvant design. [1,2]

COVID-19 virtual patient

Since it was officially declared a pandemic by the WHO in March 2020, SARS-CoV-2 has caused hundreds of millions of patients to become seriously ill. COVID-19 virtual patients describe the infection of lung epithelium with SARS-CoV-2 and the reaction of the immune system to infection, including antibody generation and cytokine release. They can be used to optimize vaccine efficacy. [3,4]

Tuberculosis virtual patient population

Tuberculosis virtual patients describe the *mycobacterium tuberculosis* infection in lung epithelium, as well as the innate and adaptive immune system response. The tuberculosis virtual patient population represents a diverse population and can be treated with combination therapies to support dosing and administration schedule design and optimize vaccine efficacy, or to run in silico clinical trials for a novel vaccine [5-8]

Conclusion

The examples presented herein illustrate how mechanistic models can be used effectively to complement immunoinformatics approaches in support of vaccine design. The InSilicoVACCINE suite can be applied to streamline the transition from nonclinical to clinical development. Using these computational models, the effects of vaccine design-related parameters, choice of adjuvants and dosing schemes can be investigated. Finally, the InSilicoVACCINE suite can be applied to set up in silico clinical trials for a wide variety of vaccines.

REFERENCES

1. Maleki A, Russo G, Parasiliti Palumbo GA, Pappalardo F. BMC Bioinformatics 2021; https://doi.org/10.1186/s12859-022-04581-6.
2. Pappalardo F, Fichera E, Paparone N, Lombardo A, Pennisi M, Russo G, et al. Bioinformatics 2016; https://doi.org/10.1093/bioinformatics/btw293.
3. Russo G, Pennisi M, Fichera E, Motta S, Raciti G, Viceconti M, et al. BMC Bioinformatics 2020; https://doi.org/10.1186/s12859-020-03872-0.
4. Russo G, Di Salvatore V, Sgroi G, Parasiliti Palumbo GA, Reche PA, Pappalardo F. Brief Bioinform 2022; https://doi.org/10.1093/BIB/BBAB403.
5. Pennisi M, Russo G, Sgroi G, Bonaccorso A, Parasiliti Palumbo GA, Fichera E, et al. BMC Bioinformatics 2019; https://doi.org/10.1186/s12859-019-3045-5.
6. Russo G, Pennisi M, Fichera E, Motta S, Raciti G, Viceconti M, et al. BMC Bioinformatics 2020; https://doi.org/10.1186/s12859-020-03872-0.
7. Juárez MA, Pennisi M, Russo G, Kiagias D, Curreli C, Viceconti M, et al. BMC Bioinformatics 2020; https://doi.org/10.1186/s12859-020-03776-z.
8. Curreli C, Pappalardo F, Russo G, Pennisi M, Kiagias D, Juarez M, et al. Int j numer method biomed eng 2021; https://doi.org/10.1002/CNM.3470.