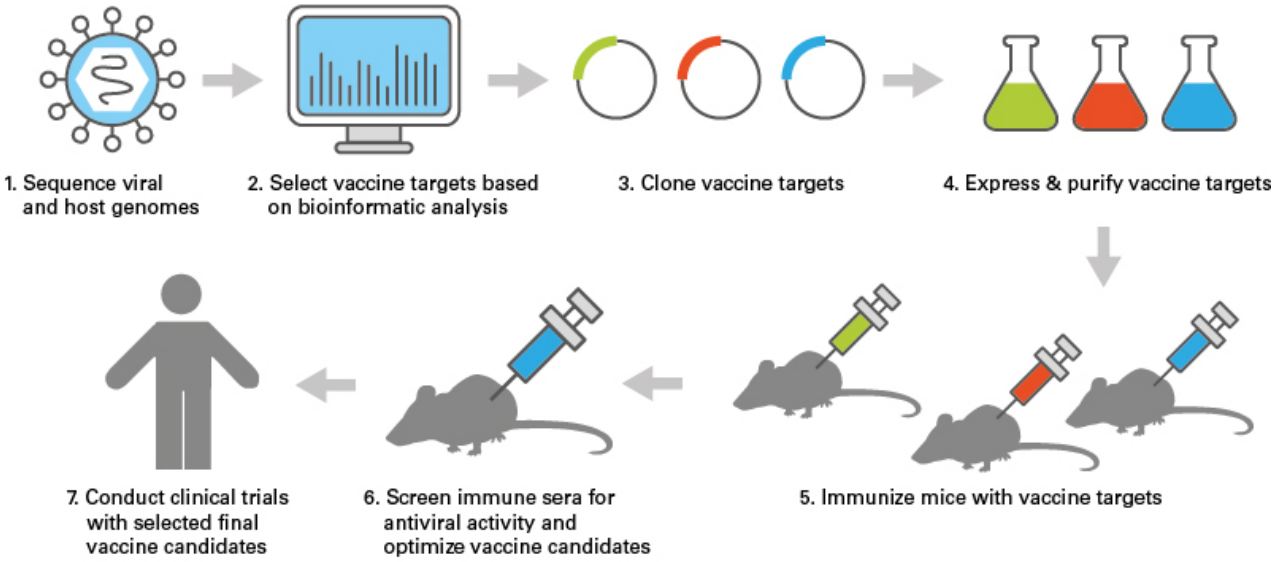
Vaccine development

Innovative tools to accelerate vaccine research and development

Viral & host genomics | Bioinformatic analysis | Clone vaccine targets | Express & purify vaccine targets | Immunize mice | Clinical trials

SARS-CoV-2 research is happening at breakneck speed, and scientists are trying to identify epitopes that could trigger an immune response to the virus, an important step in the development of novel vaccines. Takara Bio offers an array of innovative technologies to support this endeavor. The development of a vaccine involves an analysis of the viral and host genomes using sequencing and bioinformatics to identify potential targets, cloning and isolation of candidate epitopes, testing immune response in animal models, and finally conducting clinical trials with the lead candidates.



Viral and host genomics

Whole-genome sequencing of the SARS-CoV-2 virus can provide valuable information on potential antigenic epitopes that could trigger an immune response. Takara Bio's SMARTer Stranded Pico v2 kit has been used in China to sequence SARS-CoV-2, providing a full-length viral genome sequence. Immune profiling of COVID-19 infected or recovered individuals via RNA-seq can provide additional information to further fuel the process of antigen and vaccine target identification. Our highly sensitive SMARTer Human BCR and TCR profiling kits can be used to monitor changes in BCR (B-cell receptor) and TCR (T-cell receptor) clonotype repertoires throughout disease progression, from infection to recovery.

For single-prep purification of SARS-CoV-2 RNA from bodily fluids and swab samples, we recommend NucleoSpin RNA Virus, which employs a streamlined 30-minute protocol. For high-throughput processing, NucleoMag Pathogen employs scalable, automation-friendly magnetic beads, with scripts available for many common platforms.

Bioinformatic analysis

The next step is bioinformatic analysis of the viral genome and host BCR and TCR immune profiles to reveal SARS-CoV-2 antigens and select vaccine targets (viral surface receptors). Takara Bio Immune Profiler Software can be used along with the SMARTer Human BCR IgG IgM H/K/L Profiling Kit to parse out information about clonotype numbers and V(D)J sequence information.

Clone vaccine targets

Researchers can speed up viral receptor and vaccine construct generation using NucleoSpin gel and PCR cleanup and plasmid purification kits as well as our In-Fusion HD Cloning technology for high-throughput cloning:

- Highly efficient—over 95% cloning efficiency for inserts ranging from 0.5 to 15 kb
- Sequence independent—clone ANY insert, into ANY vector, at ANY locus
- Seamless construction—no extra base pairs (or scar sequences) at cloning junctions
- Versatile—multiple-insert cloning and site-directed mutagenesis with a single kit

Researchers have already published work utilizing In-Fusion HD Cloning technology within their workflows to study and develop vaccines against coronaviruses, including SARS-CoV-2:

- Kato, H. *et al.* Development of a recombinant replication-deficient rabies virus-based bivalent-vaccine against MERS-CoV and rabies virus and its humoral immunogenicity in mice. *PLoS One.* **14,** DOI:10.1371/journal.pone.0223684 (2019).
- Letko, L., Marzi, A., & Munster, V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. *Nat. Microbiol.* **6,** 562–569 (2020).
- Terada, Y., Kawachi, K., Matsuura, Y., Wataru, W., Kamitani, W. MERS coronavirus nsp1 participates in an efficient propagation through a specific interaction with viral RNA. *Virol.* **511,** 95–105 (2019).

Express and purify vaccine targets

NucleoSpin 96 Plasmid Transfection-grade is a popular choice for manual or automated high-throughput purification of expression constructs. When it's time for scale-up, NucleoBond Xtra midi and maxi kits combine gravity flow filtration and anion-exchange technology to deliver higher yields in less time than conventional alternatives. Our BacPAK Baculovirus Expression System uses a baculovirus backbone to express your protein of interest for vaccine development. This technology is easy to scale up, has high levels of protein expression, and is nonpathogenic to humans. In addition, the target proteins produced with this system are similar in structure, biological activity, and immunological reactivity to the naturally occurring protein. Once expressed from these purified constructs, his-tagged vaccine candidate proteins can be rapidly purified using our revolutionary Capturem high-capacity membrane-based purification technology:

- Fast, convenient workflow—5- to 30-minute room-temperature protocol using convenient spin columns/plates/filtration devices featuring Capturem nickel-functionalized membranes
- High purity—small bed volumes trap fewer contaminants
- Compatible with a wide range of additives—including EDTA, DTT, BME, glycerol, TCEP, etc. (see compatibility table)
- Versatile—easy purification from mammalian/bacterial cell lysates and supernatants

Researchers have already published work utilizing our Capturem His technology within their vaccine development workflows:

- Do, V. T. *et al.* Recombinant adenovirus carrying a core neutralizing epitope of porcine epidemic diarrhea virus and heat-labile enterotoxin B of *Escherichia coli* as a mucosal vaccine. *Arch. Virol.* **165,** 609–618 (2020).
- Martínez-Hernández, S. L. *et al.* An anti-amoebic vaccine: generation of the recombinant antigen LC3 from Entamoeba histolytica linked to mutated exotoxin A (PEΔIII) via the Pichia pastoris system. *Biotechnol. Lett.* **39,** 1149–1157 (2017).

Immunize mice with vaccine targets, screen sera for antiviral activity, and optimize promising candidates

Takara Bio's SMARTer Mouse BCR and TCR profiling kits can be used to speed up the process of immune sera screening for antiviral activity of target vaccines by monitoring changes in the BCR and TCR

clonotype repertoires. Promising vaccine candidates are further optimized by analyzing and comparing antibody and T-cell responses in the vaccinated animals prior to and upon exposure to virus.

Assess effectiveness of selected final vaccine candidates in clinical trials

Monitoring the immune response is key to assessing the effectiveness of the final vaccine candidates. BCR and TCR repertoire profiling by NGS allows precise monitoring of clonotype changes and the identification of vaccine-specific clonotypes.

Explore industry-leading products that can advance your SARS-CoV-2 vaccine research and development:

Please see the Kit Components List to determine kit components. Certificates of Analysis and Kit Components Lists are located under the Documents tab.

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