Longitudinální sledování imunitní odpovědi po vakcinaci

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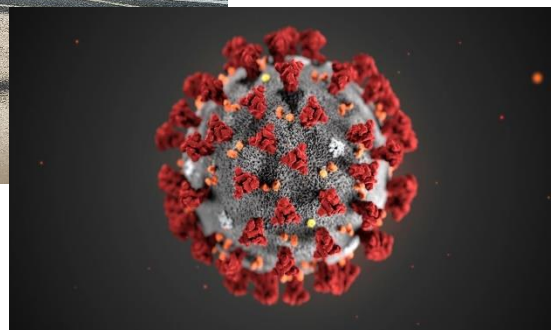
Nemocnice Na Homolce

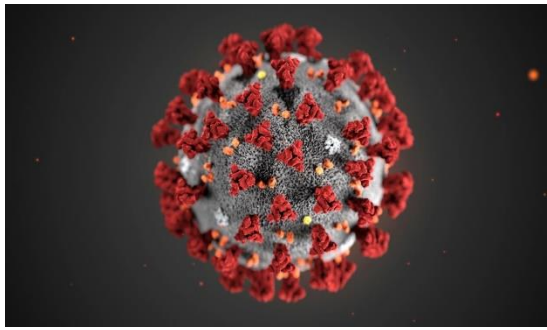
Kroměříž 23.9.2021

Dicata monumentum prof. MUDr. Danuši Táborské, DrSc.



Imunopatogeneze COVID 19

- In addition to SARS-CoV-2, six human coronaviruses (hCoVs) are known: four seasonal coronaviruses (hCoV-229E, -NL63, -HKU1, and -OC43) which cause mild upper respiratory diseases, and the two most recently discovered viruses, SARS-CoV-1 and MERS-CoV, originating from recent zoonotic events



Article

SARS-CoV-2-specific T cell immunity in cases of COVID-19 and SARS, and uninfected controls

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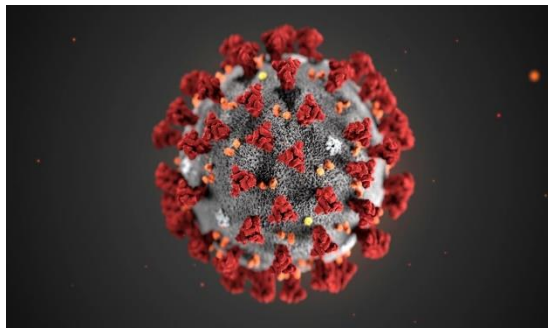
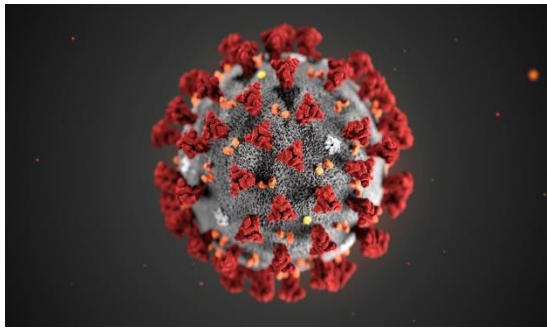


Memory T cells induced by previous pathogens can shape susceptibility to, and the clinical severity of, subsequent infections[1]. Little is known about the presence in humans of pre-existing memory T cells that have the potential to recognize severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Here we studied T cell responses against the structural (nucleocapsid (N) protein) and non-structural (NSP7 and NSP13 of *ORF1*) regions of SARS-CoV-2 in individuals convalescing from coronavirus disease 2019 (COVID-19) ($n = 36$). In all of these individuals, we found CD4 and CD8 T cells that recognized multiple regions of the N protein. Next, we showed that patients ($n = 23$) who recovered from SARS (the disease associated with SARS-CoV infection) possess long-lasting memory T cells that are reactive to the N protein of SARS-CoV 17 years after the outbreak of SARS in 2003; these T cells displayed robust cross-reactivity to the N protein of SARS-CoV-2. We also detected SARS-CoV-2-specific T cells in individuals with no history of SARS, COVID-19 or contact with individuals who had SARS and/or COVID-19 ($n = 37$). SARS-CoV-2-specific T cells in uninfected donors exhibited a different pattern of immunodominance, and frequently targeted NSP7 and NSP13 as well as the N protein. Epitope characterization of NSP7-specific T cells showed the recognition of protein fragments that are conserved among animal betacoronaviruses but have low homology to 'common cold' human-associated coronaviruses. Thus, infection with betacoronaviruses induces multi-specific and long-lasting T cell immunity against the structural N protein. Understanding how pre-existing N- and ORF1-specific T cells that are present in the general population affect the susceptibility to and pathogenesis of SARS-CoV-2 infection is important for the management of the current COVID-19 pandemic.

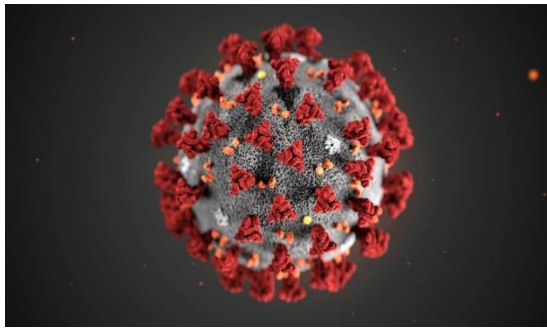
Aktuální situace a otázky

- „nejstarší“ vakcinovaní – cca 1 rok
- Účinnost vakcíny cca 90%
- Jak dlouho „vydrží“ imunita po očkování?
- Bude nutná 3 injekce?

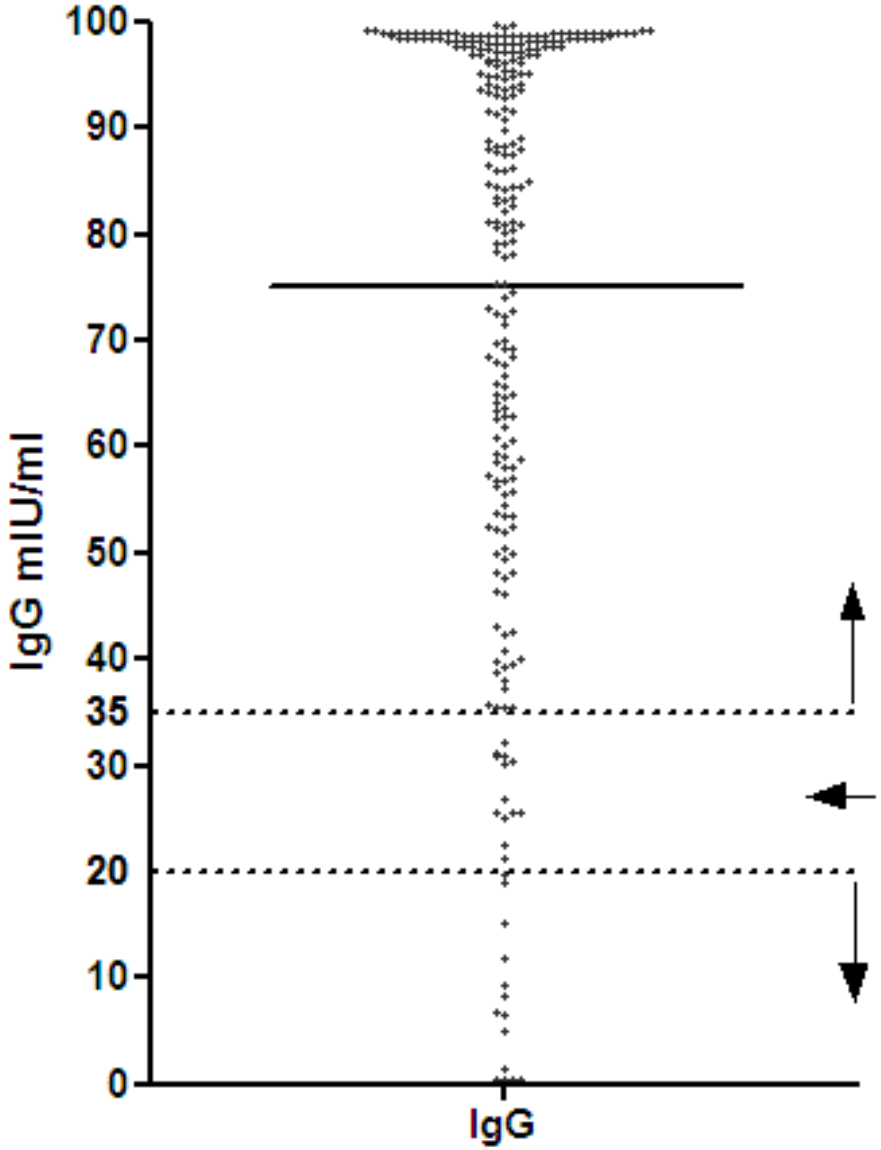


Naše zkušenosti

- Podáno cca 2800 dávek
- Bez celkové anafylaktické reakce
- Vyšetření přecitlivělosti na PEG provádíme
- NÚ – závažné – jednotky pacientů
- Indukce revmatologického onemocnění – PR, dermatomyositida



Hodnoty IgG (Anti-SARS-CoV-2 NeutraLISA)

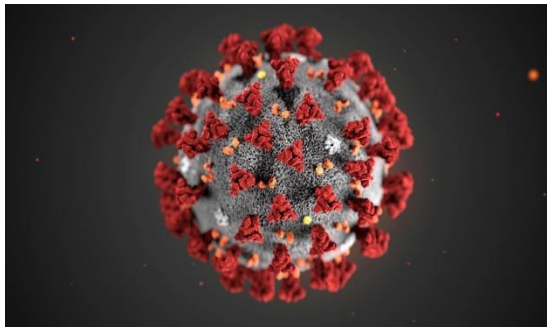


264 probandů

pozitivita: 237 (89,8%)

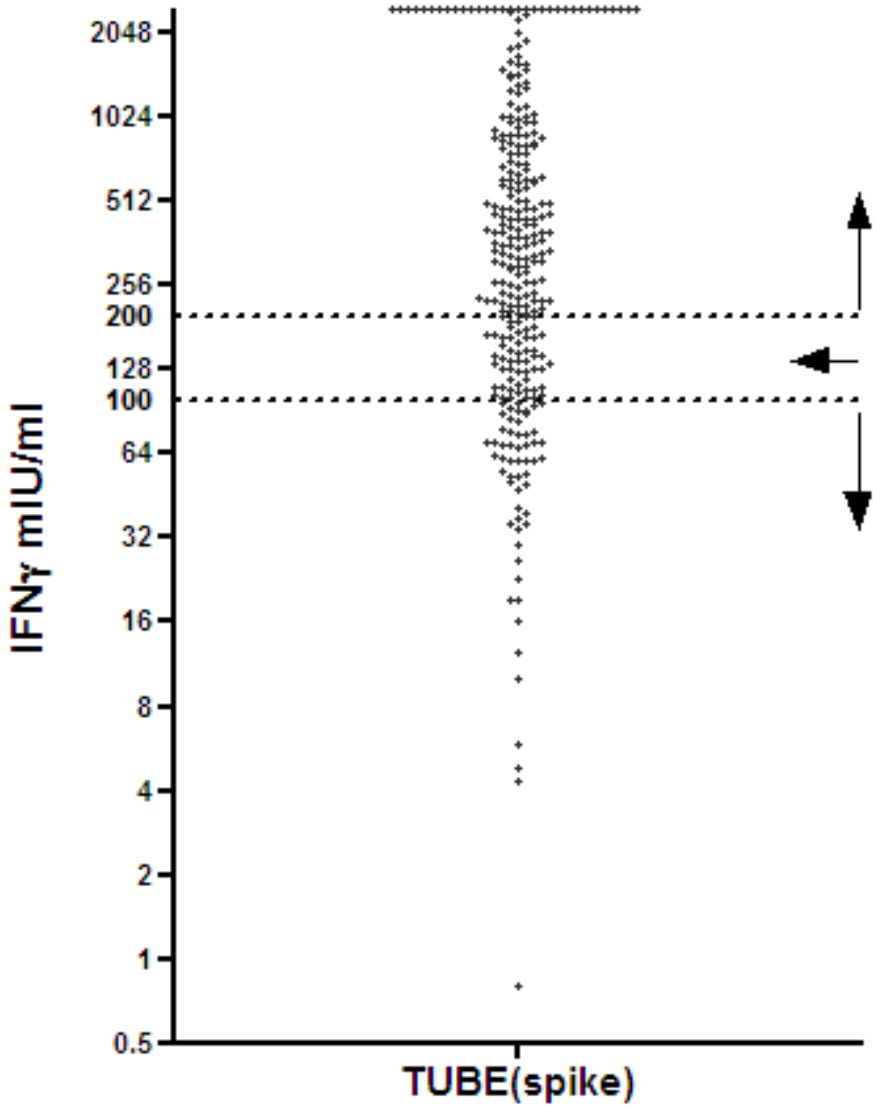
hraniční hodnoty: 13 (4,9%)

negativita: 14 (5,3%)



hodnoty IFNγ po stimulaci spike proteinem

(IGRA Quan T cell, CE IVD)

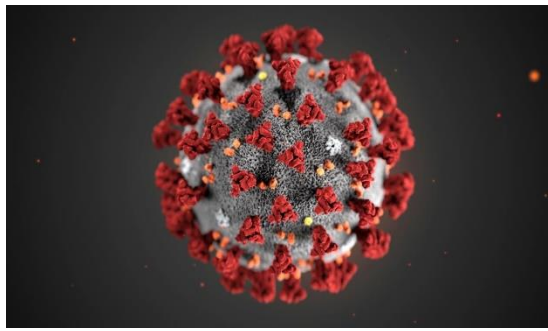


297 probandů

pozitivita: 188 (63,3%)

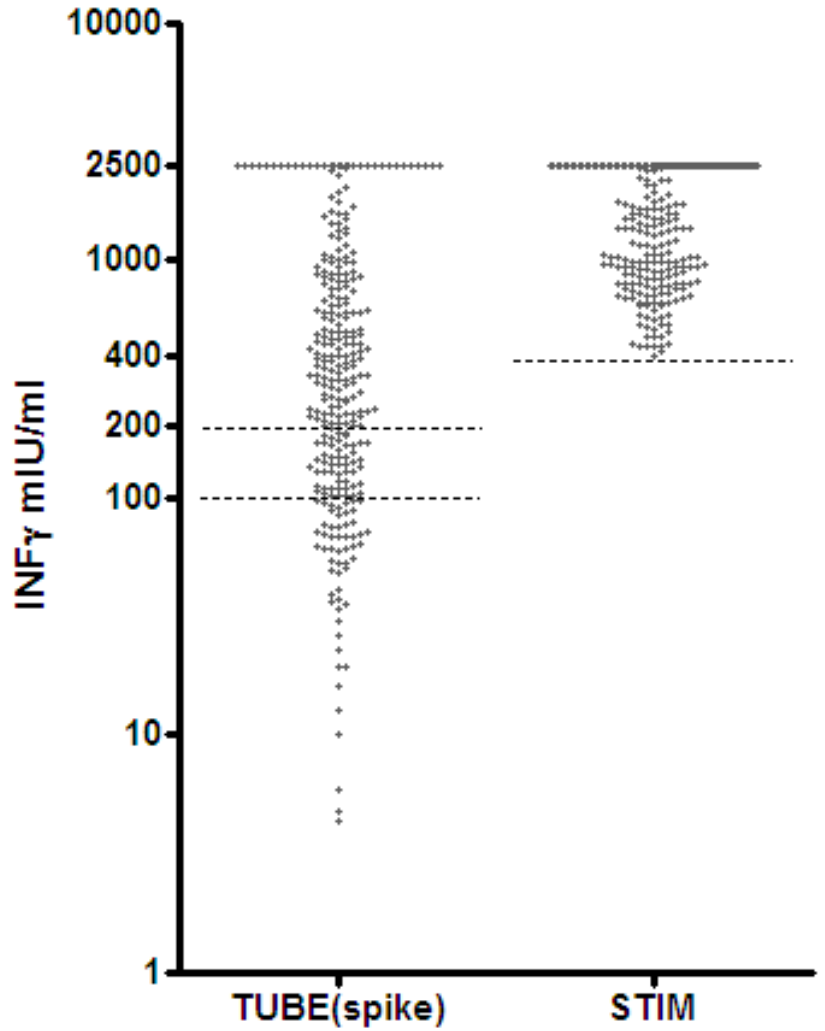
hraniční hodnoty: 52 (17.5%)

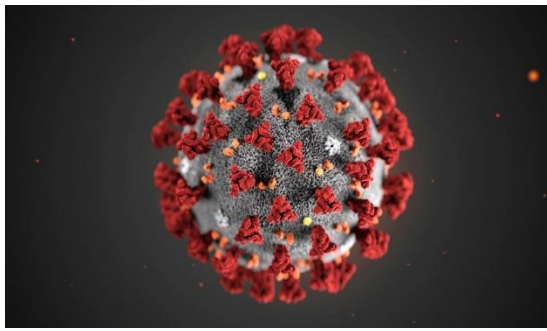
negativita: 57 (19.2%)



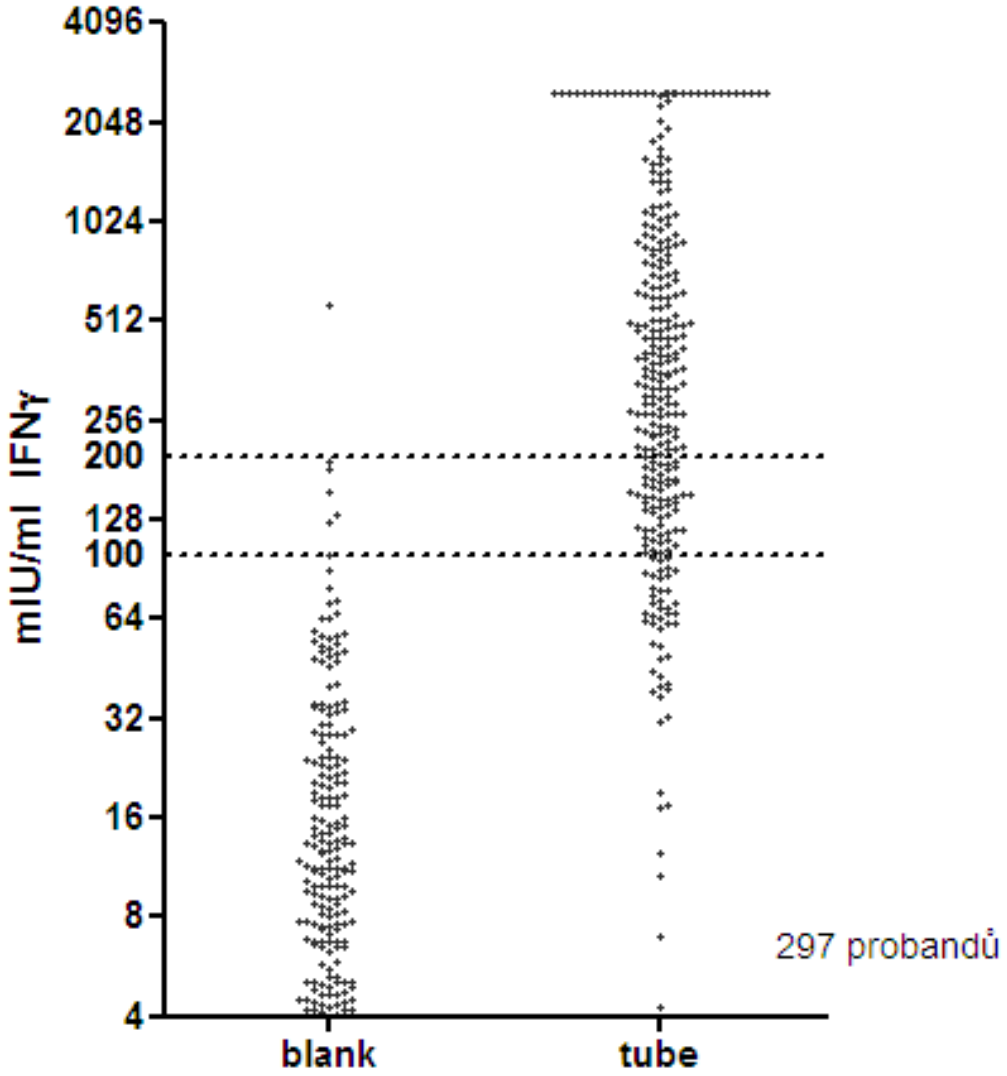
Hodnoty IFNγ Stimulace spike proteinem(TUBE -spike) a mitogenem(STIM)

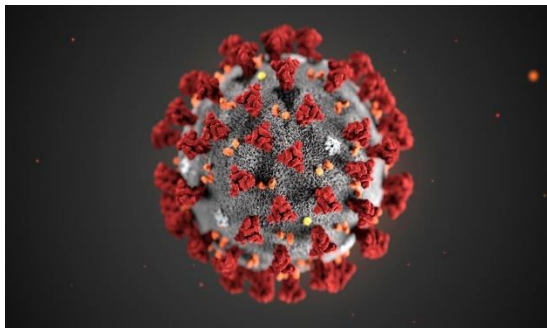
(IGRA Quan T cell, CE IVD)





Porovnání hodnot IFNγ před (*blank*) a po stimulaci spike proteinem (*tube*)





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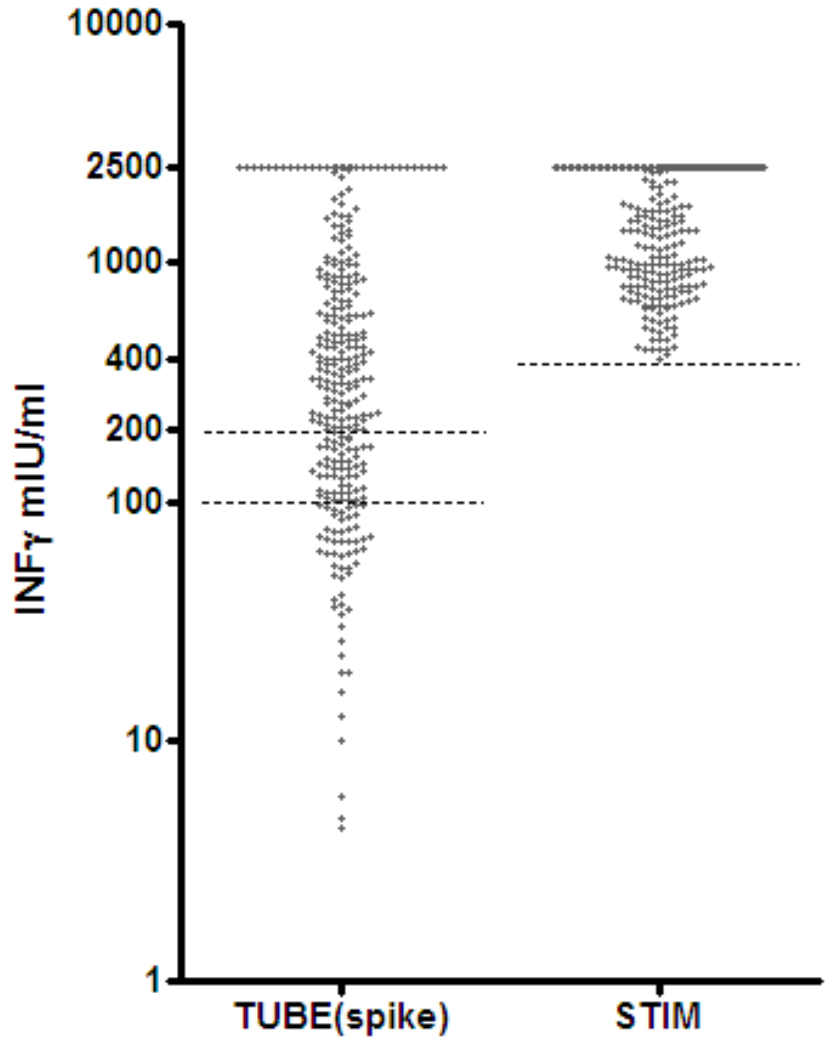
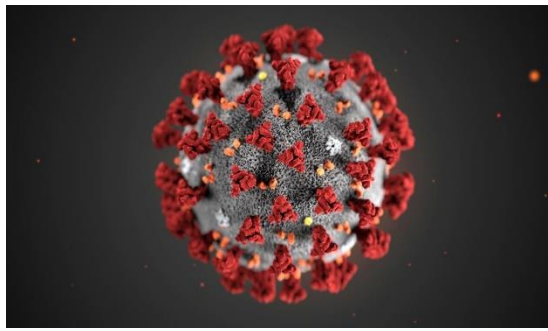
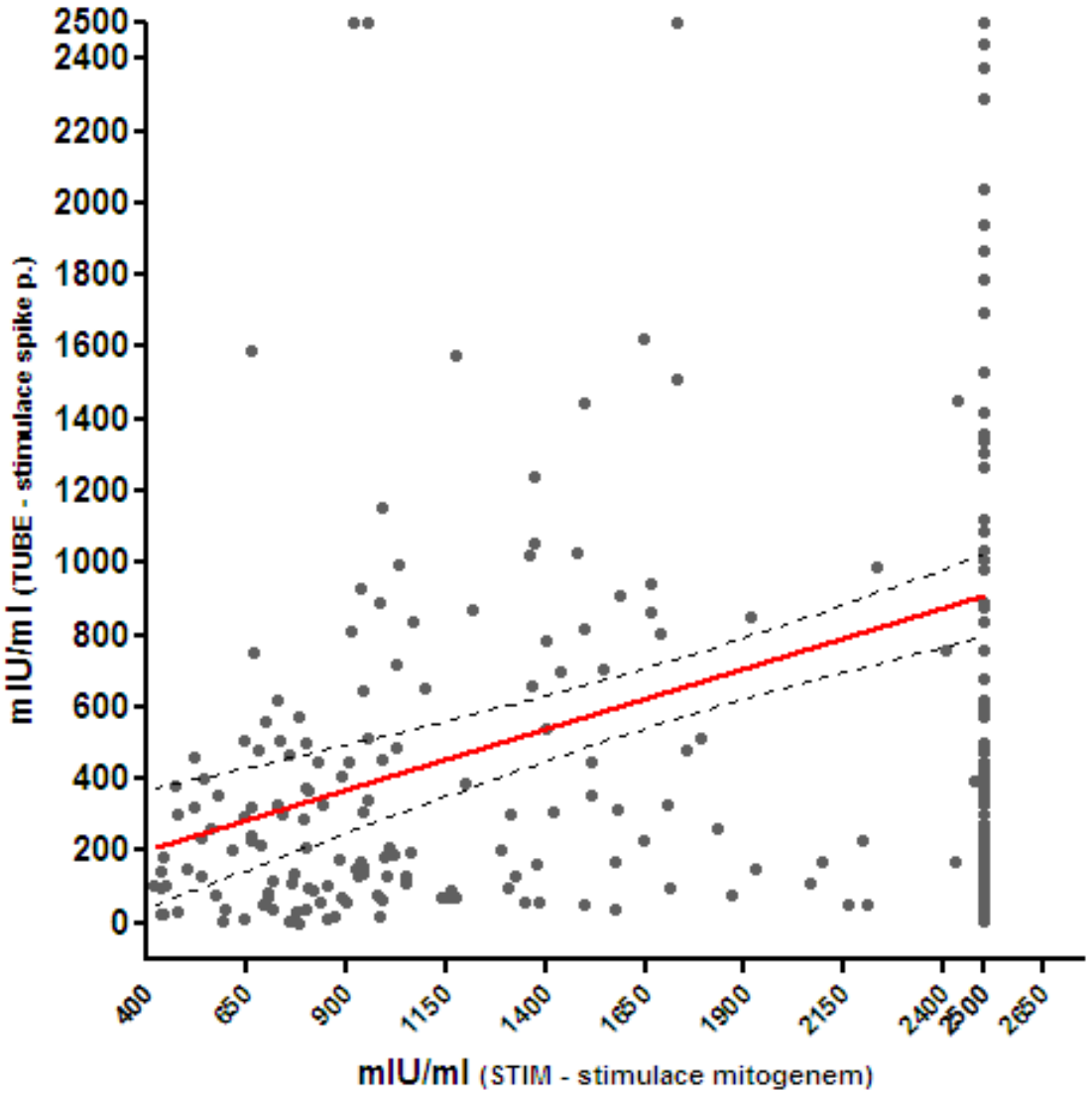


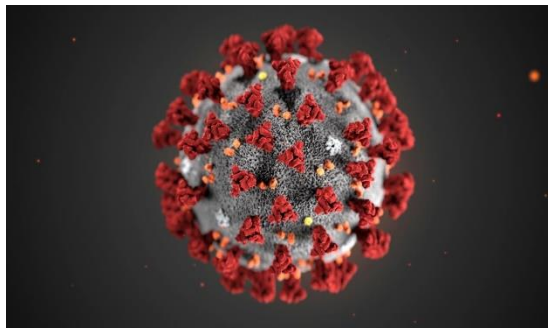


Korelace STIM a TUBE (IGRA Quan T cell, CE IVD)



počet: 297
Spearman r: 0,3046
95%CI: 0,1943-0,4072
P (two-tailed): P<0.0001
= **Signifikantní korelace**

Goodness of fit: r2 | 0.1164

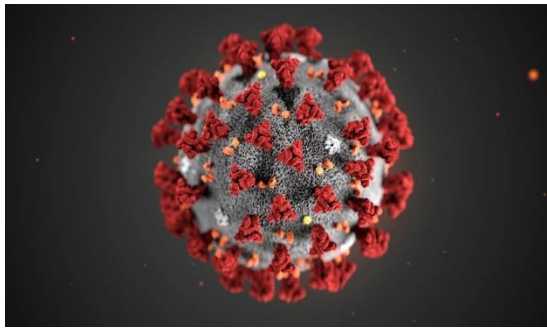


Naše zkušenosti

- Aktivní depistáž pacientů s rizikem
  – imunosuprese, autoimunitní onemocnění, st. p. transplantaci

- Cca 50% účinnost

- Po 3.dávce polovina z nereagujících zareaguje

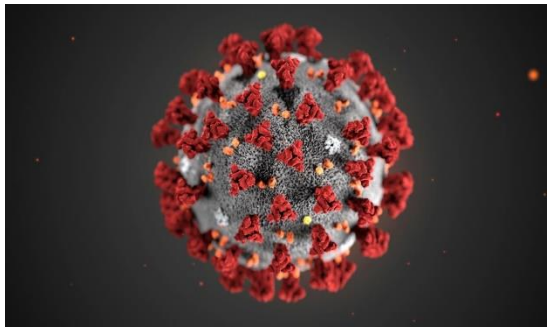


Comparing the COVID-19 Vaccines: How Are They Different?

Pfizer-BioNTech

In April, the company announced the vaccine had 91.3% efficacy against COVID-19, based on measuring how well it prevented symptomatic COVID-19 infection seven days through up to six months after the second dose. It also found it to be 100% effective in preventing severe disease as defined by the CDC, and 95.3% effective in preventing severe disease as defined by the FDA. Another study, not yet peer-reviewed, provided more new data that brought the efficacy number down to 84% after 6 months, although efficacy against severe disease was 97%.

As far as the Delta variant (first seen in India), two studies reported by Public Health England that have not yet been peer reviewed showed that full vaccination after two doses is 88% effective against symptomatic disease and 96% effective against hospitalization. But Israel later reported the vaccine's effectiveness to be 90% effective against severe disease, and 39% against infection in its population in late June and early July, based on an analysis of the country's national health statistics.



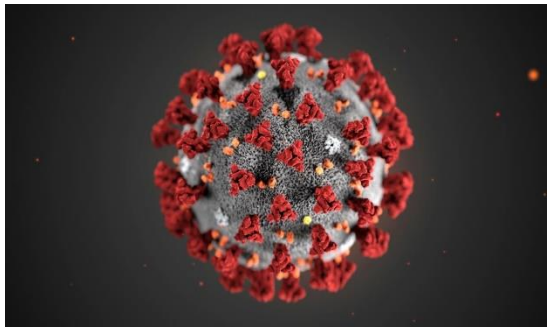
Moderna

How well it works: Greater than 90% efficacy against cases of COVID-19 and more than 95% against severe cases, with approximately 6 months median follow-up after the second dose, according to the company. Earlier Phase 3 studies showed Moderna to be 94.1% effective at preventing symptomatic infection in people with no evidence of previous COVID-19 infection (although the efficacy rate drops to 86.4% for people ages 65 and older).

In late March, a small CDC study that enrolled 3,950 health care personnel, first responders, and other essential and frontline workers showed the vaccine to be 90% effective upon full immunization (at least 14 days after the second dose) in real-world conditions.

In August, the CDC also published studies that showed mRNA vaccine protection against infection may be waning, although the vaccines were still highly effective against hospitalization. In one CDC study, data from the state of New York showed vaccine effectiveness dropping from 91.7 to 79.8% against infection.

How well it works on virus mutations: Some research has suggested that Moderna's vaccine may provide protection against the Alpha and Beta variants. In June, Moderna reported that studies showed its vaccine is effective against the Beta, Delta, Eta, and Kappa variants, although it did show it to be about two times weaker against Delta than against the original virus.

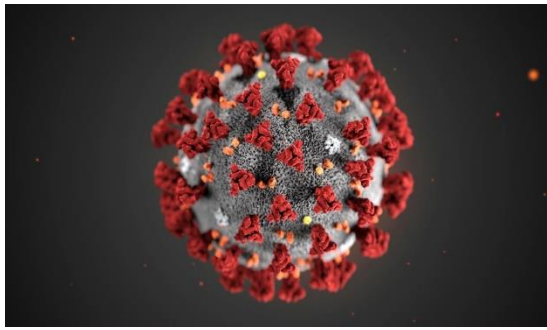


Johnson & Johnson

How well it works: 72% overall efficacy and 86% efficacy against severe disease in the U.S., according to analyses posted by the FDA in February. In August, the company announced that new data showed a booster shot at six months had a rapid and robust nine-fold increase in spike-binding antibodies in volunteers compared to 28 days after their first dose. That data has not yet been peer-reviewed or published in a scientific journal.

How well it works on virus mutations: Johnson & Johnson reported in July that its vaccine is also effective against the Delta variant, showing only a small drop in potency compared with its efficacy against the original strain of the virus, although one recent study suggested that the J&J vaccine is less effective against Delta.

But the first study to assess the vaccine against Delta in the real world reported the vaccine to be 71% effective against hospitalization and up to 95% effective against death. The vaccine's performance was slightly lower against the Beta variant in the study. This preliminary research was reported in August at a news conference by the Ministry of Health in South Africa. These studies have not yet been peer-reviewed or published in a scientific journal.



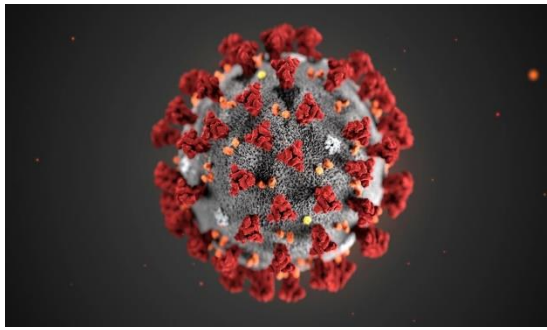
Osobní pohled

- Nejsem pro plošnou revakcinaci
- Měla by být aktivní depistáž s ohledem na rizikové faktory

Table A. SARS-CoV-2 Variants of Concern and Interest and Susceptibility to Anti-SARS-CoV-2 Monoclonal Antibodies

Who Label	Pango Lineage	CDC Variant Class	Notable Mutations	Bamlanivimab Plus Etesevimab		Casirivimab Plus Imdevimab		Sotrovimab	
				In Vitro Susceptibility[a]	Activity[b]	In Vitro Susceptibility[a]	Activity[b]	In Vitro Susceptibility[a]	Activity[b]
Alpha	B.1.1.7	VoC	N501Y	No change	Active	No change	Active	No change	Active
Beta	B.1.351	VoC	K417N, E484K, N501Y	Marked change	Unlikely to be active	No change[c]	Active	No change	Active
Gamma	P.1	VoC	K417T, E484K, N501Y	Marked change	Unlikely to be active	No change[c]	Active	No change	Active
Delta	B.1.617.2	VoC	L452R	Modest change[d]	Likely to be active	No change	Active	No change	Active
Epsilon	B.1.429/B.1.427	VoI	L452R	Modest change[d]	Likely to be active	No change	Active	No change	Active
Iota	B.1.526	VoI	E484K	Modest change[d]	Likely to be active	No change[c]	Active	No change	Active

[a] Based on the fold reduction in susceptibility reported in the FDA EUAs.[5-7]
[b] Anticipated clinical activity against the variant, based on in vitro studies.
[c] Marked change for casirivimab and no change for imdevimab. The combination of casirivimab plus imdevimab appears to retain activity.
[d] Modest change for the combination of bamlanivimab and etesevimab, although the clinical implications of this finding are not fully known.
Key: CDC = Centers for Disease Control and Prevention; VoC = variant of concern; VoI = variant of interest; WHO = World Health Organization.



Děkuji za pozornost

FDA Panel Says Boosters Aren’t Recommended for General Population

After weeks and months of speculation regarding the necessity of Covid vaccine boosters and waning immunity, an international group of scientists has announced that booster shots for the general public are not necessary at this time.

According to NPR, “In a surprising vote, a panel of advisers to the Food and Drug Administration on Friday recommended against approval of a booster dose of the Pfizer-BioNTech COVID-19 vaccine for people 16 years and older.

The 16-2 vote against broad use of the booster, which would be given about six months after completion of the two-dose immunization regimen, dealt a setback to Pfizer and complicates the FDA's approach to boosters.

After a brief intermission following the rejection, FDA officials returned to the meeting with a revised booster question. The panel then voted 18-0 in support of the agency authorizing a booster shot of the vaccine for people 65 and older or at high risk of severe COVID-19.

The FDA then polled the panel members for advice on other groups of people who might be considered for a booster. Though not an official vote, the panel members unanimously supported authorization of a Pfizer booster dose for health care workers or others at high risk of occupational coronavirus exposure.

The agency typically follows the advice of its advisory committees, though it isn't required to...

The rise of the highly infectious delta variant of the SARS-CoV-2 coronavirus and some evidence that the Pfizer vaccine's protection against infections wanes with time are two of the factors that were cited in support of a booster.

But presentations Friday generally showed that the vaccine is still effective in protecting immunized people against severe illness, hospitalization and death in the United States.

Separately, however, an analysis published Friday in the CDC's 'Morbidity and Mortality Weekly Report' found that the Pfizer vaccine's protection against COVID-19 hospitalization dropped from 91% during the first 120 days after vaccination to 77% in the days after that.

Over the course of the meeting, speakers from the FDA, Pfizer, the CDC, Israel and the U.K. presented data on the state of the coronavirus pandemic, experience with the Pfizer vaccine and lab tests.

The most direct support for the Pfizer booster came from laboratory work and a clinical study done by Pfizer that involved a little over 300 people.

'The difficulty for the committee is that you're making incredibly important policy decisions very rapidly in a situation of uncertainty,' said Jonathan Sterne, a statistician from the University of Bristol who made a presentation to the panel."