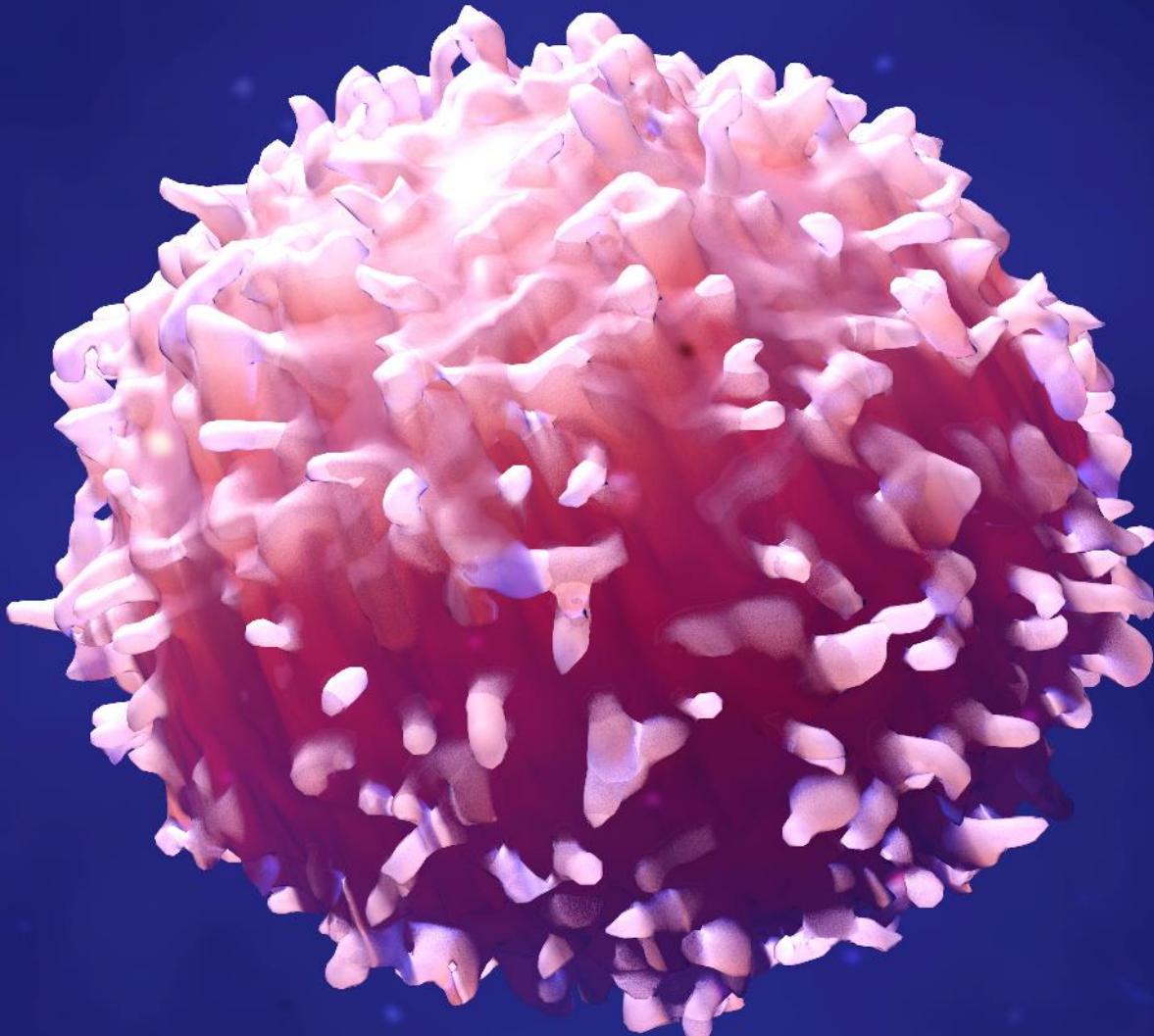
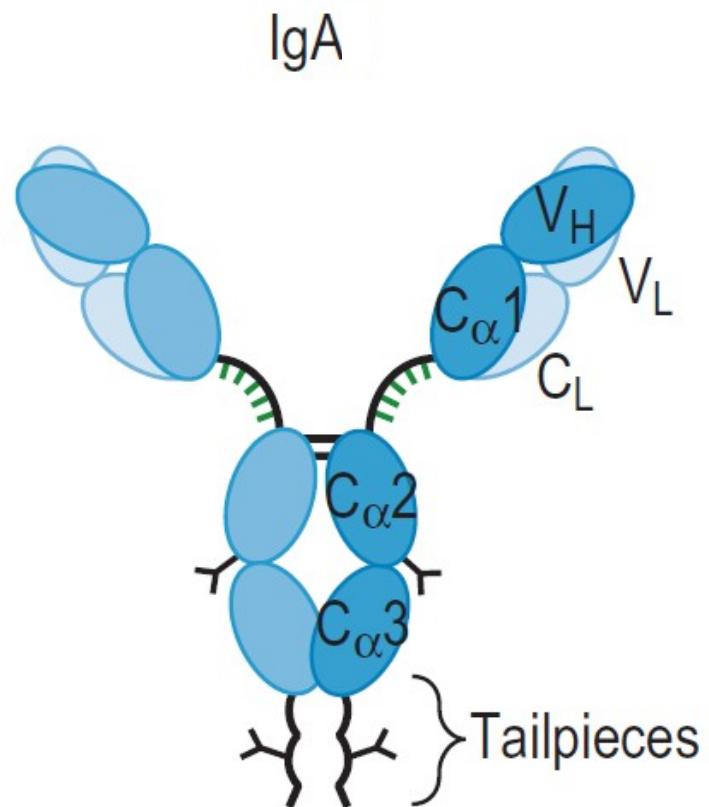


IgA och Covid 19

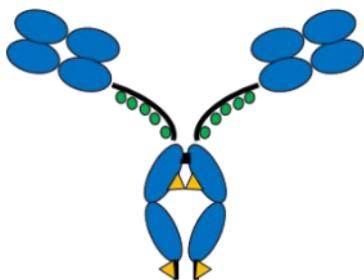


IgA upptäcktes 1953

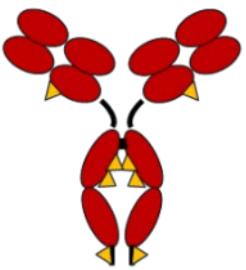


Två isoformer av IgA

IgA1



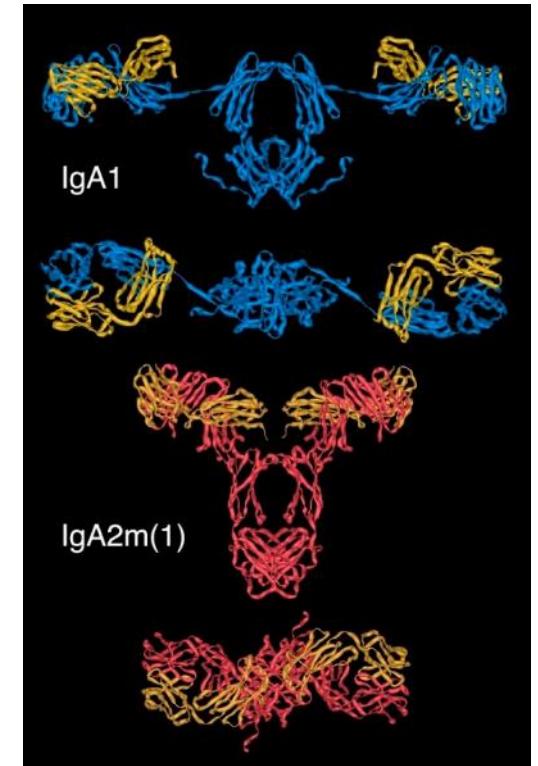
IgA2



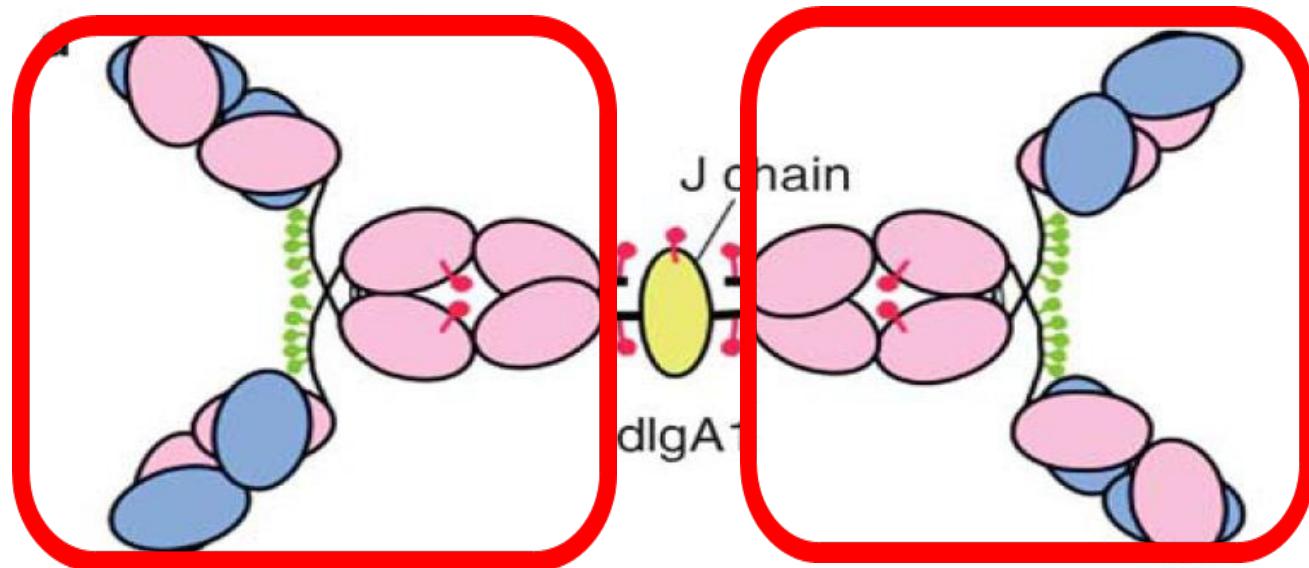
- O-linked glycosylation
- N-linked glycosylation

IgA1 ffa i blod

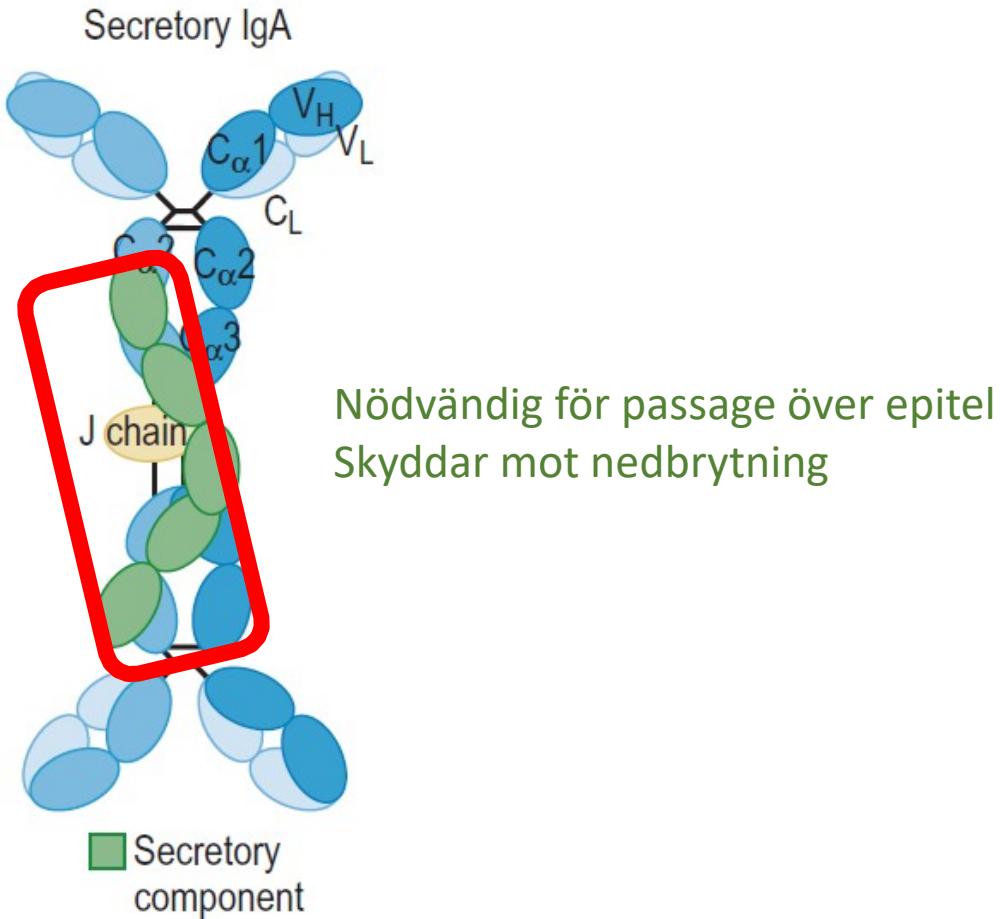
IgA2 ffa sekreterat



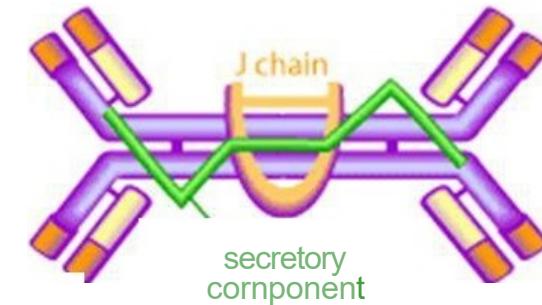
Dimerisk form- joining chain



Sekretoriskt IgA-secretory component

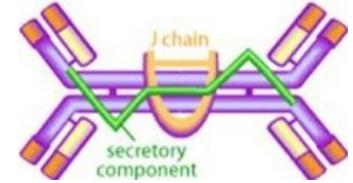


IgA



- Struktur: Dimer
- Fraktion av serum immunoglobuliner: 10-15%
- Lokal: Sekretion (tårar, saliv, mag-tarm, bröstmjölk), blod och lymfa.
- Half-life i serum: 6 d
- Komplement Fixering: Nej
- Placenta Transport: Nej
- Funktion: Lokalt skydd av slemhinnor

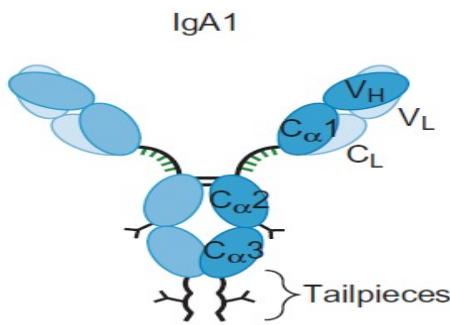
IgA



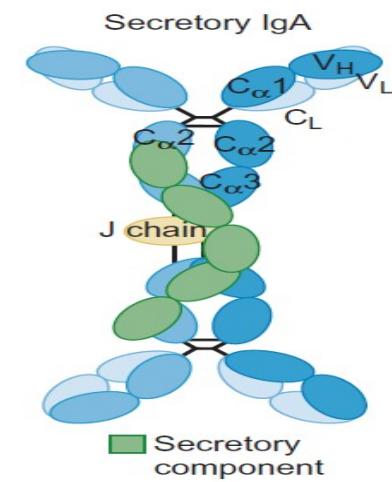
**2 g polymeriskt IgA produceras per dag
dvs 2,000,000,000,000,000 molekyler IgA/d**

60-70% av den totala Ig sekretionen

Produktion av IgA

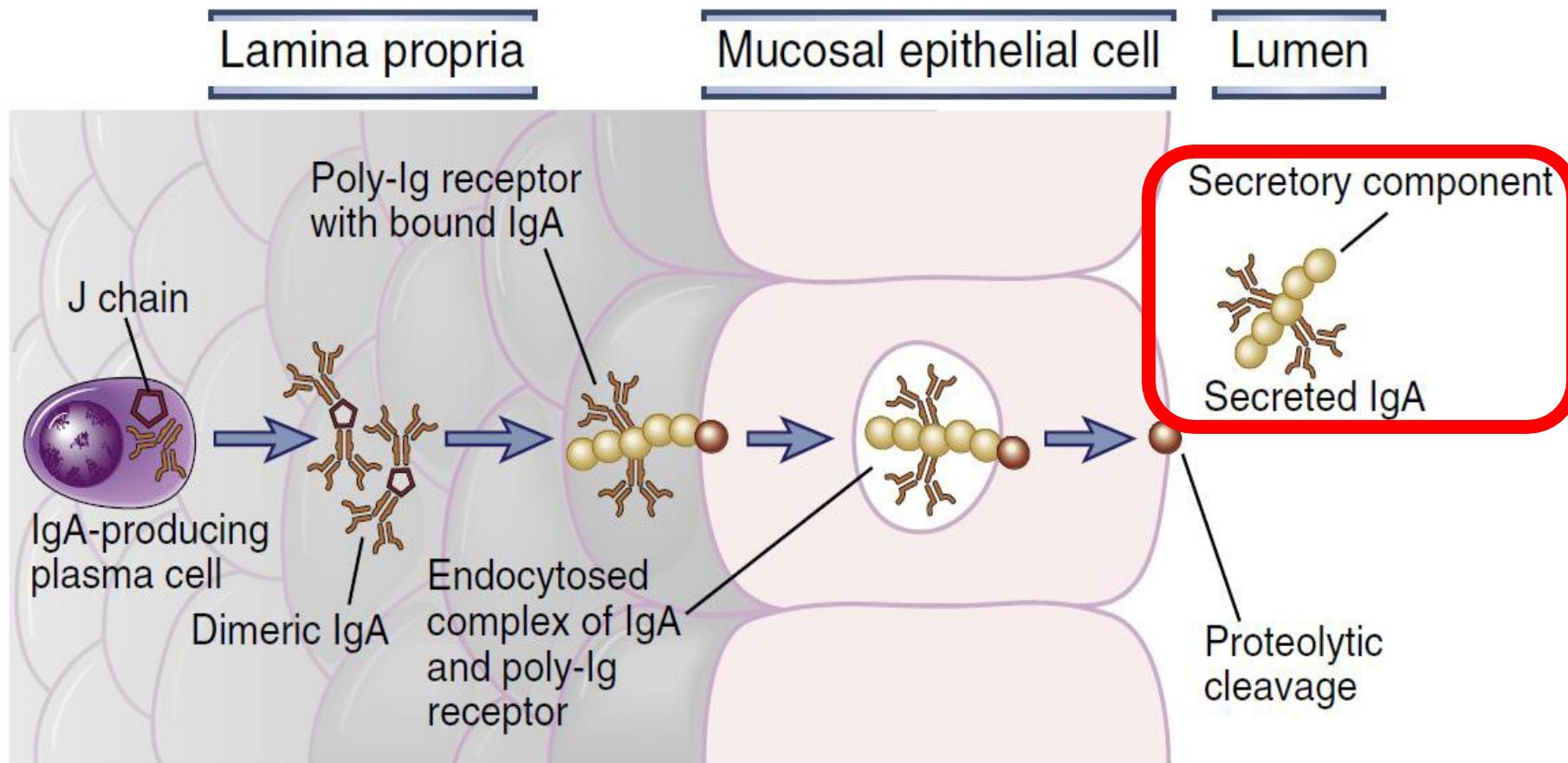


Från plasmaceller i benmärg

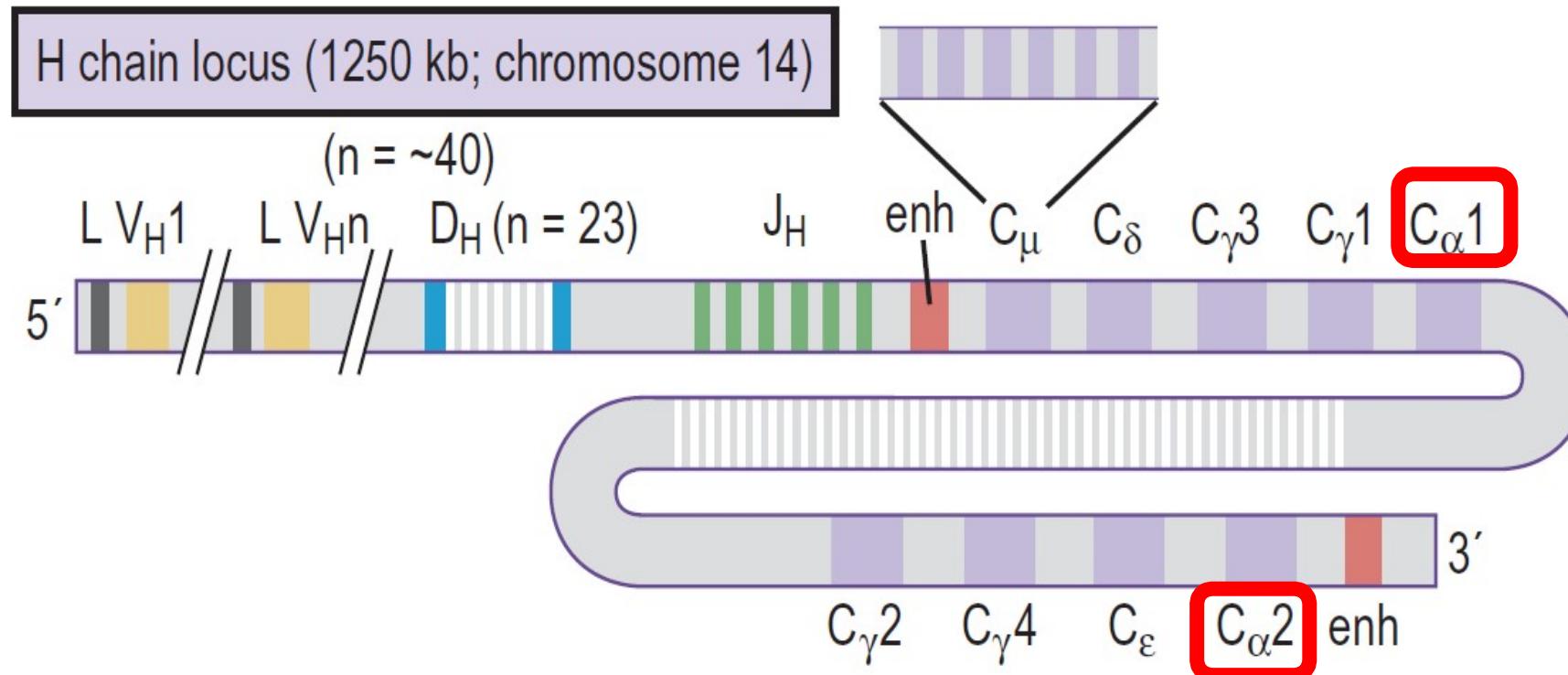


Lokal produktion i mukosa

Transport av IgA över epitel



Germline organisation av immunoglobulin gene loci



Abbas AK, Lichtman AH, Pillai S. Cellular and molecular immunology. 8th ed. Philadelphia, W.B. Saunders Company.2015.

Jelinek DF,Li JT.Immunoglobulin Structure and Function In: Adkinson NF,Bochner BS,Burks AW,Busse WW,Holgate ST, Lemanske RF,O'Hehir RE, editors. Middleton's allergy: principles & practice. 8 th ed. Philadelphia: Mosby-Elsevier; 2014.

Selektiv IgA brist-beskrevs först 1964

The screenshot shows the homepage of the **TRANSLATIONAL RESEARCH** journal, which is "The Journal of Laboratory and Clinical Medicine". The header includes links for RSS Feeds, Mobile, Login, Register, and Subscribe. A search bar at the top right allows for "All Content" or "Advanced Search". The main navigation menu includes Articles & Issues, Collections, For Authors, Journal Info, Press Releases, CSCTR, CSCTR in the News, Subscribe, and More Periodicals.

The central content area displays an article from **February 1964**, Volume 63, Issue 2, Pages 205-212. The title of the article is **Beta-2A aglobulinemia in two healthy men**. The authors listed are **John H. Rockey*, Lars A. Hanson**, Joseph F. Heremans***, Henry G. Kunkel**. Below the authors, it states "From the Rockefeller Institute New York, N. Y. USA". There are footnotes: * Present address: Department of Microbiology, School of Medicine, University of Pennsylvania, Philadelphia, Pa.; ** Present address: Crown Princess Lovisa's Children's Hospital, Stockholm K, Sweden; *** Present address: Hospital St. Pierre, 69 rue Bruxelles, Louvain, Belgium. The text "Received: August 15, 1963; Accepted: November 8, 1963;" is also present.

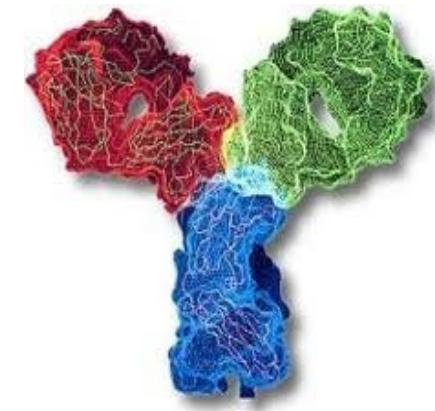
To the right of the article abstract, there is a link to "Access this article on ScienceDirect". Below the article abstract, a red sidebar titled "Article Tools" provides links for PDF download (573 KB), Email Article, Add to My Reading List, Export Citation, Create Citation Alert, and Cited by in Scopus (29).

Rockey JH, Hanson LA, Heremans JF, Kunkel HG. BETA-2AAGLOBULINEMIA IN TWO HEALTHY MEN. The Journal of laboratory and clinical medicine. 1964;63:205-12.

Selektiv IgA brist

Selective IgA deficiency (SIgAD) vanligaste immunbristen

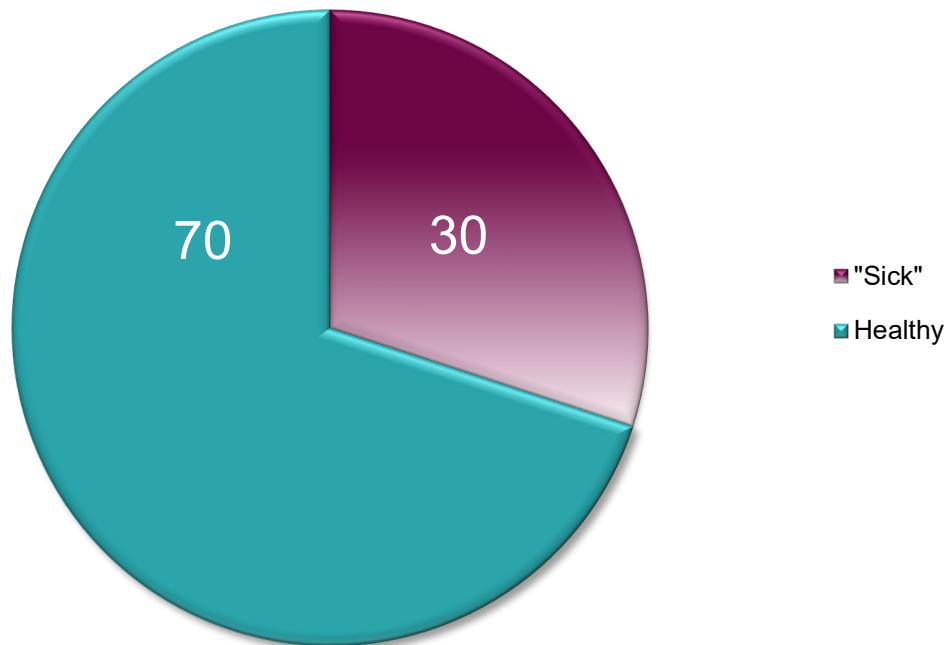
Definition: Serum IgA <0.07 g/L, Normal IgG och IgM
Normalt IgG svar mot vaccination

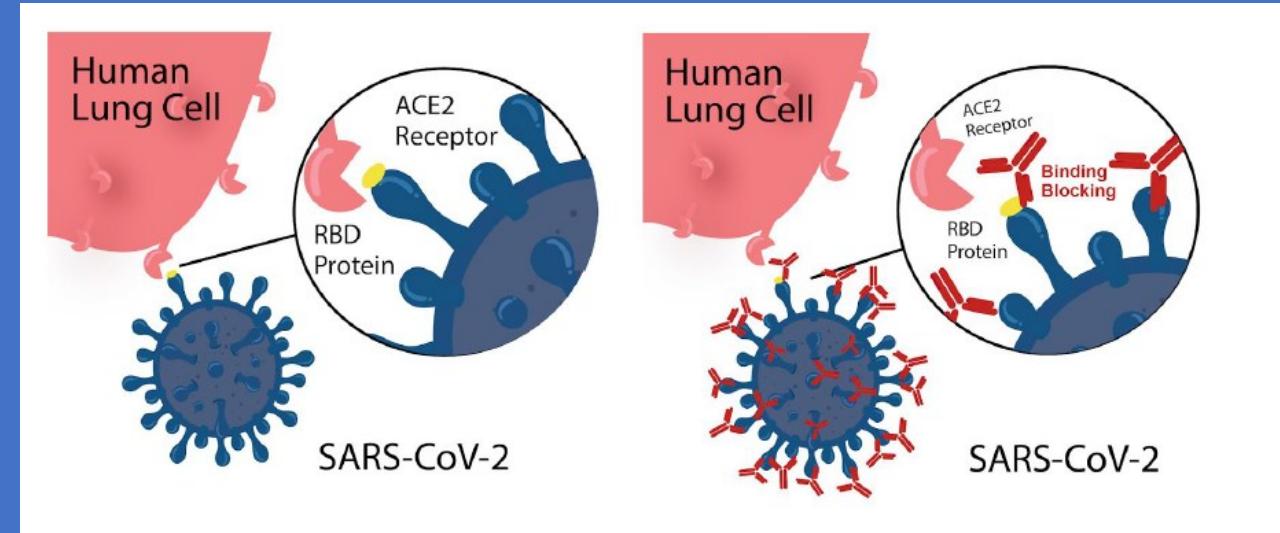


Patogenes: IgA B lymfocyter utmognar inte till IgA producerande plasmaceller

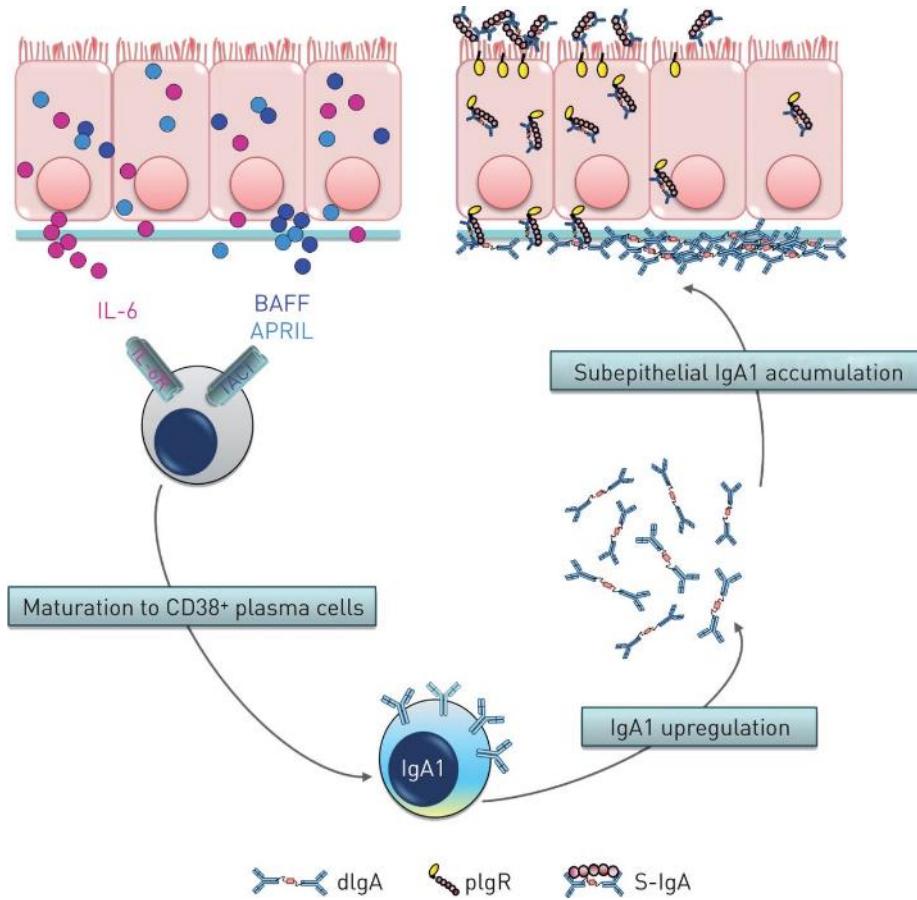
Selektiv IgA brist

Ökat antal infektioner, autoimmunitet, allergi

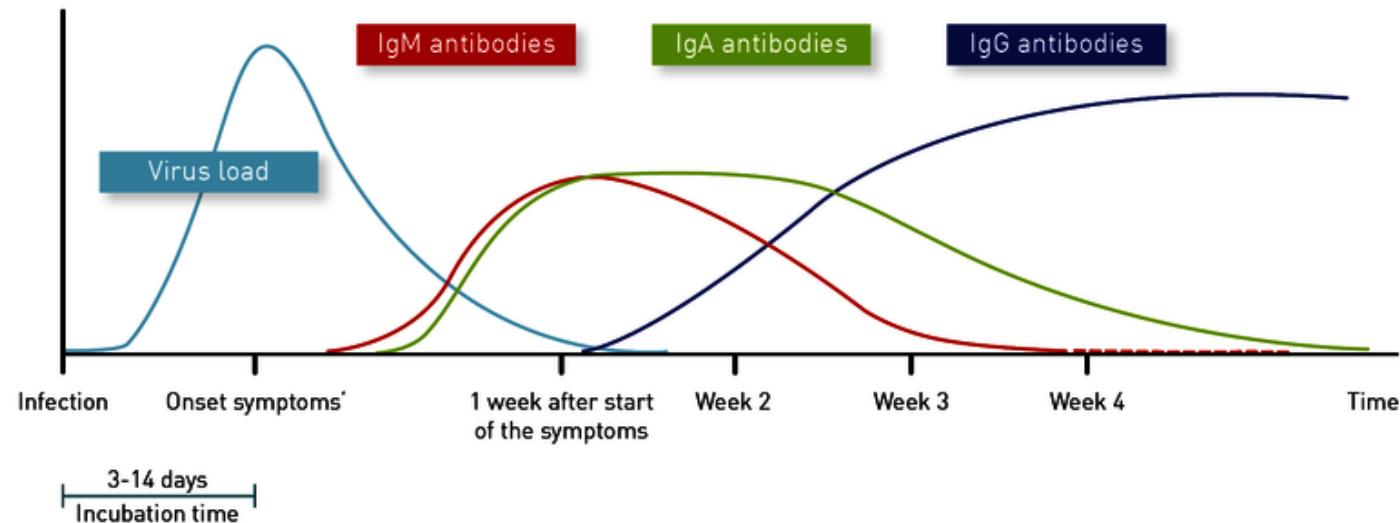




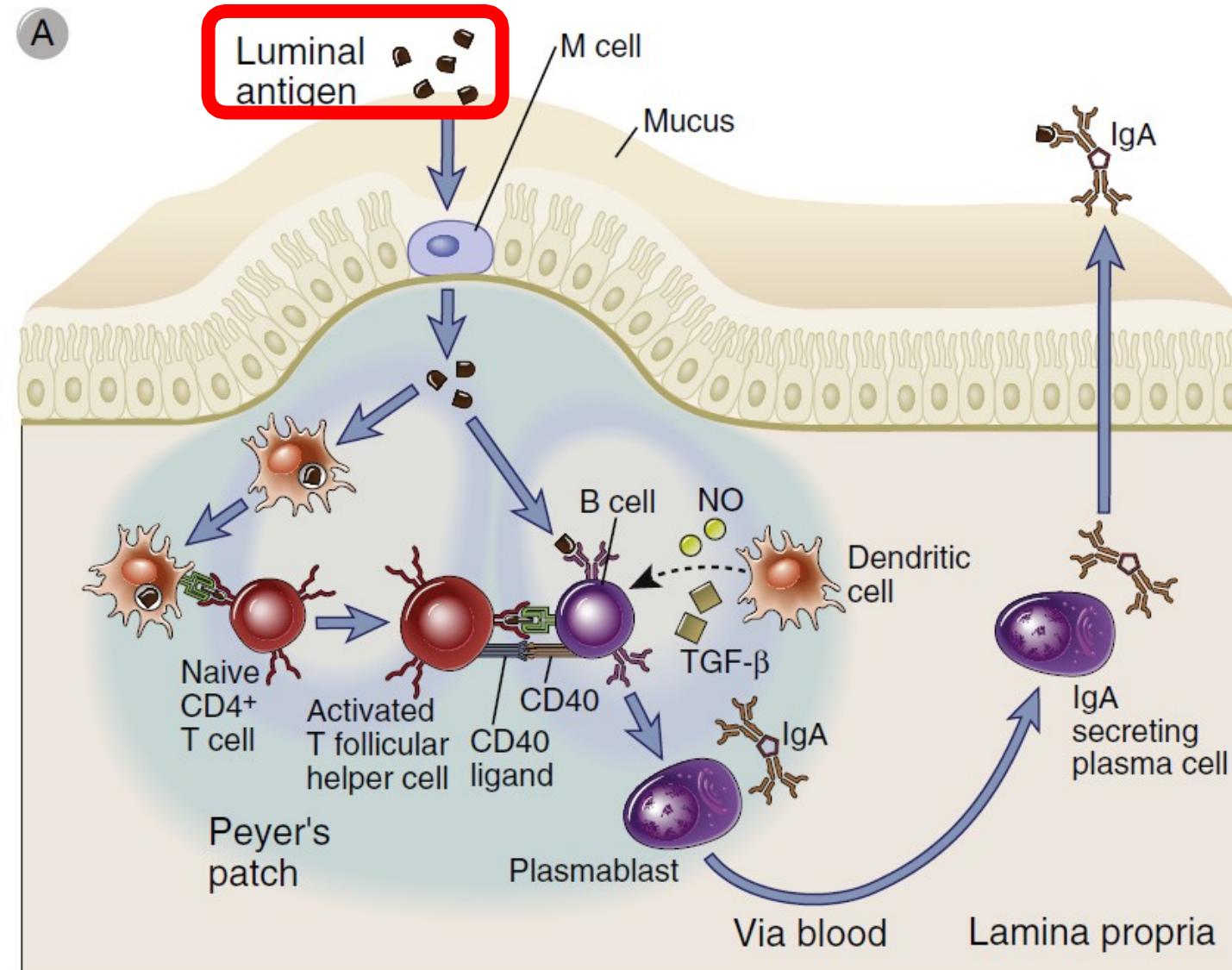
Skydd mot COVID 19 sannolikt neutraliseraende IgA antikroppar mot Spike proteinet



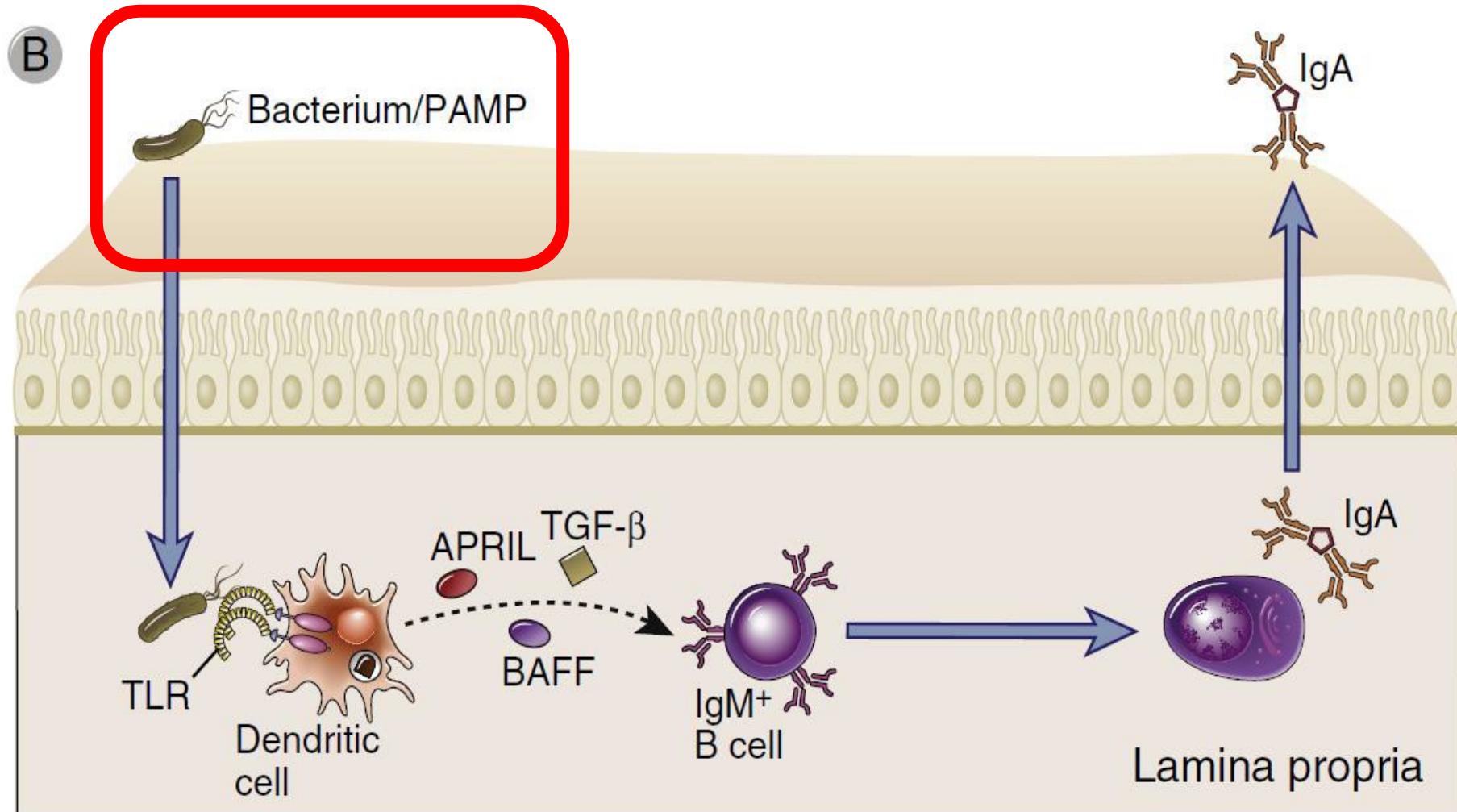
Antikroppssvar efter Covid-19



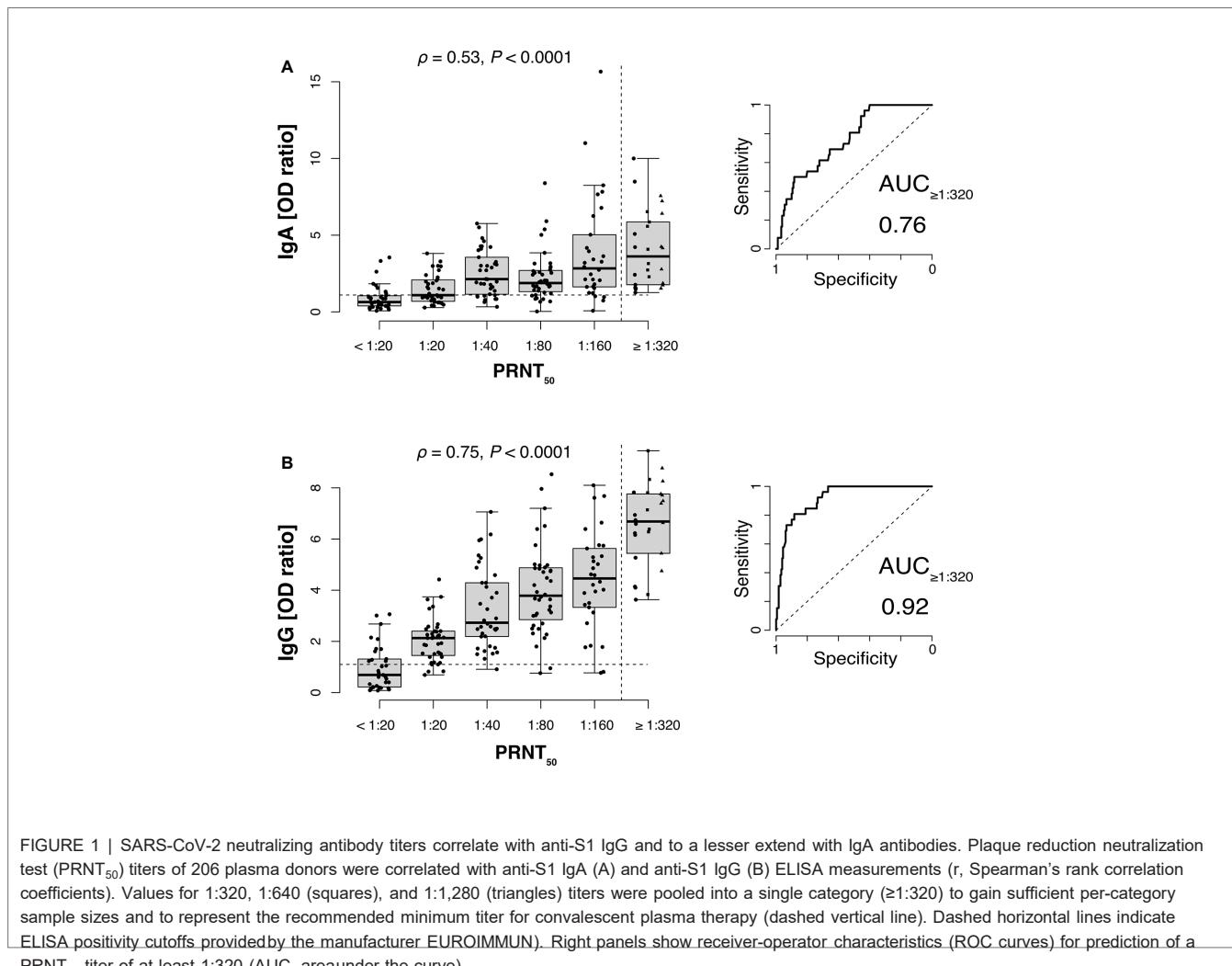
IgA class switching -T-dependent IgA class switching



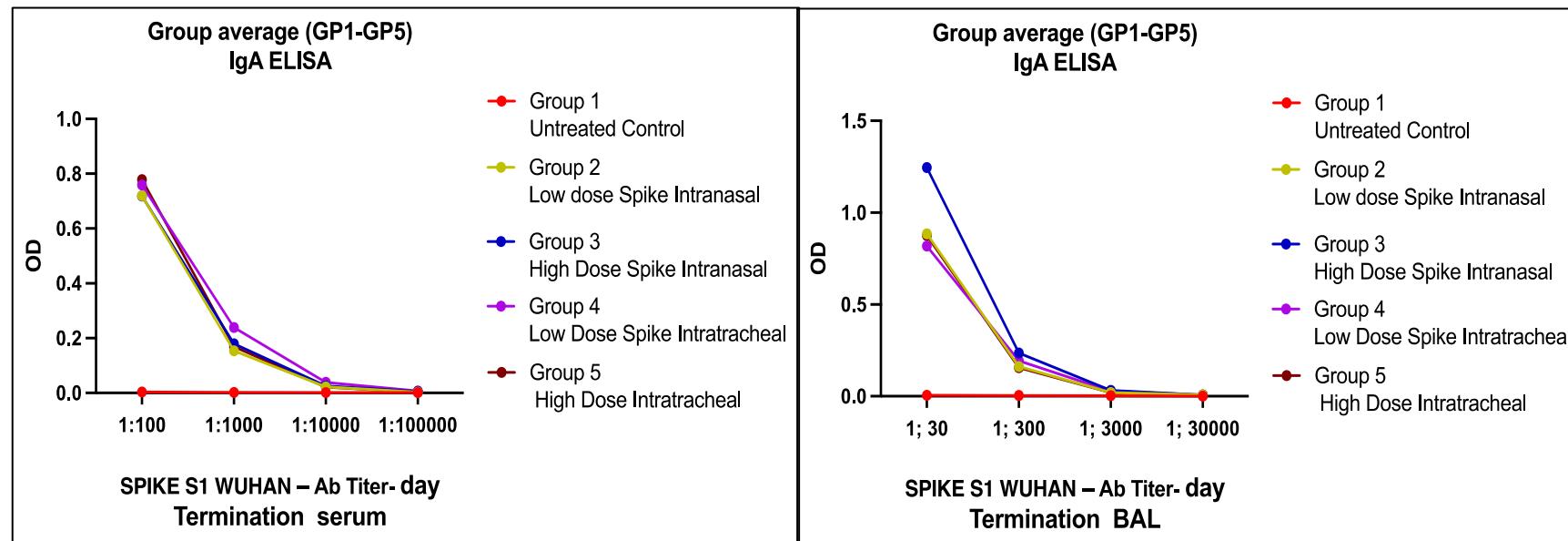
IgA class switching. T-independent IgA class switching



Neutraliserande antikroppar korrelerar med anti S1 IgG och IgA i konvalescensprover



Inhalation eller intranasal installation av spike i musmodell ger IgA svar i lunga och i serum



SERUM

BAL



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE CORONAVIRUS

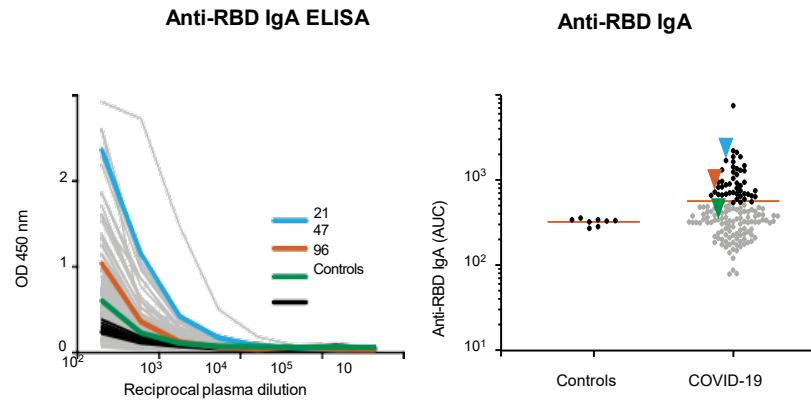
Enhanced SARS-CoV-2 neutralization by dimeric IgA

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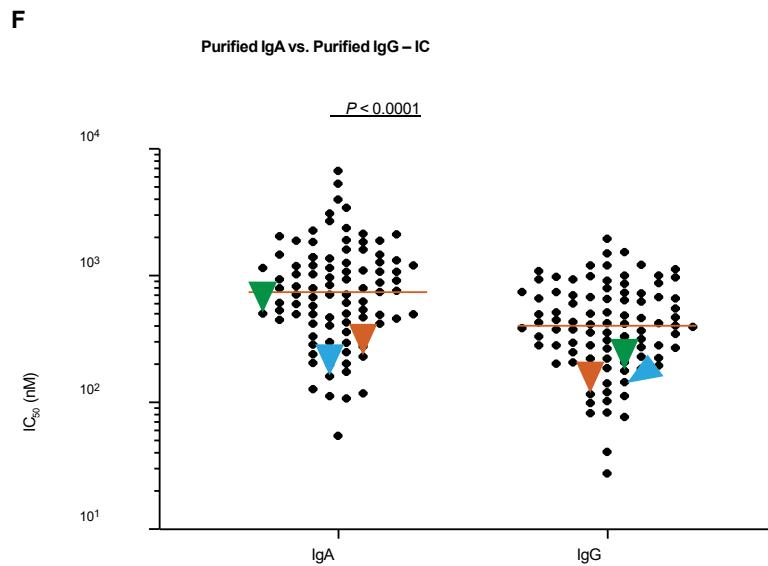
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Zijun Wang^{1*}, Julio C. C. Lorenzi^{1*}, Frauke Muecksch^{2*}, Shlomo Finkin^{1*}, Charlotte Viant¹,
Christian Gaebler¹, Melissa Cipolla¹, Hans-Heinrich Hoffman³, Thiago Y. Oliveira¹,
Deena A. Oren⁴, Victor Ramos⁵, Lilian Nogueira⁶, Eleftherios Michailidis⁷, Davide F. Robbiani⁸,
Anna Gazumyan¹, Charles M. Rice³, Theodora Hatzioannou², Paul D. Bieniasz^{2,6}, Marina Caskey¹, Michel C. Nussenzweig^{1,6†}

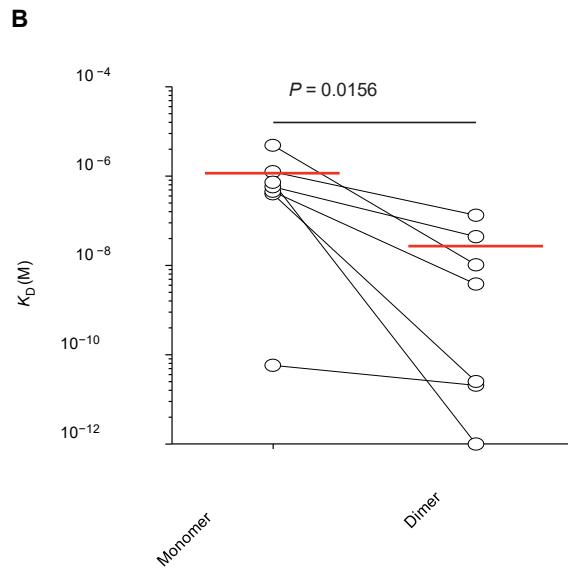
RBD bindande IgA antikroppar ökade i plasma från Covid patienter



Pseudovirus neutralising IgA vs IgG



Dimeriskt IgA har högre affinitet än monomert IgA för RBD domänet



Although the monomeric form of IgA found in serum is, on average, twofold less potent than IgG, the dimeric, secretory form of IgA found in mucosa is more than one log more potent than their respective monomer forms against authentic SARS-CoV-2, suggesting that dimeric IgA is a more potent neutralizer than IgG.

PUB MED

Sök term	Utfall
Selective IgA deficiency	1176
Covid-19	194 745
Selective IgA deficiency AND Covid-19	4

Releationship between selective IgA deficiency and Covid-19 prognosis

Patientmaterial

423 patienter Covid 19

11 patienter SIgAD

IgA brist ser ut att ge ökad risk för svår Covid-19

Slutsatser:

Risken för svår Covid-19 sjukdom var 7.7 ggr högre i SIgAD gruppen

Serum IgA nivåer korrelerade med lymfocytantal

Serum IgA korrelerade negativt med CRP

Original Article

Association between selective IgA deficiency and COVID-19

Yuji Naito,^{1,*} Tomohisa Takagi,¹ Tetsuro Yamamoto,² and Shaw Watanabe³

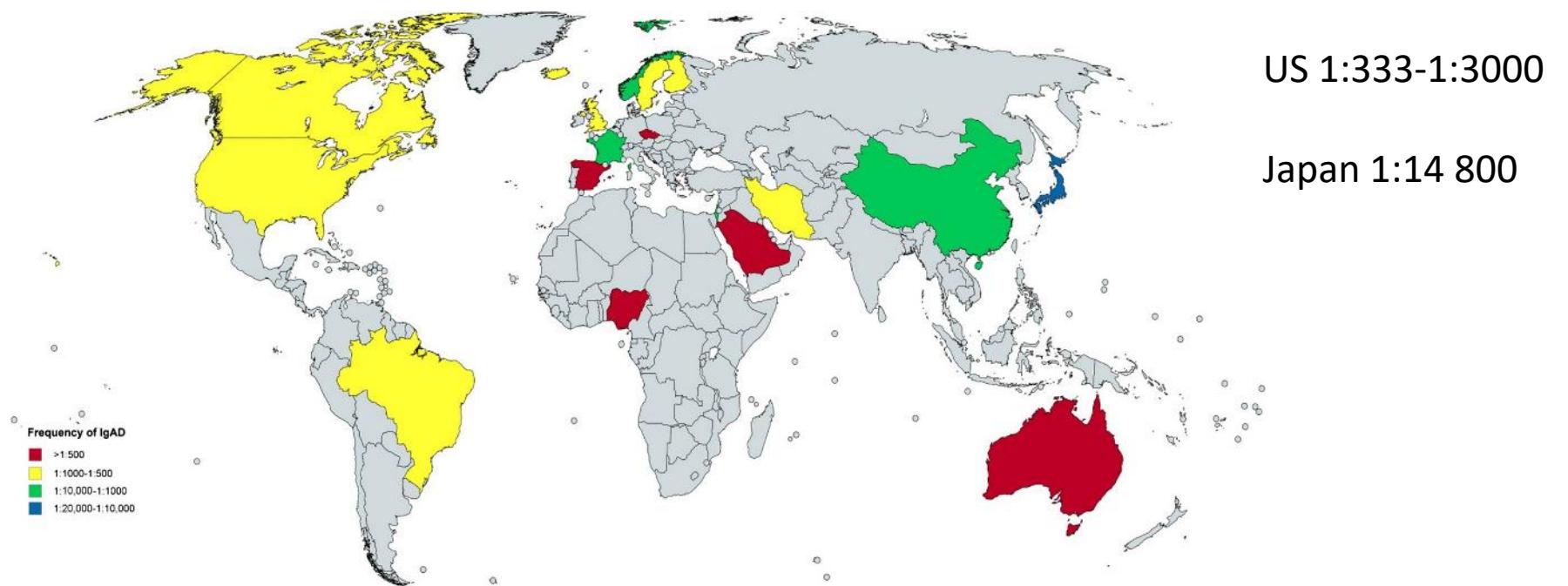
¹Department of Gastroenterology and Hepatology, Kyoto Prefectural University of Medicine, 465 Kajii-cho, Kamigyo-ku, Kyoto 602-8066, Japan

²TTC Co. Ltd., 1-20-2 Ebisu-nishi, Sibuya-ku, Tokyo 150-0021, Japan

³Asia Pacific Clinical Nutrition Society, Life Science Promoting Association, 25-3-1004 Daijyo-cho, Shinjuku, Tokyo 160-0015, Japan

(Received 12 June, 2020; Accepted 24 June, 2020; Published online 21 August, 2020)

Prevalens av IgA brist i världen



Antalet Covid-19 fall och incidens av selektiv IgA brist

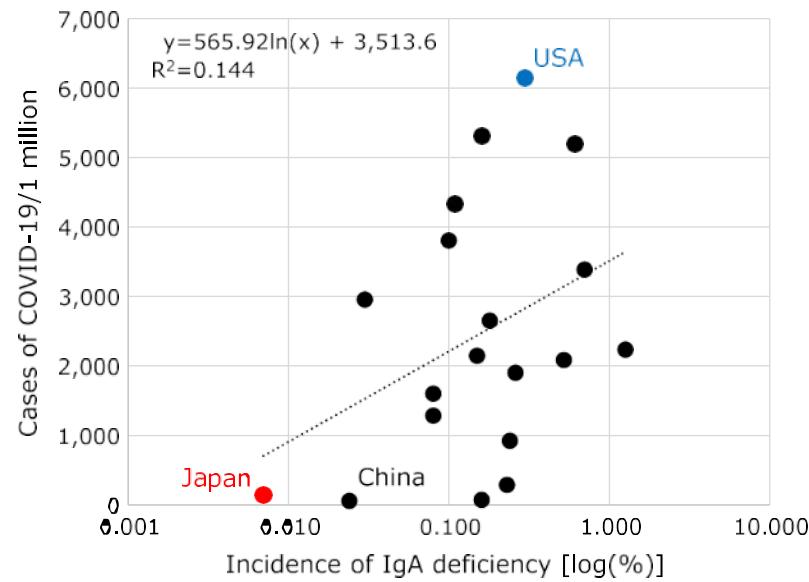


Fig. 3. Correlation between the COVID 19 infection rate and frequency of selective IgA deficiency.

Autoimmunity complicating SARS-CoV-2 infection in selective IgA-deficiency

Steffen Pfeuffer, MD, Matthias Pawlowski, MD, PhD, Gunther S. Joos, Jens Minnerup, MD, Sven G. Meuth, MD, PhD, Rainer Dziewas, MD, and Heinz Wiendl, MD

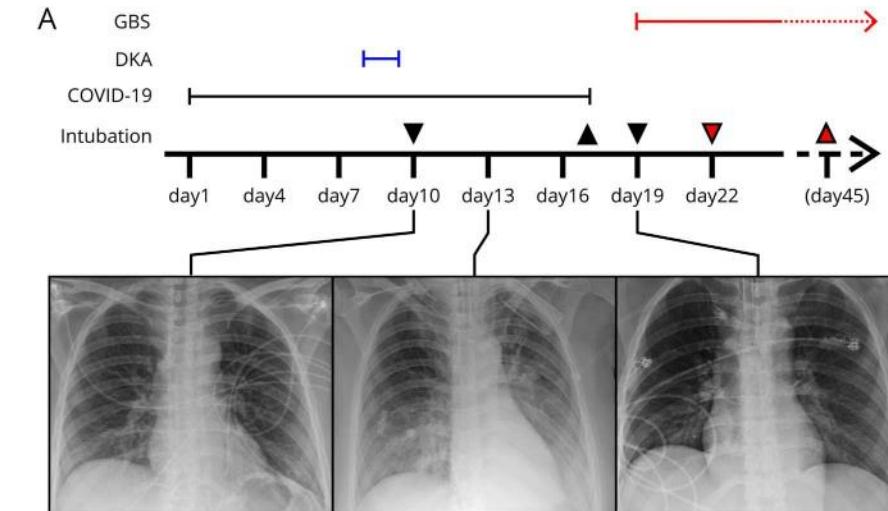
Neurol Neuroimmunol Neuroinflamm 2020;7:e881. [doi:10.1212/NXI.0000000000000881](https://doi.org/10.1212/NXI.0000000000000881)

35 årig tid frisk kvinna presenterar med feber och hosta och blir diagnosticerad med positiv PCR SARS-CoV-2 efter 1 vecka

Dag 8 Diabetes ketoacidos GAD 65 antikropp positiv HbA1C% 6.4

Dag 10 Försämrad syresättning pga Covid, läggs i respirator

Dag 17 extuberad



Behandling

5 plasmafereser med snabb återhämtning

Kvarstående bulbär pares och trachestomerad med ventilator dag 22-45

Därefter mild svalgpares

Insulinberoende diabetes

Tolkning

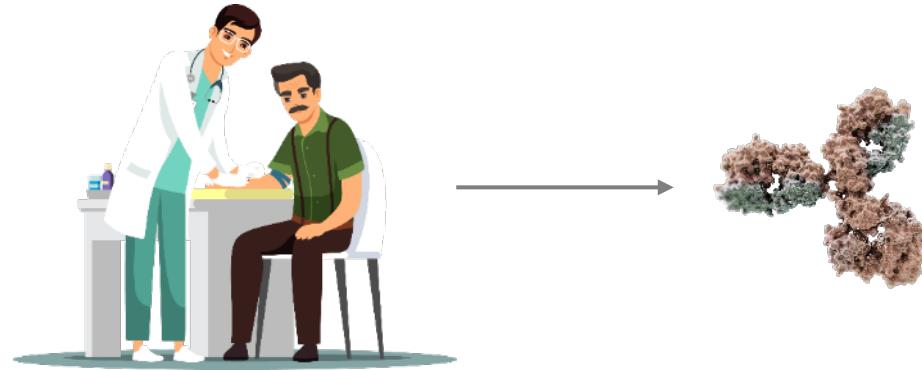
Odiagnosticerad IgAD

vilket går med ökad risk för autoimmunitet
ökad risk svår Covid?

SARS-CoV-2 finns beskrivet att kunna utlösa GBS
spike kan binda till ganglioside antigen och ge upphov till immunisering

Snabbt uppkommen T1D (lågt HbA1C)
T cells medierad

Utveckling av SARS-CoV-2 neutraliserande IgA för terapi

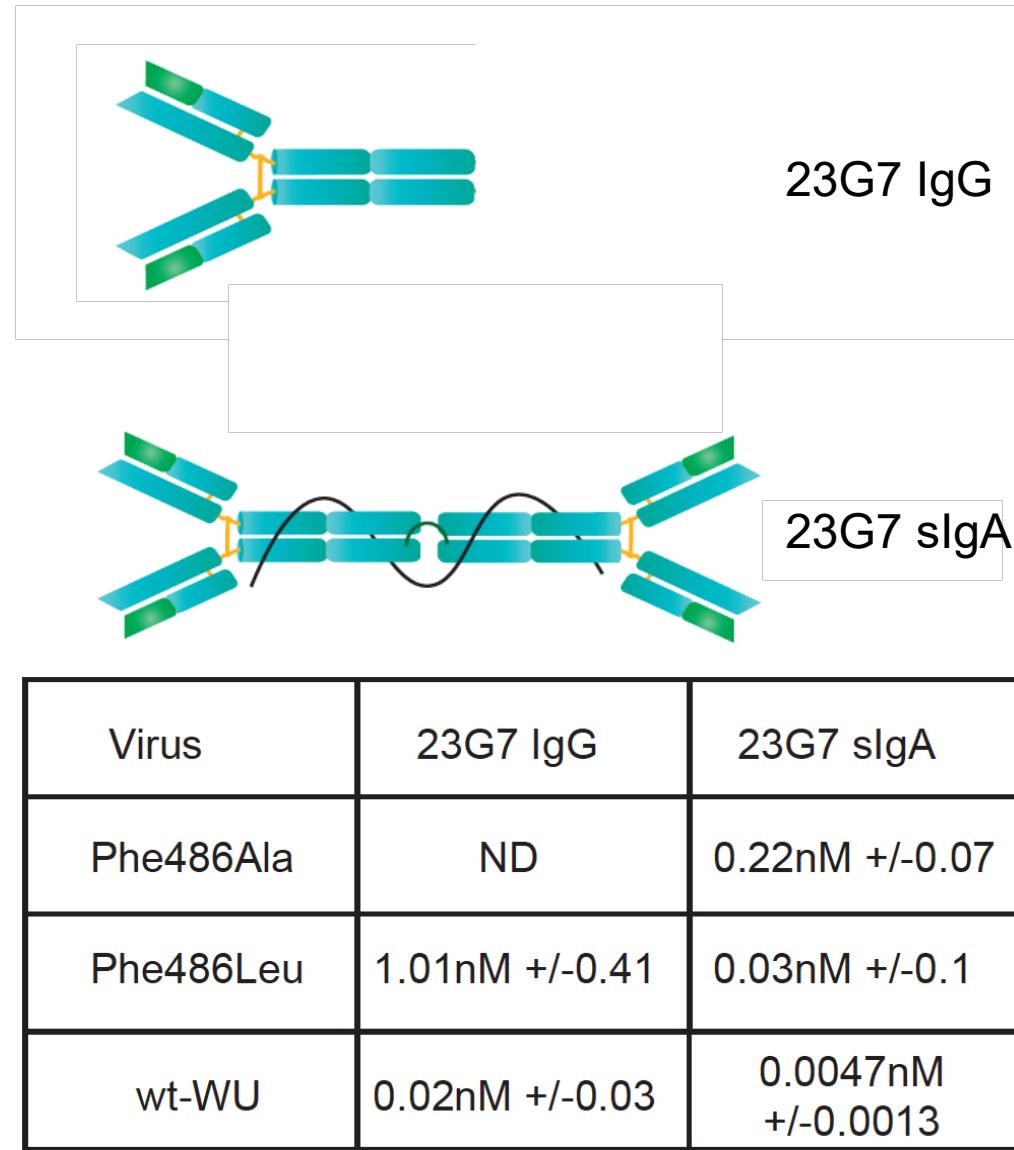
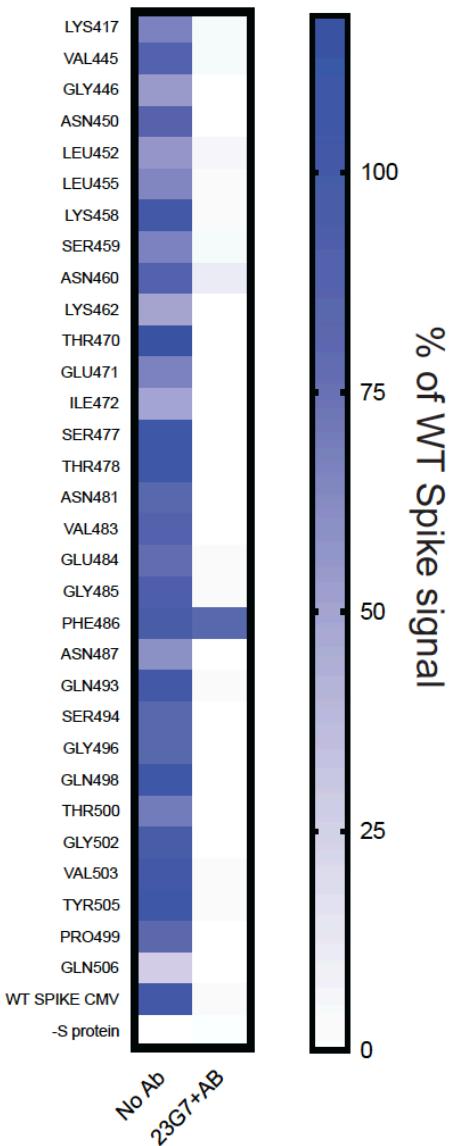


**Blod från
patienter
tillfrisknade från
Covid-19**

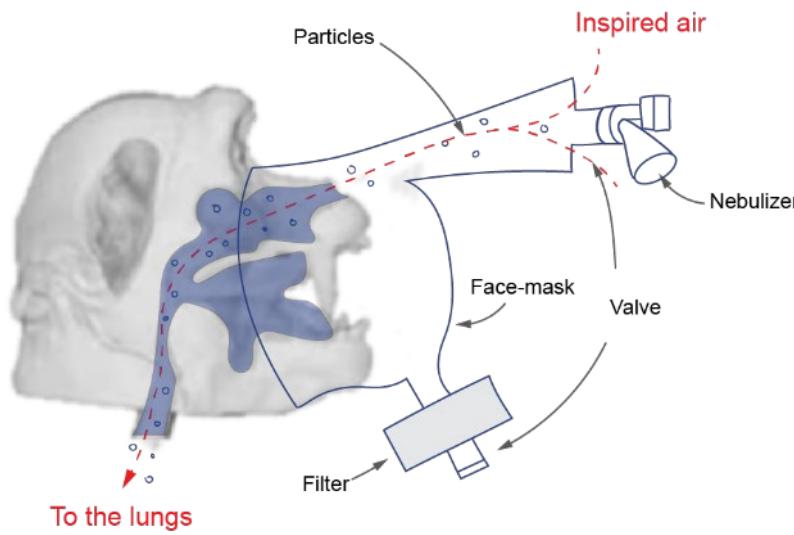
**Isolera SARS-CoV-2
neutraliserande
antikroppar**

slgA är mer potent och resistent mot mutationer i RBD domänet

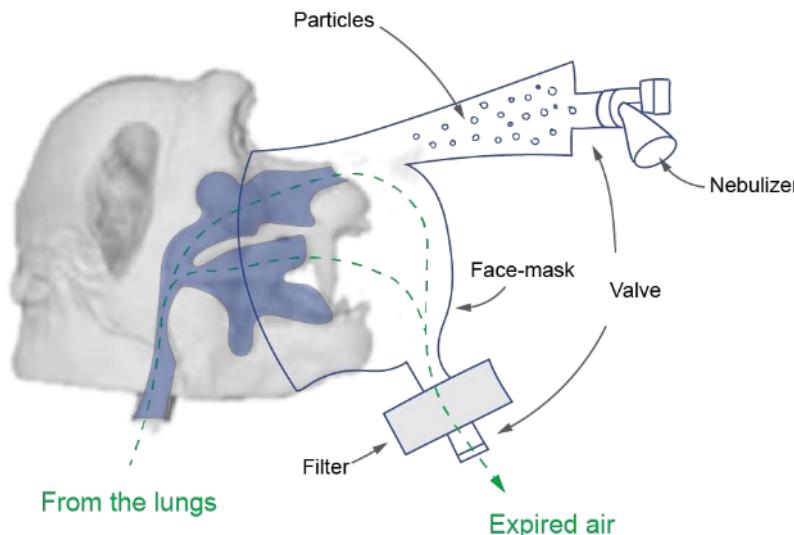
RBD Ala scanning



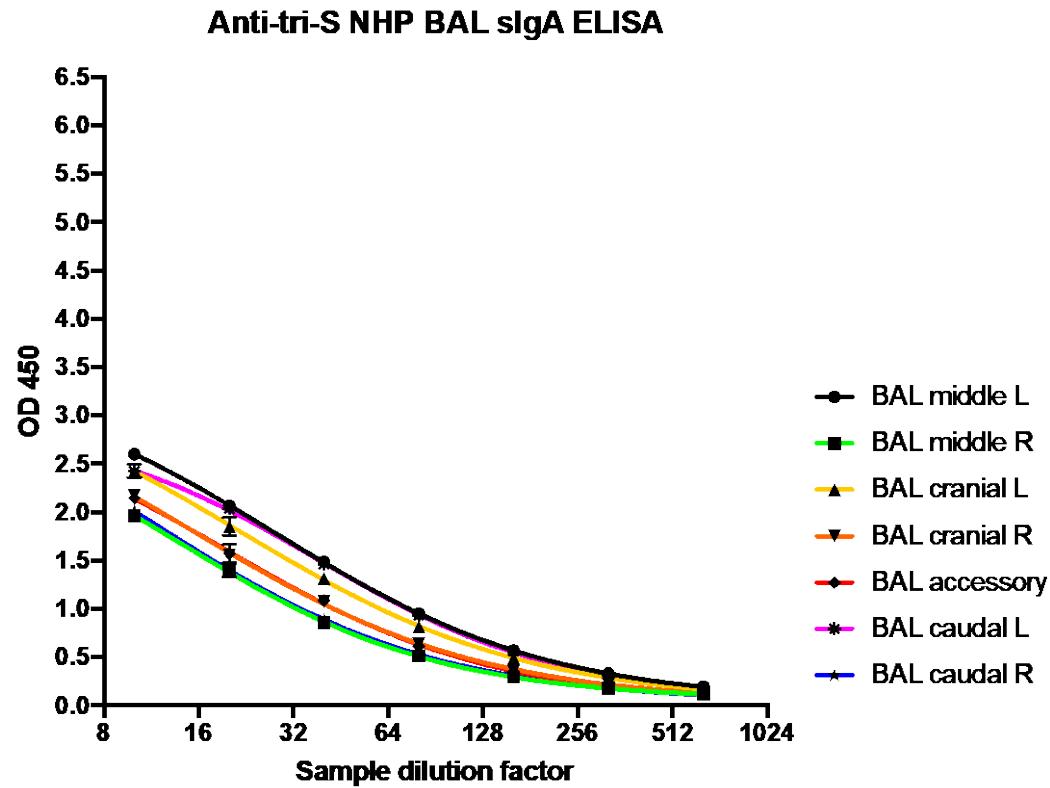
Leverans av SARS-CoV-2 neutraliserande antikroppar genom nebulisering



- Antikroppsbehandling mot svår Covid-19 har försöks med blandad framgång
- I.V administrering begränsar SARS-CoV-2 antikroppseffekt
- Antikropps nebulisering av SARS-CoV-2 neutraliserande sIgA till lungan skulle kunna vara en intressant terapeutisk möjlighet



sIgA detekteras i BAL efter nebulisering





IgA antikroppar neutraliseringande ev. med högre affinitet mot SARS-CoV-2

I liten serie ser det ut att vara en högre risk att bli svårt sjuk om man har IgA brist

Det finns antydan i epidemiologiska data att förekomst av SlgAD varierar med insjuknande

Spike specifikt IgA kommer kanske kunna erbjudas i framtiden för behandling