

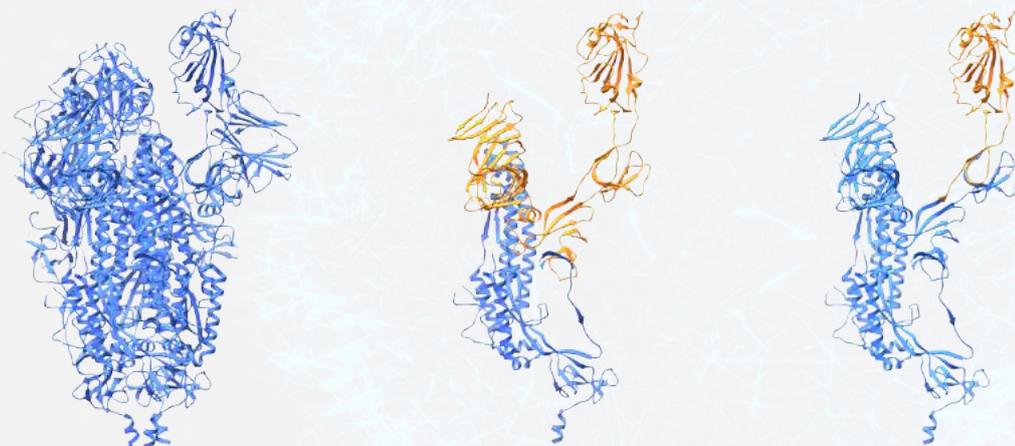
Coronavirus Reagents

SARS-CoV-2 Antigens

The Native Antigen Company offers a growing range of antigens for the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which are suitable for a variety of applications including assay development, neutralisation testing, immunofluorescence, surface plasmon resonance or basic research. Our proprietary VirtuE (HEK293) expression system ensures complete glycosylation and proper folding of antigens to ensure full biological and antigenic activity. If we don't currently provide a product you are looking for, our team has decades of experience in antigen production and assay development and is also able to undertake a range of custom projects to suit your needs.

Spike Protein

Spike protein is a large type I transmembrane trimer that studs the surface of SARS-CoV-2 and gives it its characteristic crown-like appearance. Each Spike protein comprises three segments: A large ectodomain (comprising S1 and S2), a transmembrane anchor, and a short intracellular tail. The S1 subunit of the ectodomain mediates binding of the virion to host cell-surface receptors through its receptor-binding domain (RBD), whereas the S2 subunit fuses with both host and viral membranes, by undergoing dramatic structural changes.



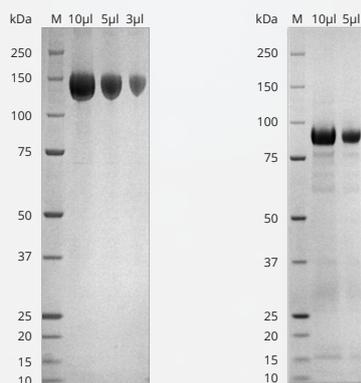
3D crystal structures of the SARS-CoV-2 Spike protein. Left: Spike protein trimer in the open conformation. Centre: Spike protein monomer in open conformation with S1 subunit labelled orange and S2 subunit labelled blue. Right: Spike protein monomer in open conformation with receptor-binding domain labelled orange.

Emerging studies suggest that the serology of SARS-CoV-2 is highly complex and differs significantly from other betacoronaviruses. Antibody responses to SARS-CoV-2 appear to occur later and be of lower titres than are typically observed, influencing the way in which assays are designed to diagnose both acute and historic infections. An important consideration is the potential for antibody cross-reactivity to other co-circulating coronaviruses, requiring close attention to the binding specificity of antigens used. The choice of antibody class is also important for measuring antibodies such as IgA.

S1 & S2 Subunits

The S1 and S2 subunits of Spike are a popular choice for the development of immunoassays as they are highly exposed to the virus's external environment and can readily induce potent antibody responses. In particular, Spike antibodies that bind the RBD of S1 may be able to neutralise virus by preventing binding with ACE2.

The Native Antigen Company offers an S1 antigen that comprises the C-terminus of the SARS-CoV-2 Spike protein (residues 1-674) and an S2 antigen that comprises the N-terminus of the SARS-CoV-2 Spike protein (residues 685-1211). Both proteins are available from a range of expression systems and come with monomeric sheep Fc-tags or His-tags for ease of purification and detection.



SDS-PAGE images of SARS-CoV-2 Spike S1 proteins following Protein G chromatography. Far left: HEK293-expressed S1 (REC31806). Left: Insect cell-expressed S1 (REC31828). Difference in molecular weights is explained by use of Fc- and His-tags, respectively.

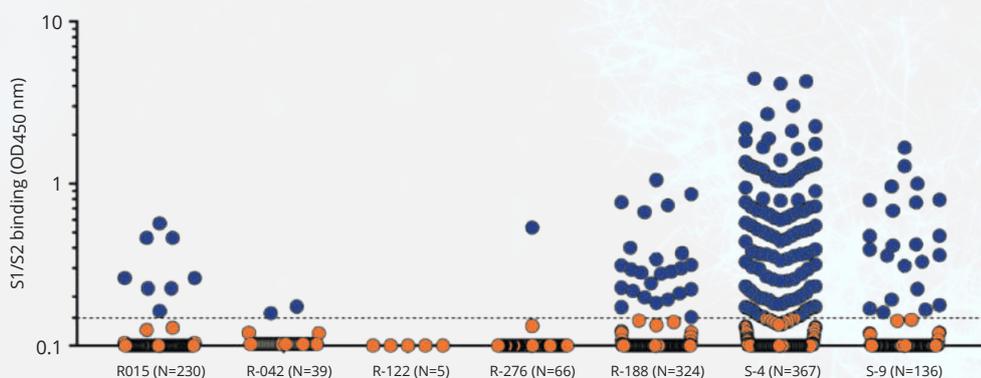
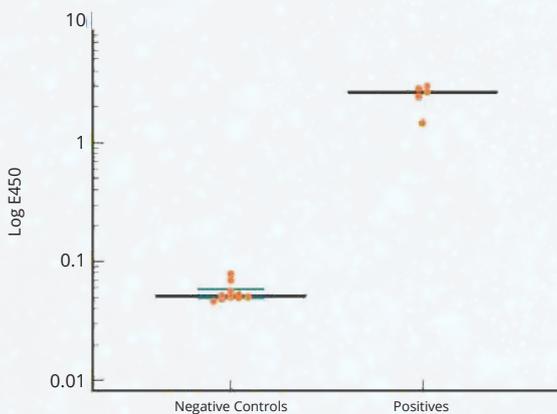


Chart showing results of SARS-CoV-2 supernatant binding to S1 (REC31806) & S2 (REC31807). Blue dots represent mAbs which bind S1 + S2; orange dots represent mAbs which do not bind S1 + S2. Results from preprint by Andreano et al., "Identification of neutralizing human monoclonal antibodies from Italian COVID-19 convalescent patients."

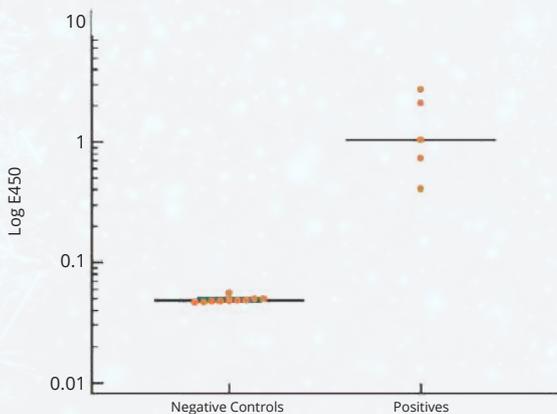
Receptor-Binding Domain

The Spike receptor-binding domain (RBD) functions to mediate cell-surface attachment and internalisation by binding human ACE2 receptors. Given RBD's role in host-cell entry, it is able to elicit highly neutralising antibody responses and is a popular target for the development of vaccines. The RBD also shows high sequence divergence between other coronavirus Spike proteins, making it a popular antigen for the development of sensitive and specific immunoassays.

The Native Antigen Company offers SARS-CoV-2 RBDs from HEK293, CHO and *E. coli* expression systems, all with C-terminal His-tags for ease of purification and detection.



Spike RBD (REC31849) tested as solid-phase bound capture antigen at 2µg/ml with a SARS-CoV-2 IgG ELISA. 5 SARS-CoV-2 PCR-positive patient samples vs. 11 negative controls at 1:400 sample dilution.



Spike RBD (REC31849) tested as solid-phase bound capture antigen at 2µg/ml in combination with an RBD-biotin conjugate as soluble detector/tracer at 1µg/ml with a SARS-CoV-2 IgG ELISA. 5 SARS-CoV-2 PCR-positive patient samples vs. 11 negative controls at 1:160 sample dilution.

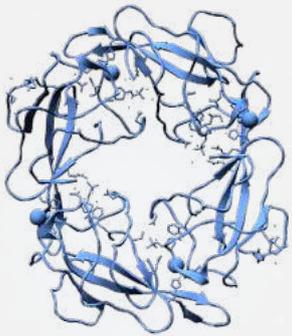
N-Terminal Domain

The N-terminal domain of the SARS-CoV-2 Spike protein shows the highest sequence variability across the coronavirus family, making it a popular choice of antigen for maximising the specificity of diagnostic assays. The Native Antigen Company offers a SARS-CoV-2 Spike NTD (aa 1-260) from our HEK293 expression system, which includes a C-terminal sheep Fc tag for ease of purification and detection.

Nucleoprotein

Nucleoproteins are found within the coronavirus virion, where they bind viral RNA and play an important role in virion structure, replication and transcription. Unlike Spike, Nucleoproteins are unglycosylated and bind phosphate groups to mediate interaction with RNA. As nearly all vaccines for SARS-CoV-2 target the Spike protein, Nucleoproteins are a popular antigen for the development of diagnostics that can distinguish vaccine-induced immune responses from those that have occurred due to natural infection. Nucleoprotein is also commonly used in the development of immunoassays that detect acute and historic SARS-CoV-2 infection.

The Native Antigen Company offers a full-length SARS-CoV-2 Nucleoprotein expressed in *E. coli* with a C-terminal His-tag for ease of purification and to immobilise on surfaces for detection in immunoassays.



3D crystal structure of the SARS-CoV-2 Nucleoprotein RNA-binding domain.



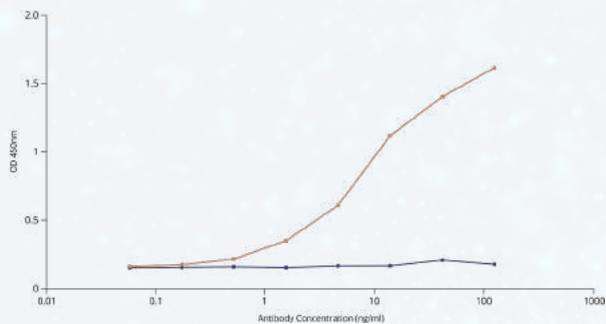
*SDS-PAGE image of SARS-CoV-2 Nucleoprotein expressed from *E. coli*.*

Mosaic Proteins

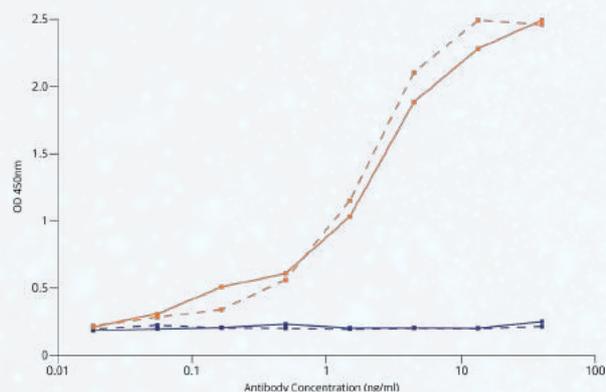
The Native Antigen Company offers a mosaic protein comprising the immunodominant regions of the Spike, Envelope and Membrane proteins to allow researchers to assess serological responses to different SARS-CoV-2 proteins using a single reagent. This protein is highly pure and includes a C-terminal His-tag for ease of purification and detection.

SARS-CoV-2 Antibodies

The Native Antigen Company offers a variety of SARS-CoV-2 Spike-specific antibodies from clone CR3022 for the development of immunoassays, neutralisation assays, surface plasmon resonance and X-ray crystallography. We offer CR3022 antibodies in both human and rabbit IgG variants, as well as a human IgM.

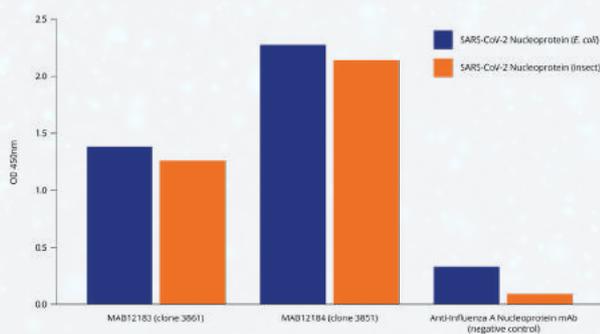


Affinity of human CR3022 IgG to plate coated with SARS-CoV-2 S1 and S2 at 5 µg/ml. Primary antibodies were titrated on a 3-fold serial dilution starting at 125 ng/ml. Antibody recognised SARS-CoV-2 S1 (orange), but not SARS-CoV-2 S2 (blue).



Affinity of human CR3011 IgG to plate coated with SARS-CoV-2 S1 and S2, SARS-CoV S1 and SARS-CoV Spike mosaic at 5 µg/ml. Primary antibodies were titrated on a 3-fold serial dilution starting at 41.6 ng/ml. Secondary antibody anti-human IgG conjugated to HRP at 1:4000 concentration. Antibody recognised SARS-CoV S1 (blue) and SARS-CoV-2 S1 (orange), produced in mammalian (dotted) and insect cells (solid), respectively. Antibody did not recognise SARS-CoV-2 S2 or Spike mosaic protein (blue dotted), containing S1 residues 12-53, 90-115, 171-203.

We also offer two mouse monoclonal antibodies that have shown to bind to both SARS and SARS-CoV-2 Nucleoproteins.



Data from indirect ELISA showing binding of two anti-Nucleoprotein monoclonal antibodies (MAB12183 and MAB12184) to *E. coli* and insect cell-expressed Nucleoproteins.

Additional Coronavirus Reagents

In addition to our range of antigens and antibodies for SARS-CoV-2, we offer cell-surface viral receptors, antigens and antibodies for the SARS, MERS, 229E and NL63 coronaviruses. These reagents can be used to assess potential cross-reactivity of antibodies developed for SARS-CoV-2 assays.

Human Receptors

The Native Antigen Company offers highly purified human angiotensin-converting enzyme 2 (ACE2), bound by the SARS-CoV-2 Spike protein. These proteins have been tested for functional RBD binding in ELISA and include C-terminal human Fc-tags for ease of purification and detection.

SARS-CoV Antigens & Antibodies

The Native Antigen Company offers a range of proteins and antibodies for the development of Severe Acute Respiratory Syndrome-Related Coronavirus (SARS-CoV) assays and vaccines. Our SARS-CoV proteins include S1, S2, Nucleoprotein, envelope protein, membrane protein and a combination of S1/S2 mosaic proteins. These antigens have been expressed in *E. coli* and are over 95% pure. We are currently developing mammalian-expressed S1 and Nucleoprotein.

MERS-CoV Antigens & Antibodies

The Native Antigen Company offers two S1 proteins and three anti-S1 mouse monoclonal antibodies for the Middle East Respiratory Syndrome-Related Coronavirus (MERS-CoV). Our MERS S1 proteins are available from mammalian cells with a camel Fc-tag, or from *E. coli* with a His-Tag for ease of expression and purification. We offer three mouse monoclonal antibodies (clones 3871, 3872, 3873) to the MERS S1 protein, which do not cross-react with our SARS-CoV S1 antigens and are suitable for use in ELISAs and IFAs.

Endemic Coronavirus Antigens

The Native Antigen Company also offers antigens for the 229E and NL63 alphacoronaviruses. Our 229E Nucleoprotein is expressed in *E. coli*, with a His-Tag and is over 95% pure. Our NL63 Nucleoprotein is also expressed in *E. coli* and shows over 95% purity. These antigens are ideal for use in ELISAs and other immunoassays. We are developing Spike S1 for the 229E, NL63, HKU1 and OC43 coronaviruses, as well as Nucleoprotein for HKU1-CoV and OC43-CoV.

Antigens	Product Code	Source	Format
SARS-CoV-2 Spike Glycoprotein (Full-Length) *	REC31850	HEK293 Recombinant	Liquid
SARS-CoV-2 Spike Glycoprotein (S1)	REC31806	HEK293 Recombinant	Liquid
SARS-CoV-2 Spike Glycoprotein (S1)	REC31828	Insect Cell Recombinant	Liquid
SARS-CoV-2 Spike Glycoprotein (S1) RBD	REC31849	HEK293 Recombinant	Liquid
SARS-CoV-2 Spike Glycoprotein (S1) RBD	REC31845	<i>E. coli</i> Recombinant	Liquid
SARS-CoV-2 Spike Glycoprotein (S1) RBD	REC31831, REC31843	CHO Recombinant	Liquid
SARS-CoV-2 Spike Glycoprotein (S2)	REC31807	HEK293 Recombinant	Liquid
SARS-CoV-2 Spike Glycoprotein (S2)	REC31830	Insect Cell Recombinant	Liquid

* Product currently in development

Antigens	Product Code	Source	Format
SARS-CoV-2 Spike Glycoprotein (S2) (aa 1000-1200)	REC31846	<i>E. coli</i> Recombinant	Liquid
SARS-CoV-2 Spike Glycoprotein (S2) (aa 800-1000)	REC31844	<i>E. coli</i> Recombinant	Liquid
SARS-CoV-2 Nucleoprotein	REC31812	<i>E. coli</i> Recombinant	Liquid
SARS-CoV-2 Spike N-Terminal Domain (NTD)	REC31835	HEK293 Recombinant	Liquid
SARS-CoV-2 Spike-E-M Mosaic Protein	REC31829	<i>E. coli</i> Recombinant	Liquid
SARS-CoV-2 Membrane-Envelope Fusion Protein	REC31848	<i>E. coli</i> Recombinant	Liquid
SARS-CoV Spike Glycoprotein (S1)	REC31809	HEK293 Recombinant	Liquid
SARS-CoV Spike Glycoprotein (S1) Mosaic	REC31842	<i>E. coli</i> Recombinant	Liquid
SARS-CoV Spike Glycoprotein (S1) Mosaic (N-Term)	REC31840	<i>E. coli</i> Recombinant	Liquid
SARS-CoV Spike Glycoprotein (S2) Mosaic (C-Term)	REC31841	<i>E. coli</i> Recombinant	Liquid
SARS-CoV Envelope Protein	REC31839	<i>E. coli</i> Recombinant	Liquid
SARS-CoV Nucleoprotein	REC31744	HEK293 Recombinant	Liquid
SARS-CoV Nucleoprotein (N-Term)	REC31836	<i>E. coli</i> Recombinant	Liquid
SARS-CoV Nucleoprotein (C-Term)	REC31837	<i>E. coli</i> Recombinant	Liquid
SARS-CoV Membrane Protein (Matrix)	REC31838	<i>E. coli</i> Recombinant	Liquid
MERS Coronavirus Spike Glycoprotein (S1)	REC31847	HEK293 Recombinant	Liquid
MERS Coronavirus Spike Glycoprotein (S1)	REC31760	<i>E. coli</i> Recombinant	Liquid
229E Coronavirus Nucleoprotein	REC31758	<i>E. coli</i> Recombinant	Liquid
NL63 Coronavirus Nucleoprotein	REC31759	<i>E. coli</i> Recombinant	Liquid
Antibodies	Product Code	Source	Format
Human SARS-CoV-2 Spike (S1) IgG mAb (CR3022)	MAB12422	Hybridoma	Liquid
Human SARS-CoV-2 Spike (S1) IgM mAb (CR3022)	MAB12423	Hybridoma	Liquid
Rabbit SARS-CoV-2 Spike (S1) IgG mAb (CR3022)	MAB12424	Hybridoma	Liquid
Mouse SARS-CoV Nucleoprotein IgG mAb (3851)	MAB12184	Hybridoma	Liquid
Mouse SARS-CoV Nucleoprotein IgG mAb (3861)	MAB12183	Hybridoma	Liquid
Mouse SARS-CoV Nucleoprotein IgG mAb (3862)	MAB12425	Ascities Fluid	Liquid
Mouse SARS-CoV Nucleoprotein IgG mAb (3863)	MAB12426	Ascities Fluid	Liquid
Mouse SARS-CoV Nucleoprotein IgG mAb (3864)	MAB12427	Ascities Fluid	Liquid
Mouse MERS-CoV Spike (S1) IgG mAb (3871)	MAB12395	Hybridoma	Liquid
Mouse MERS-CoV Spike (S1) IgG mAb (3872)	MAB12396	Hybridoma	Liquid
Mouse MERS-CoV Spike (S1) IgG mAb (3873)	MAB12397	Hybridoma	Liquid
Receptors	Product Code	Source	Format
ACE2 (18-615)(Human)	REC31832	HEK293 Recombinant	Liquid
ACE2 (19-740)(Human)	REC31833	HEK293 Recombinant	Liquid
CLEC4M (Human)	REC31686	HEK293 Recombinant	Liquid