Digital twins for personalized vaccine development and program optimization

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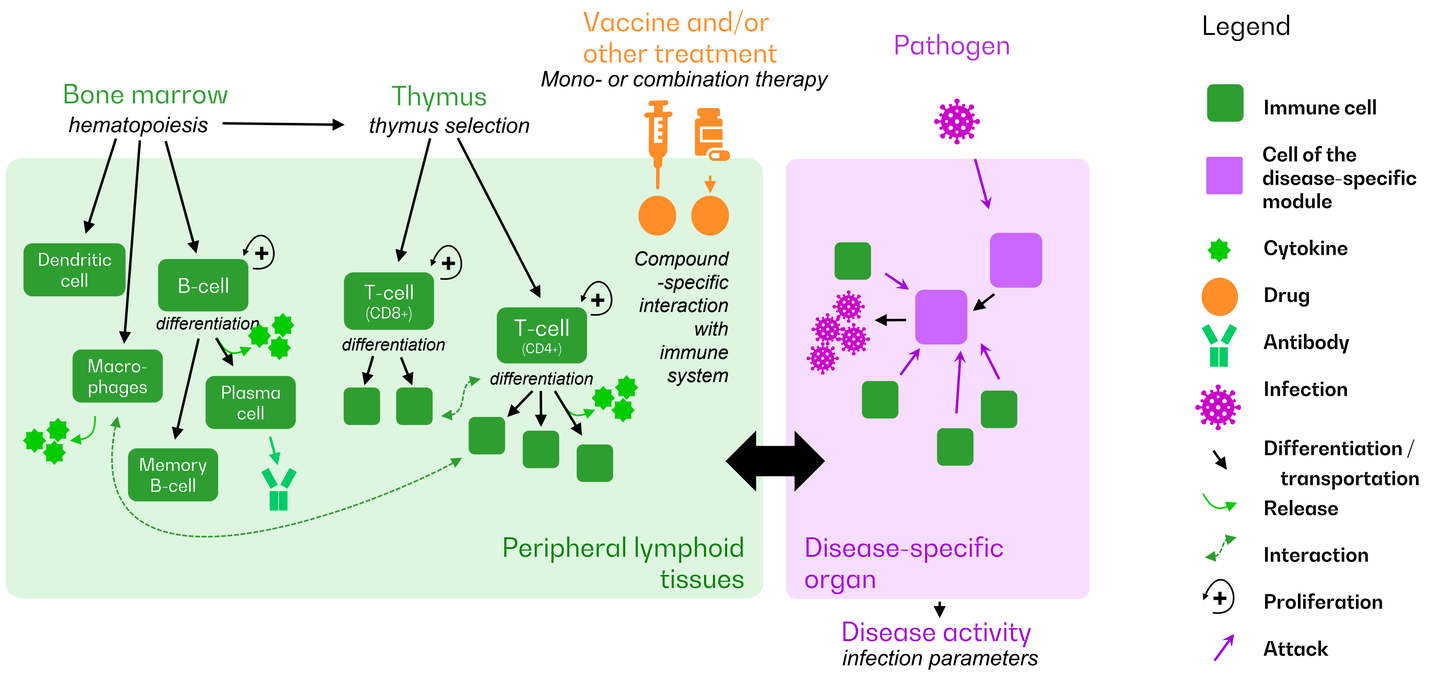
Background

Vaccination can be a key strategy to protect vulnerable individuals from serious illness; however, the most vulnerable populations and individuals may be left suboptimally protected as a result of either reduced vaccine efficacy or ineligibility for vaccination. Vulnerable populations or individuals could therefore benefit greatly from a more tailored, personalized approach to vaccination; however, developing such a personalized approach is a highly complex task. In order to aid in the optimization and personalization of vaccination strategies, we have developed the InSilicoVACCINE suite (http://insilicotrials.com). The suite encompasses a collection of individualizable immune system simulators that can be used to inform vaccination strategies with in silico evidence.

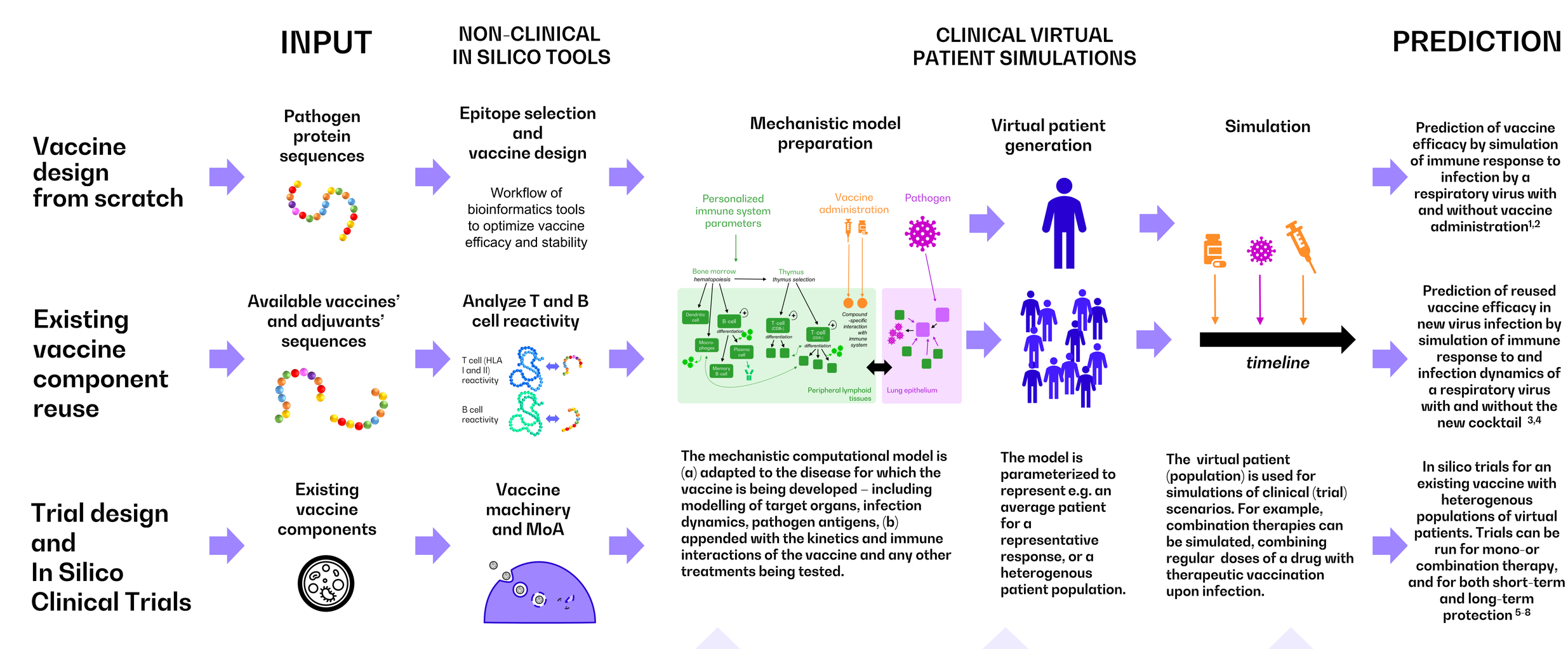
Virtual Patients based on an Agent-Based model

The InSilicoVACCINE suite's individualizable immune system models are based on a versatile immune system simulator. This simulator encompasses an agent-based model which has been applied to a variety of chronic and infectious diseases, and incorporates immune system heterogeneity, immune memory and personal characteristics that affect immune system function

Through personalization of the input characteristics, the effect of a parameter such as age on immune function can be investigated. Three infectious diseases extensions were developed so that the immune system simulator can be applied to vaccine development, representing the pathology of influenza A [1-2], COVID-19 [3-4] and tuberculosis [5-8]. The disease modules were created by modelling the affected tissues, the pathophysiology, and the immune system response. The disease modules were further tested by generation of virtual patients or diverse patient populations. Finally, the models were extended to include vaccination modules by incorporating in detail the affinity between heterogeneous immune receptors and pathogen epitopes. Several existing and hypothetical vaccines and adjuvants were implemented in the simulators, representing a wide variety of vaccine methodology and targets. The resulting simulators can be applied to change vaccine, adjuvants or vaccination schedule for patients with diverse immune systems, in various stages of disease.



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

In conclusion, our personalized vaccine and immune system modelling suite InSilicoVACCINE provides a versatile basis for personalized modelling of populations and at-risk individuals and their response to vaccination in various types of infectious diseases. The suite can be a valuable tool to aid development of vaccine and (personalized) vaccination program design. Following validation in vulnerable populations and individuals, the platform can be a key resource in optimizing vaccine strategies for patients and populations who are left suboptimally protected in the regular vaccination program, by serving as a digital twin of vulnerable populations or patients.

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