



Laboratuvarda COVID-19 Aşı Etkisinin Araştırılması

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Koç Üniversitesi İş Bankası Enfeksiyon Hastalıkları Araştırma Merkezi (KUISCID)

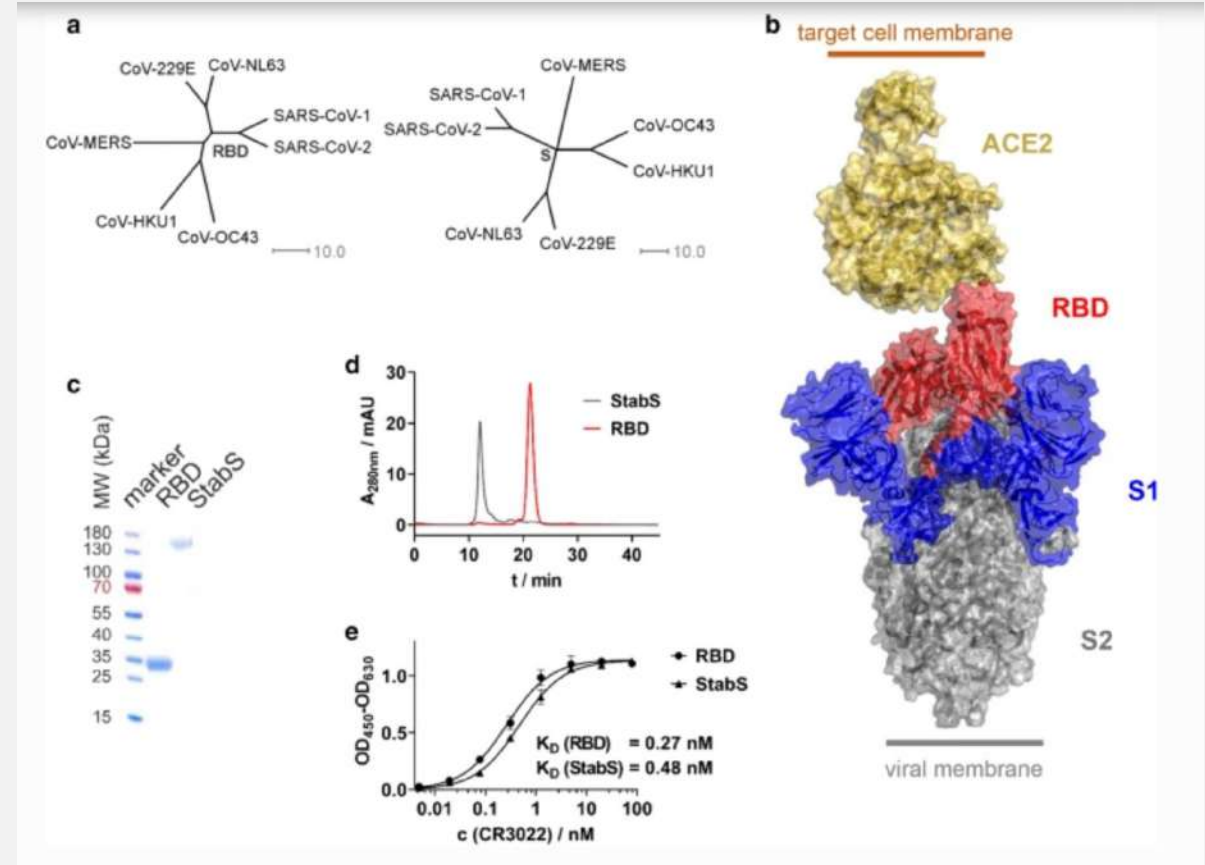
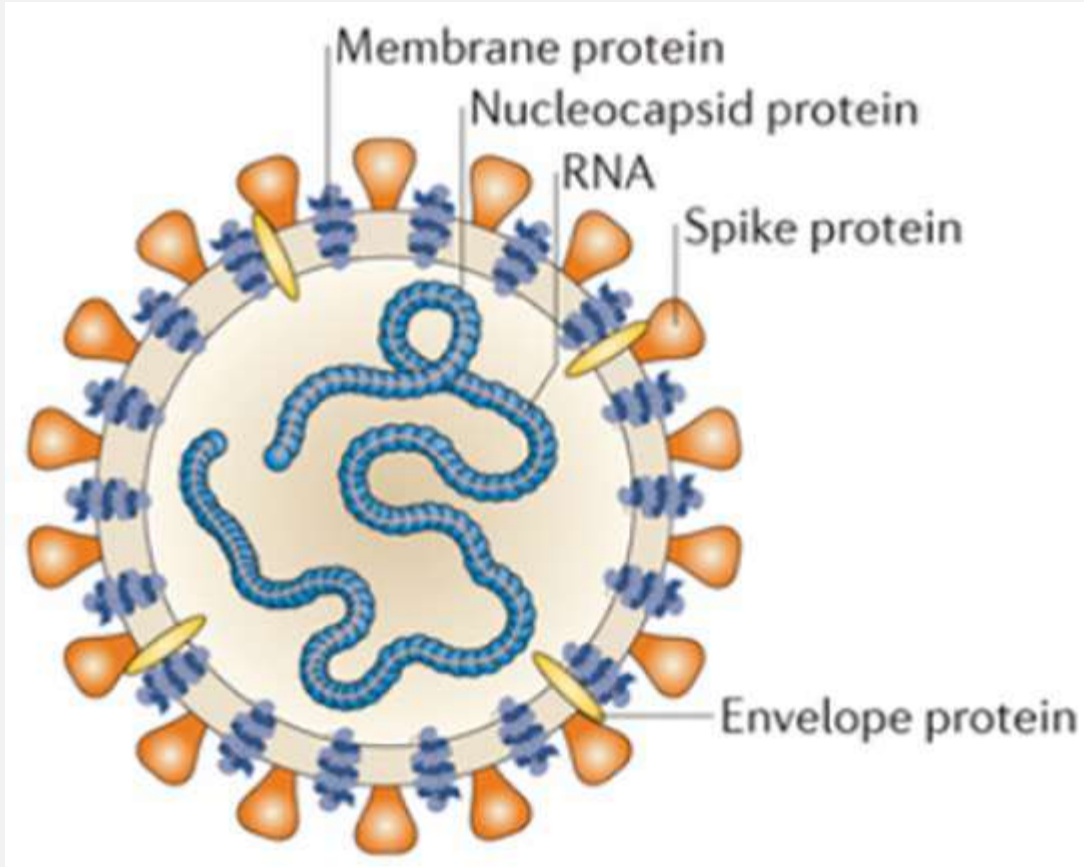


Sunum Planı

- COVID-19 antikor yanıtı
- Antikorlar testleri tanı amaçlı kullanılmalı mı
- Aşı etkinliği ölçümünde serolojik testler
- Aşı sonrası bağışıklığın takibinde kullanılmalı mı
- Ülkemizde aşı sonrası immun yanıt verilerimiz



Antikor testlerinde hedef antijenler





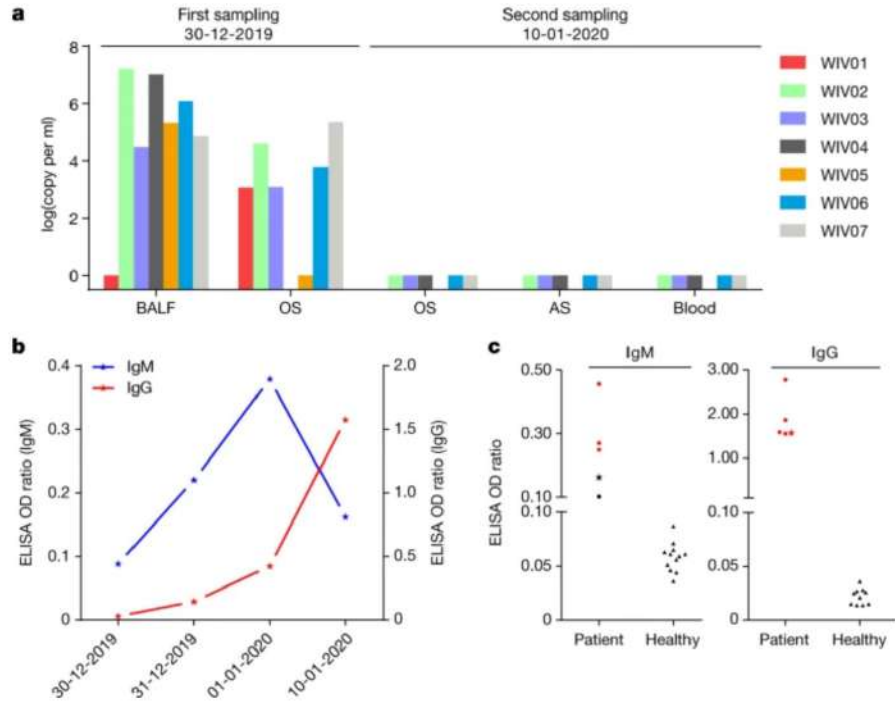
Farklı antikor test stratejileri farklı

- Binding antikor testleri: IgM, IgG, IgA
 - POC
 - Laboratuvar, ELISA, CIA
- Nötralizan antikor testleri
 - Virüs nötralizasyon testi
 - Pseudovirüs nötralizasyon testi
 - Kompetitif nötralizasyon testleri



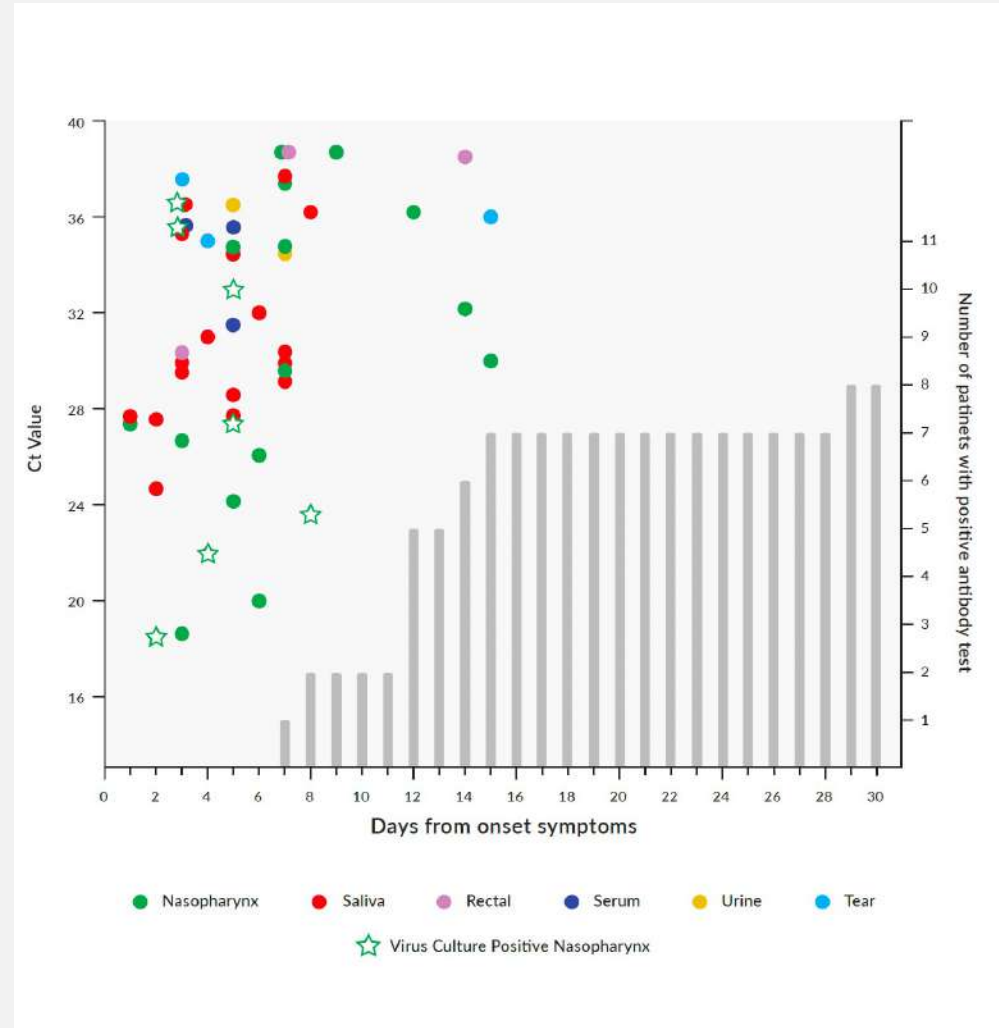
Antikor testleri COVID-19 enfeksiyon tanısında kullanılmamalı

Fig. 2: Molecular and serological investigation of patient samples.



a, Molecular detection of 2019-nCoV in seven patients. Patient information can be found in Extended Data Tables 1, 2. Detection methods are described in the Methods. AS, anal swab; OS, oral swab. **b**, Dynamics of 2019-nCoV antibody levels in one patient who showed signs of disease on 23 December 2019 (ICU-06). OD ratio, optical density at 450–630 nm. The right and left y axes indicate ELISA OD ratios for IgM and IgG, respectively. **c**, Serological test of 2019-nCoV antibodies in five patients (Extended Data Table 2). The asterisk indicates data collected from patient ICU-06 on 10 January 2020. **b, c**, The cut-off was to 0.2 for the IgM analysis and to 0.3 for the IgG analysis, according to the

Zhau ve ark. Nature,2020

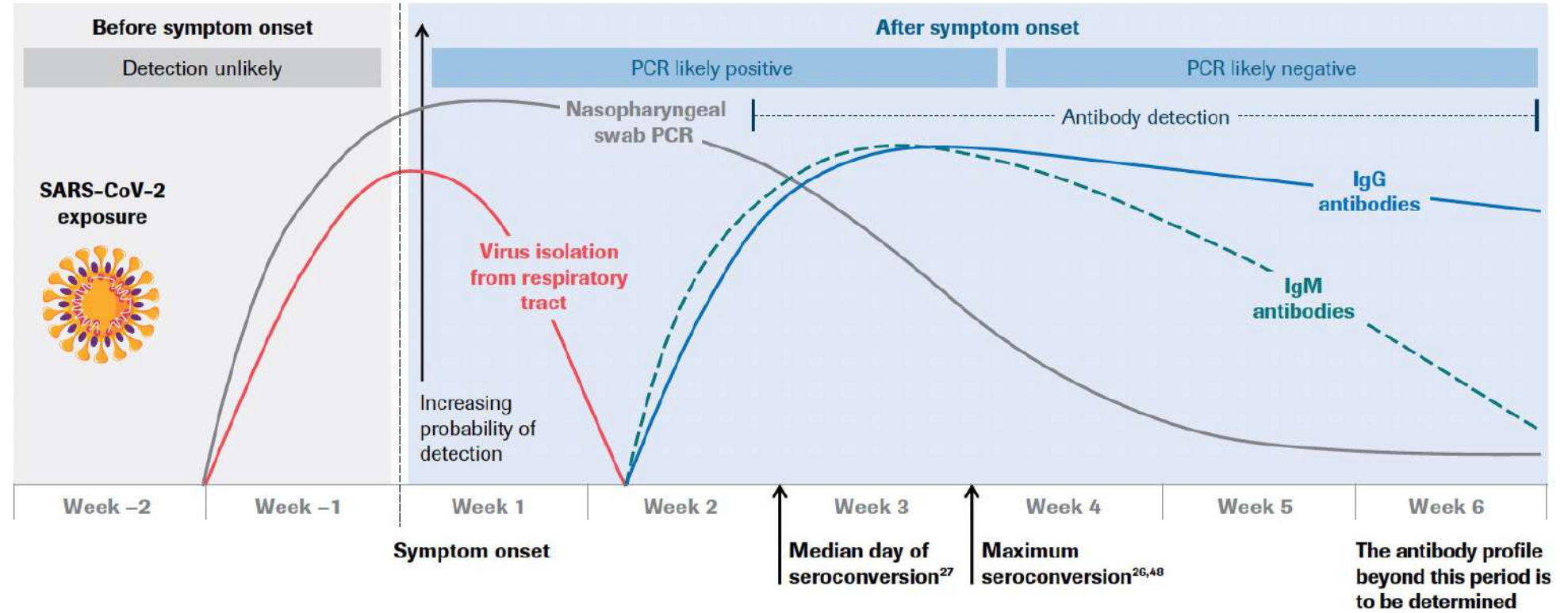


Kapmaz M ve ark. IDCM,2020



Geçirilmiş enfeksiyonun veya aşı yanıtının tanımlanması: Spike protein tanıyan IgG antikor testleri en güvenilir testler

Estimated course of markers in SARS-CoV-2 infection⁴⁷





Antikor testlerinin performansları önemli

TABLE 1 Performance indicators for the 6 serological assays (n=125)

Assay (n)	% (95% CI) by indicator				
	Sensitivity	Specificity	PPV	NPV	Overall agreement with PRNT results
Genscript-cPass (125)	71.07 (58.8–81.3)	94.64 (85.1–98.8)	94.23 (84.1–98.8)	72.60 (60.9–82.4)	81.6 (73.7–87.9)
Diasorin-S1/S2 IgG (104)	75.47 (61.7–86.2)	94.12 (83.8–98.8)	93.02 (80.9–98.5)	78.69 (66.3–88.1)	84.61 (76.2–90.9)
Alinity IgG II (104)	98.11 (89.9–99.9)	70.59 (56.1–82.5)	77.61 (65.8–86.9)	97.30 (85.8–99.9)	84.62 (76.22–90.94)
Diasorin-TrimericS IgG (103)	84.91 (72.4–93.2)	90 (78.1–96.6)	90 (78.1–96.6)	84.91 (72.4–93.2)	87.37 (79.4–93.1)
Roche Elecsys (96)	100 (92.6–100)	41.67 (27.6–56.7)	63.16 (51.3–73.9)	100 (83.1–100)	70.83 (60.7–79.7)
AESKULISA (99)	92.31 (81.5–97.9)	72.34 (57.4–84.4)	78.69 (66.3–88.1)	89.47 (75.2–97.1)	82.82 (73.9–89.7)



TABLE 3 Optimum cutoffs based on the ROC curves and their performances^a

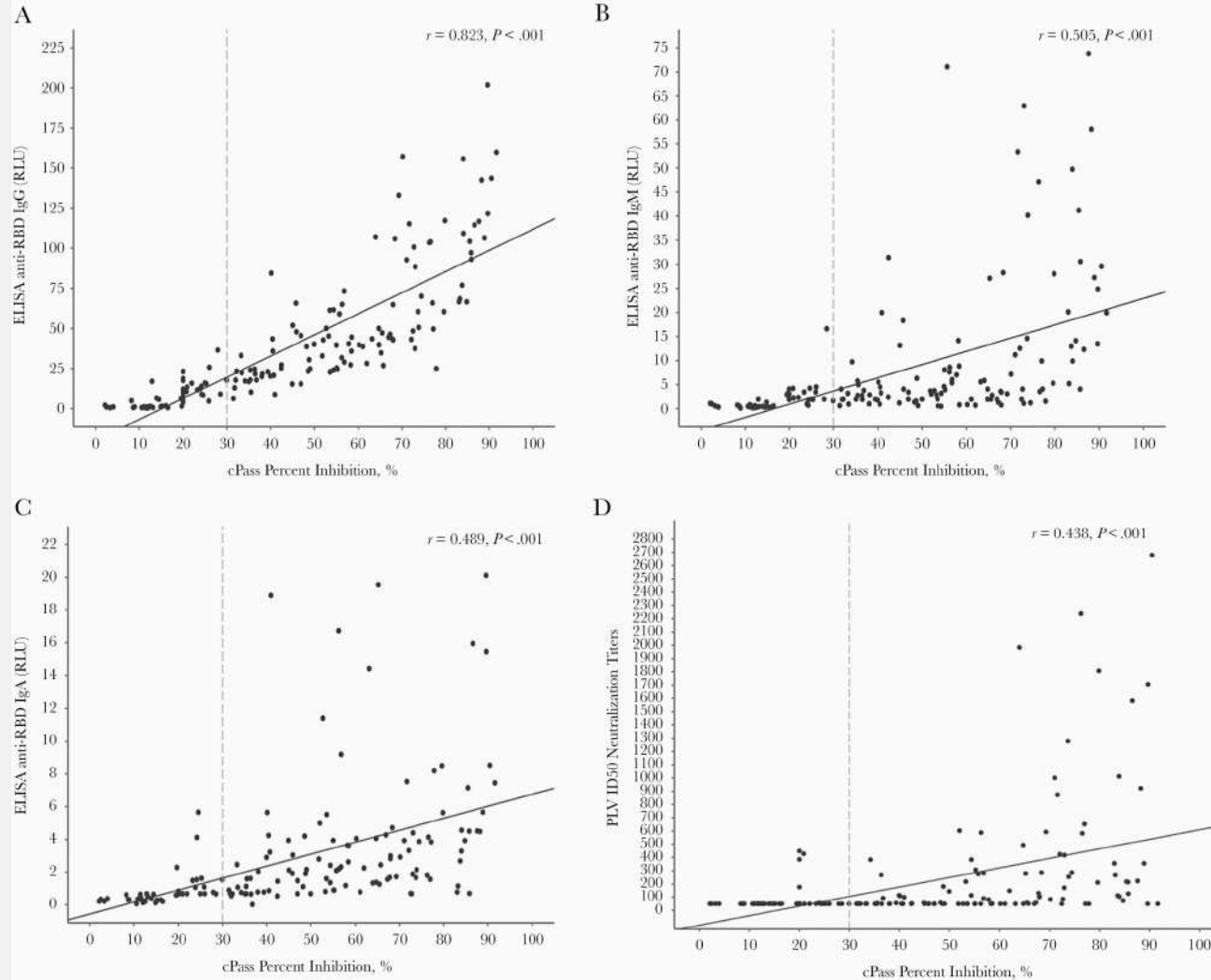
Assay (n)	Cutoff	Sensitivity	Specificity	Overall agreement (%)
Genscript cPass (125)	Manufacturer's cutoff, 30%	71%	94.23%	81.6%
	Based on ROC cutoff, 20%	92.75%	87.5%	90.4%
	<i>P</i> value	<0.001	0.065	<0.05
Diasorin-TrimericS IgG (103)	Manufacturer's cutoff, 33.8 BAU/ml	84.91%	90%	87.37%
	Based on ROC cutoff, 40 BAU/ml	84.90%	96%	90.29%
	<i>P</i> value	0.998	0.092	0.506
Roche Elecsys (96)	Manufacturer's cutoff, 0.8 U/ml	100%	41.67%	70.83%
	Based on ROC cutoff, 5 U/ml	93.75%	70.83%	82.29%
	<i>P</i> value	<0.05	<0.001	0.0616

^a The other three tests showed ROC-based cutoffs similar to the manufacturer's values.

In Roche Elecsys by raising the cut-off from 0.8 to 5U/ml, our study found that **14 out of 28 (50%)** samples that was initially reported as positive by the test were correctly reported as negative.



Genscript assay nötralizan antikor testi RBD antikor testi ile korelasyon gösteriyor

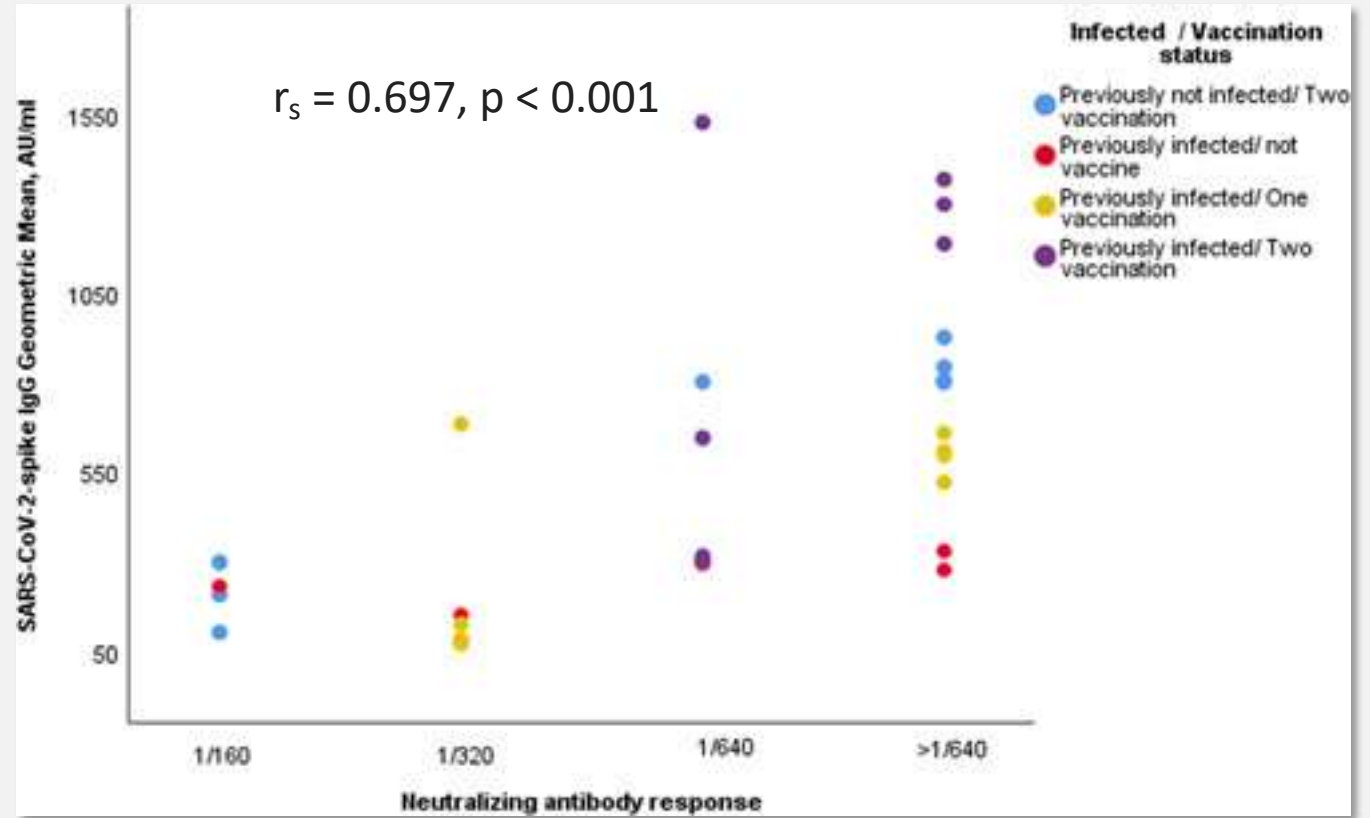
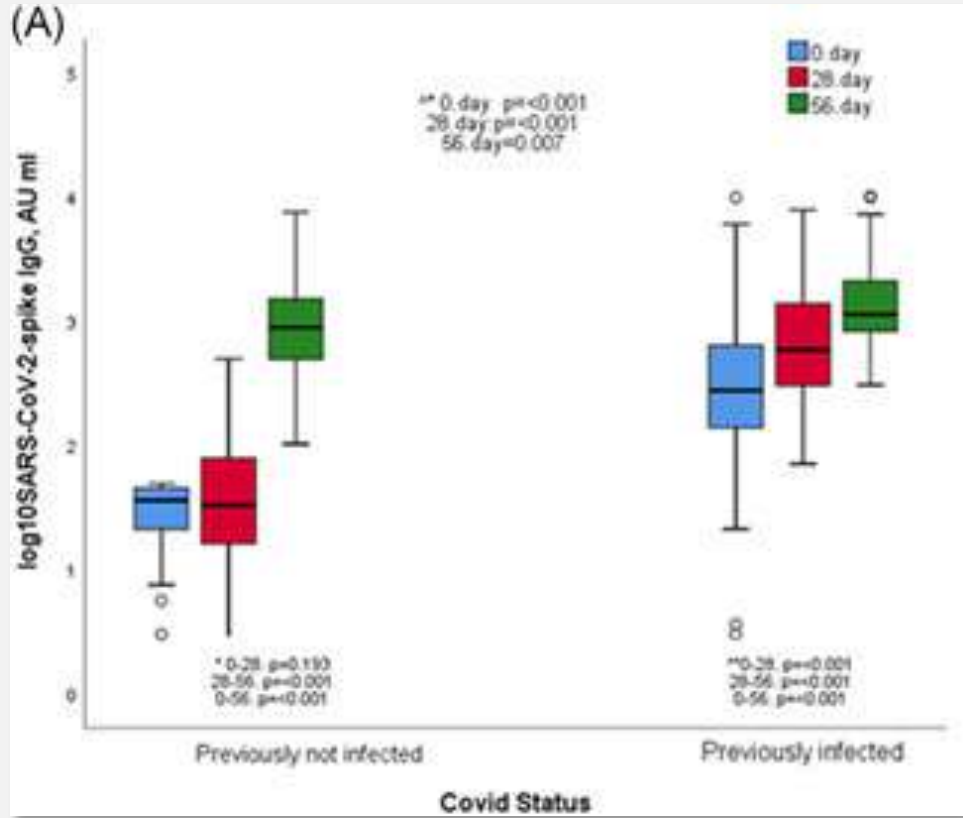


Open Forum Infect Dis, Volume 8, Issue 6, June 2021, ofab220, <https://doi.org/10.1093/ofid/ofab220>

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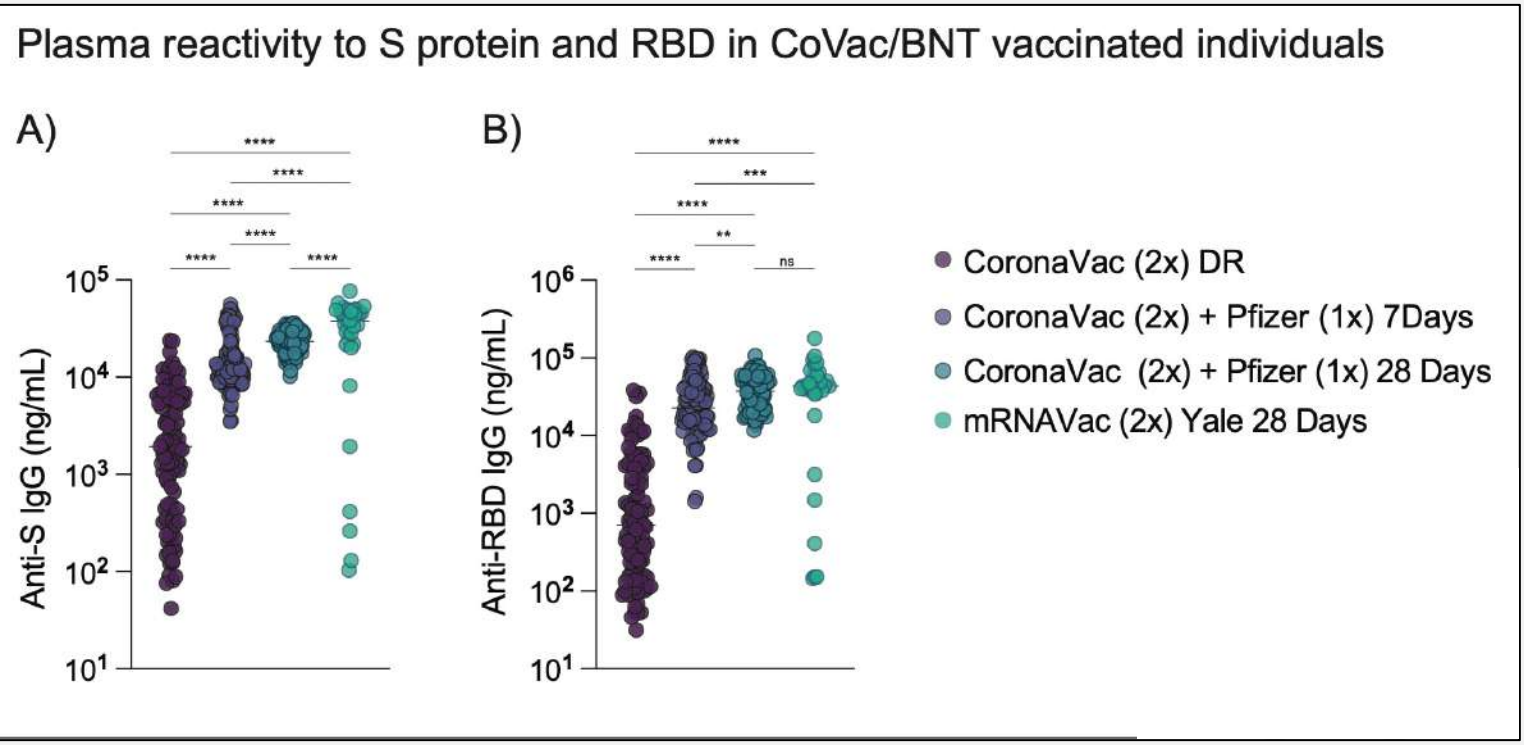
Aşılama sonrası Binding Antikor düzeyleri enfeksiyon geçirenlerde daha yüksek



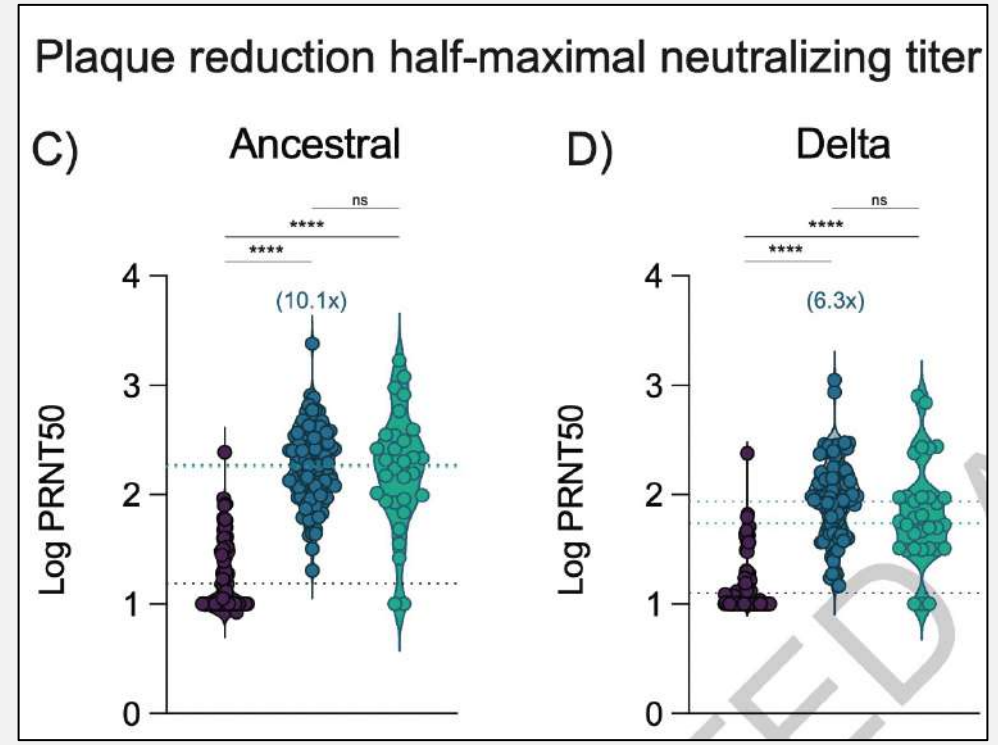
Yalcin T, J Med Virol, 2022



Neutralizing antibodies against the SARS-CoV-2 Delta and Omicron variants following heterologous CoronaVac plus BNT162b2 booster vaccination



Booster dozler ile anti-RBD titreleri belirgin artiyor



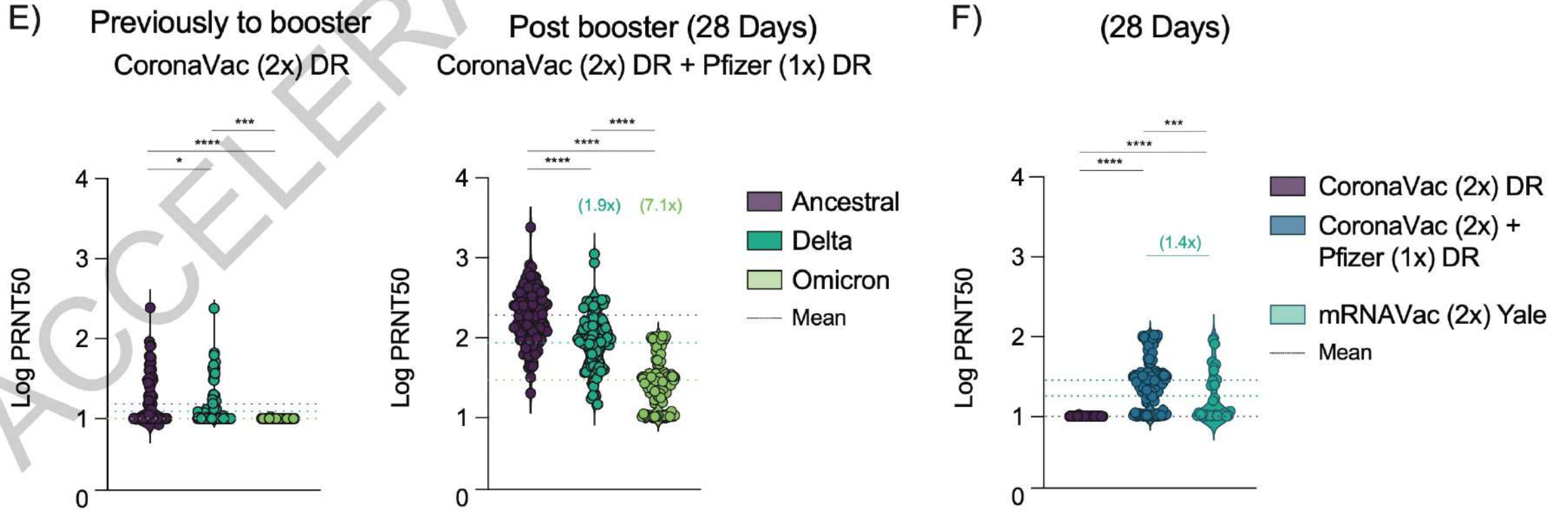
Nötralizan ab titreleri anti-RBD ile paralel

Iwasaki A, ve ark.



Aşı sonrası nötralizan antikor yanıtı: Omicron varyantına etki azalıyor

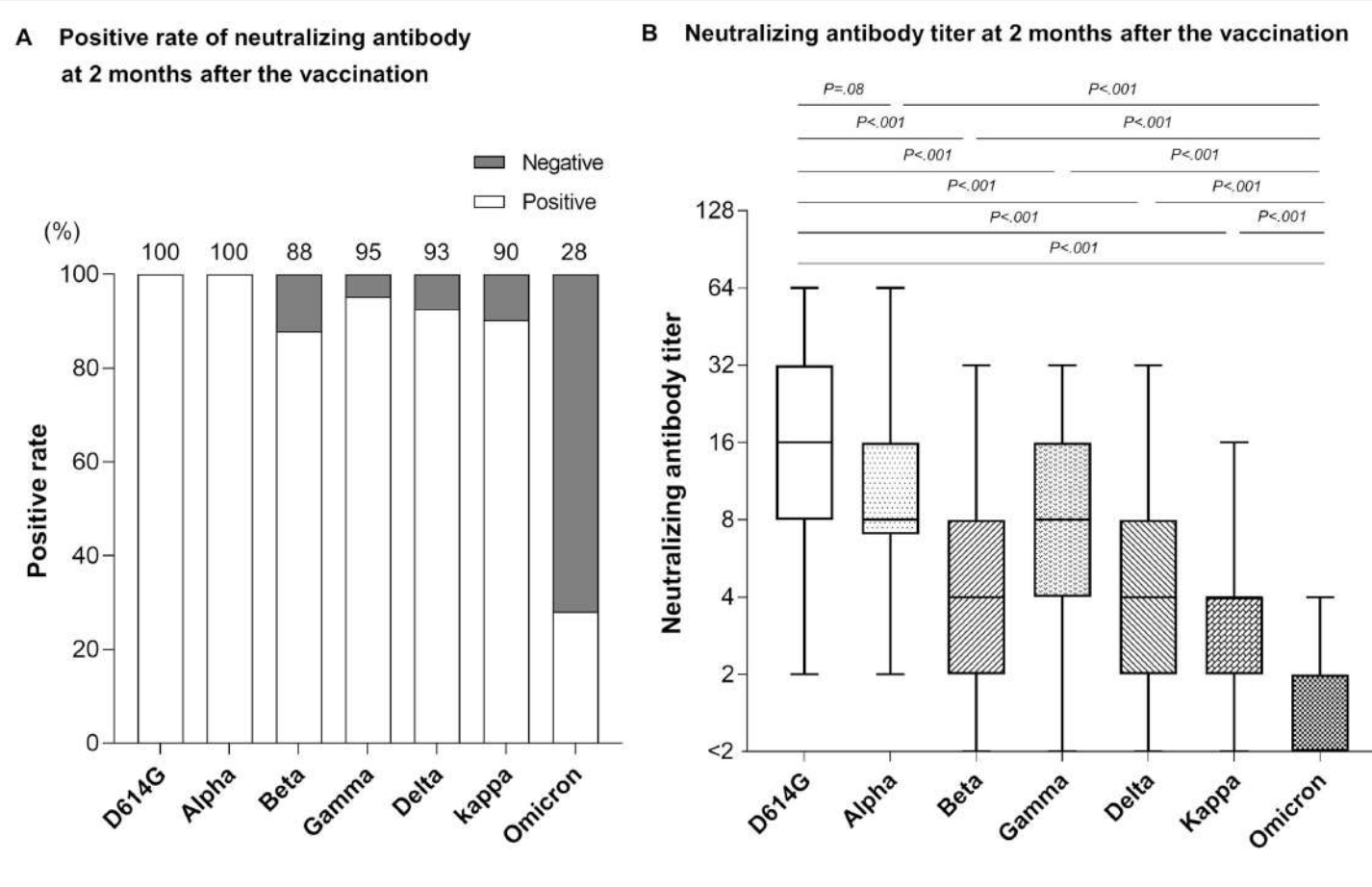
Plaque reduction half-maximal neutralizing titer (PRNT50) against Omicron variant



Iwasaki A, ve ark.



3 doz mRNA aşısı sonrası nötralizan antikor düzeyleri



Binding Antikor testleri varyantlara karşı nötralizasyon kapasitesini gösteremez



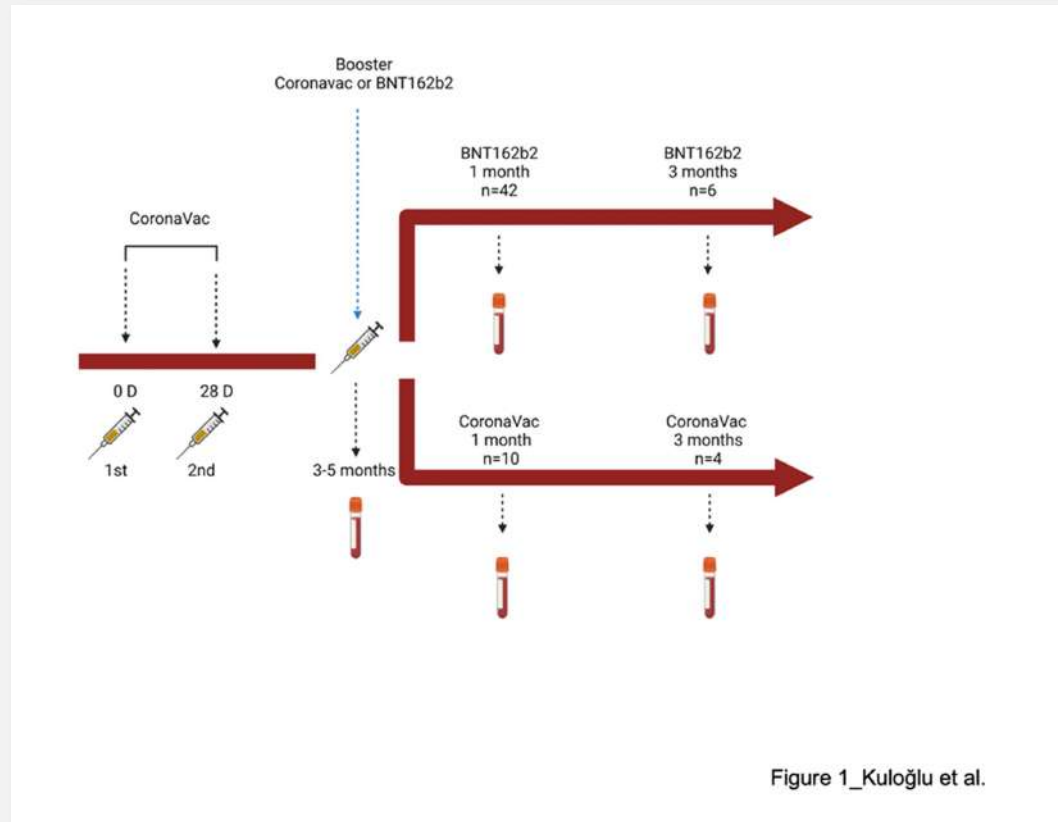
COVID-19 aşılama sonrası serolojik testler

- **Aşı sonrası Antikor Yanıtının Belirlenmesi ????**
 - Anti-S ve Anti-RBD testleri-
 - Rutin hayır
 - Surveyans-evet
- **Aşıya bağlı antikorların koruyuculuğunun belirlenmesi**
- Anti-S ve Anti-RBD testleri-hayır
- Nötralizasyon antikor testleri-evet
- Rutin????



Effect of BTN162b2 and Coronavac boosters on humoral and cellular immunity of individuals previously fully vaccinated with Coronavac against SARS-CoV-2: A longitudinal study

Zeynep Ece Kuloğlu^{1,2,*}, Rojbin El^{1,2,*}, Gülen Guney-Esken², Yeşim Tok³, Zeynep Gülçe Talay^{1,2}, Tayfun Barlas², Mert Ahmet Kuskucu^{2,3}, Özgür Albayrak⁴, Özlem Doğan^{2,5}, Serap Şimşek Yavuz⁶, Kenan Midilli³, Önder Ergönül^{2,7}, Füsun Can^{2,6,**}





2 CoronaVac+1 BNT sonrası nötralizan antikor yanıtı artıyor

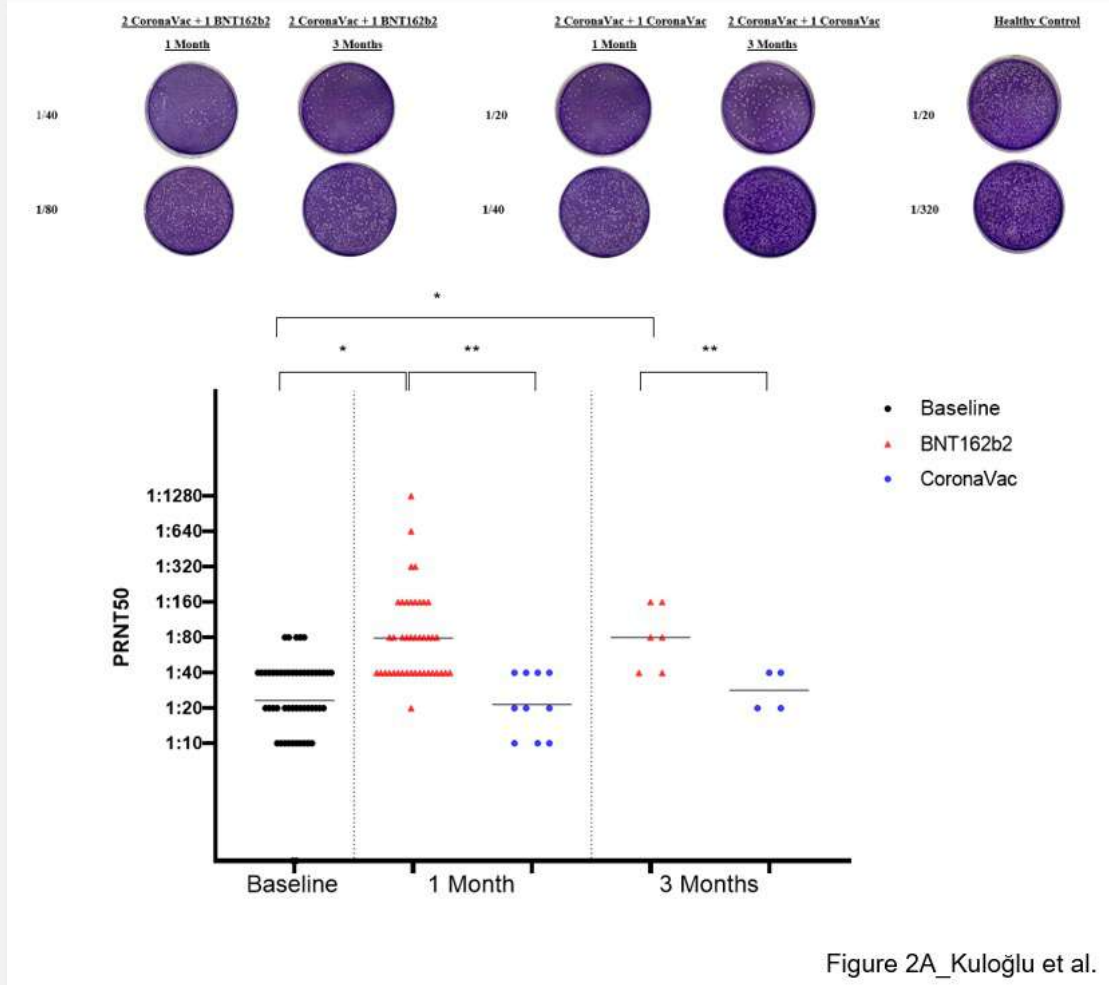


Figure 2A_Kuloğlu et al.

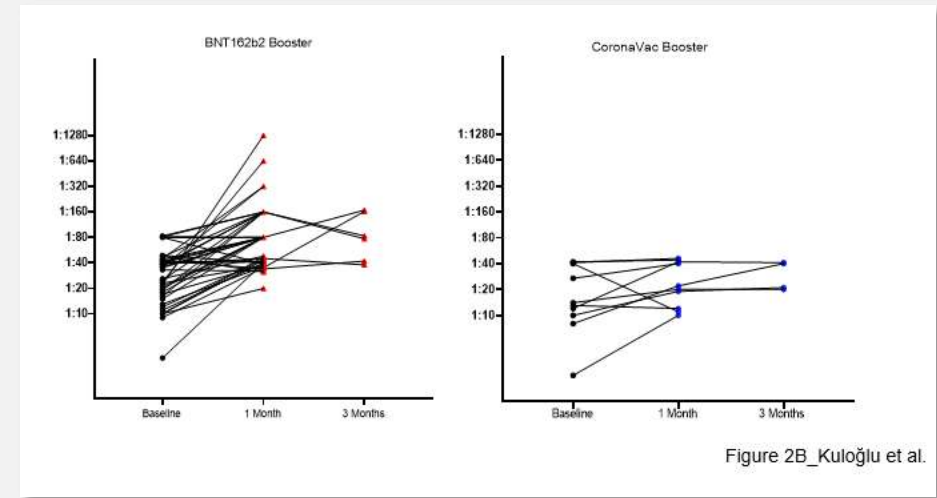


Figure 2B_Kuloğlu et al.



2 CoronaVac+1 booster sonrası T hücre sayılarında değişiklik yok

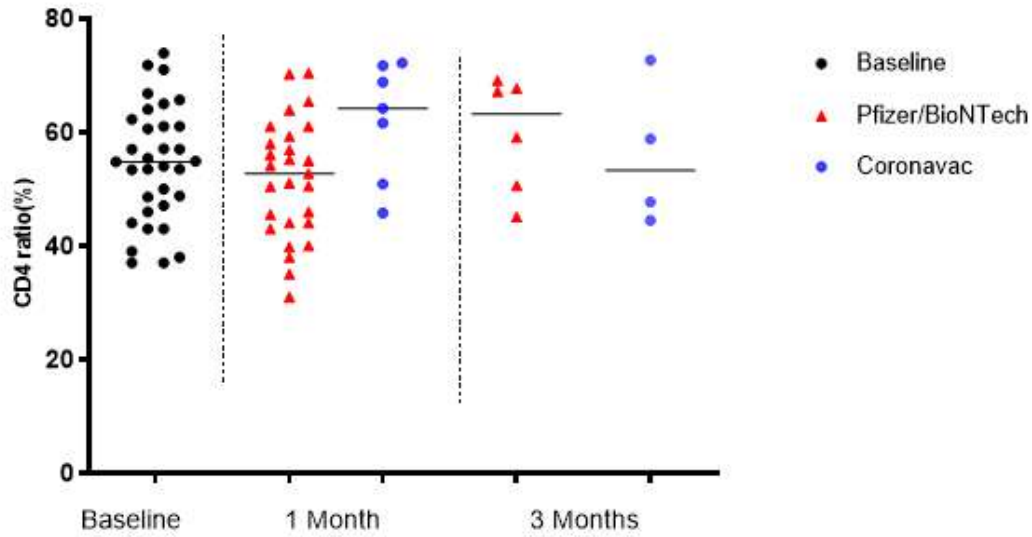


Figure 3A_Kuloğlu et al.

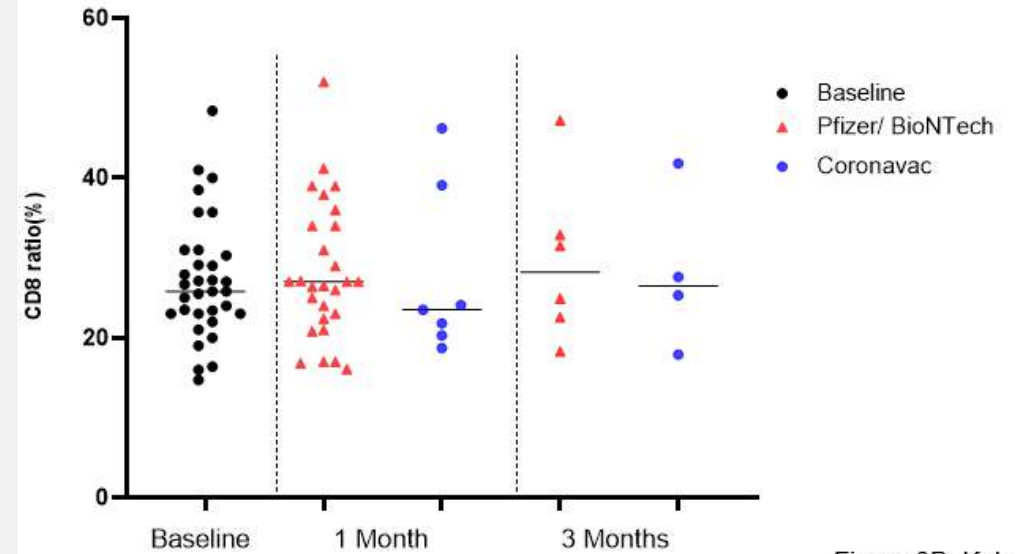


Figure 3B_Kuloğlu et al.



BNT aşısı sonrası Effector CD4+ ve CD8+ hücreler artıyor

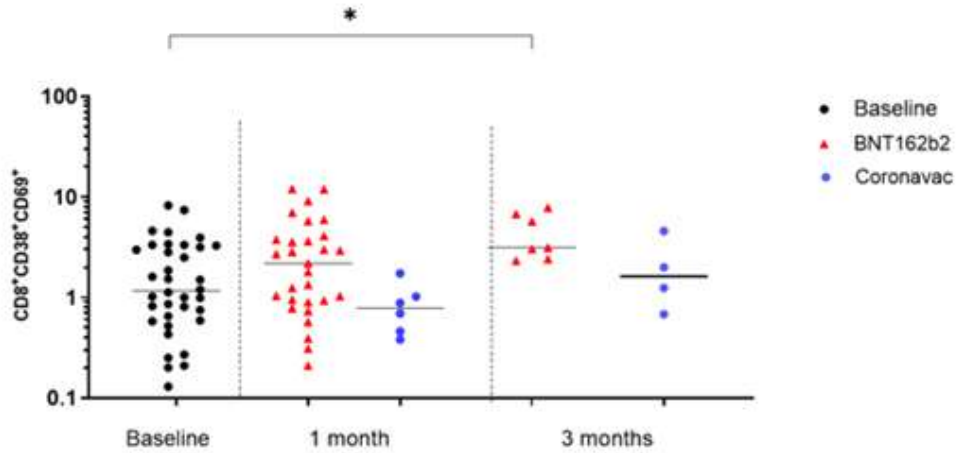


Figure 5A_Kuloğlu et al

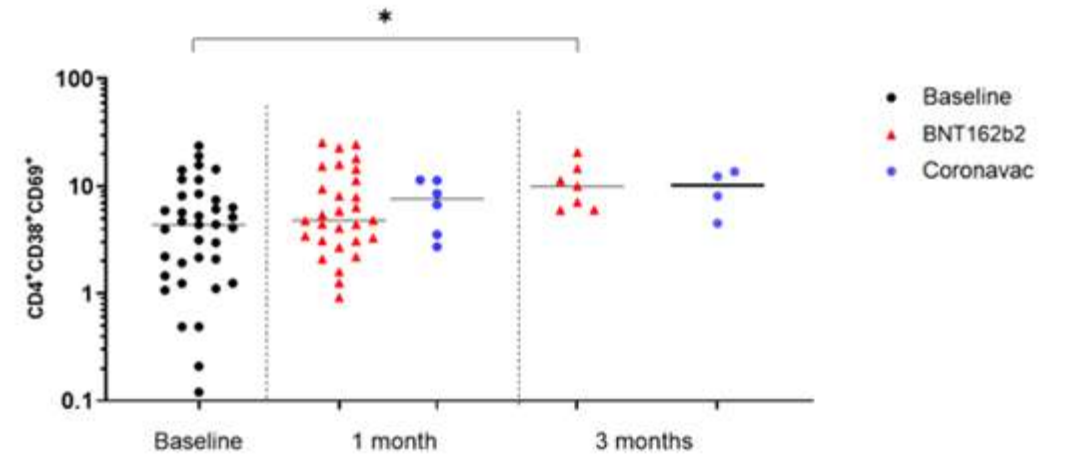


Figure 5B_Kuloğlu et al



2 CoronaVac+1 BNT sonrası IFN-gama ve IL-2 Yanıtı artıyor

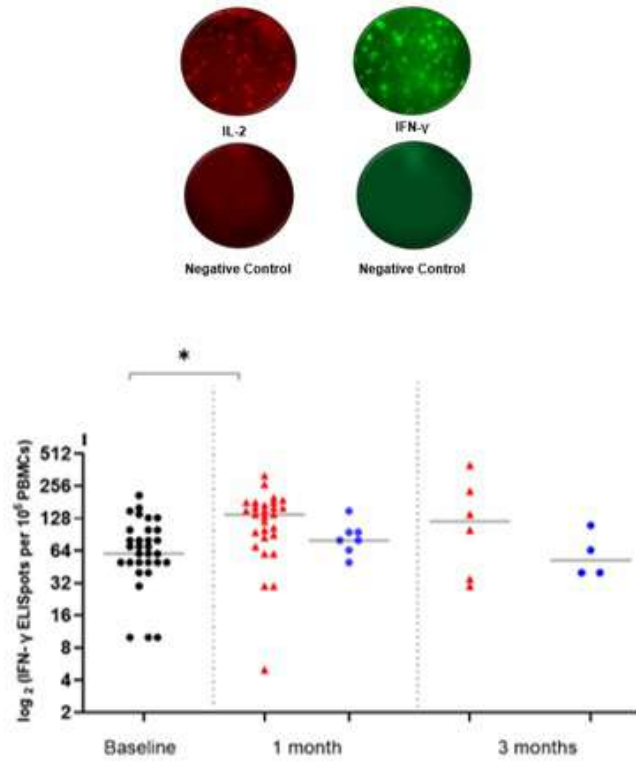


Figure 4A_Kuloğlu et al.

BNT sonrası IL-2 yanıtı bazal ve CV yanıtına göre yüksek

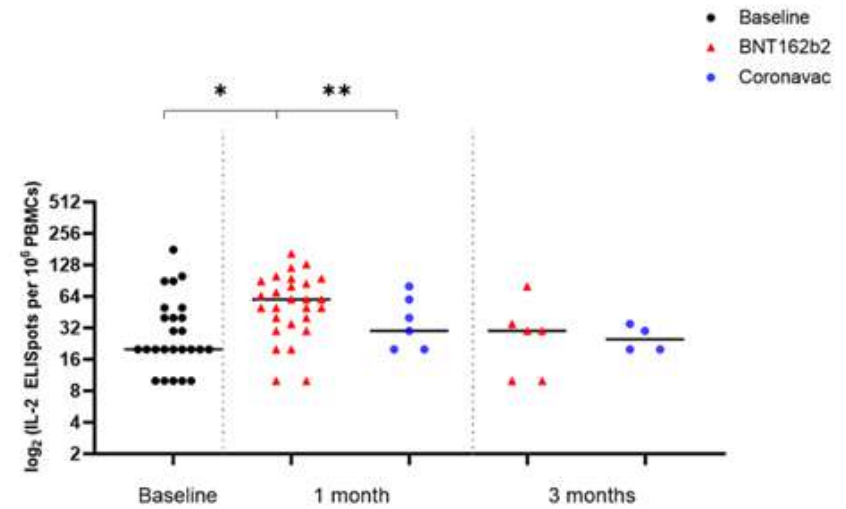


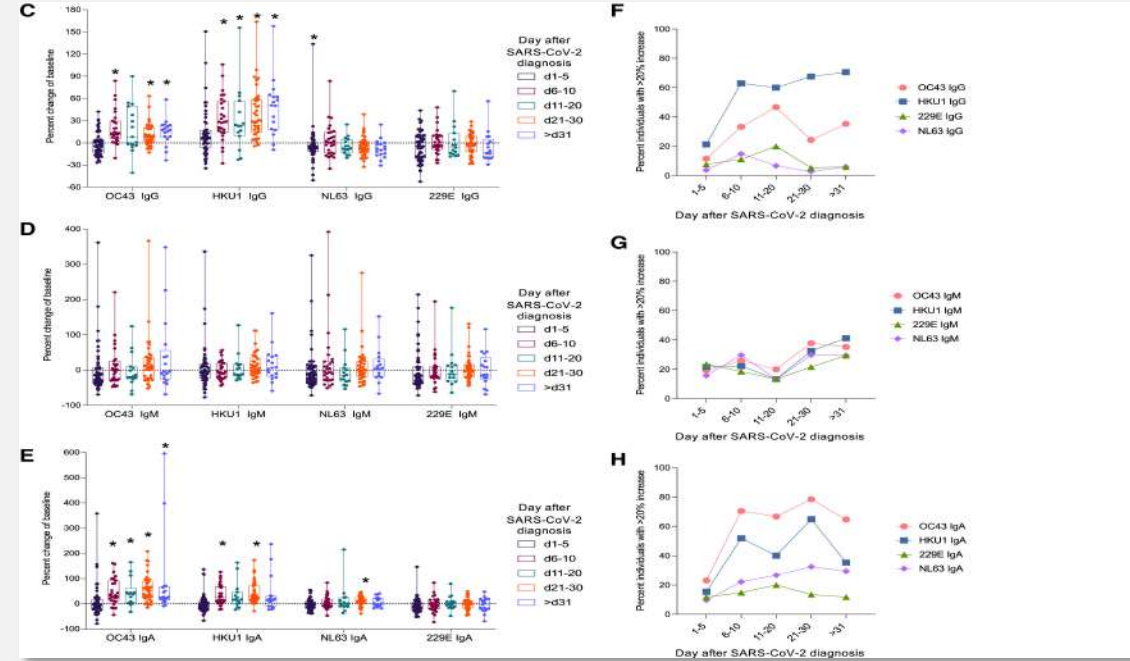
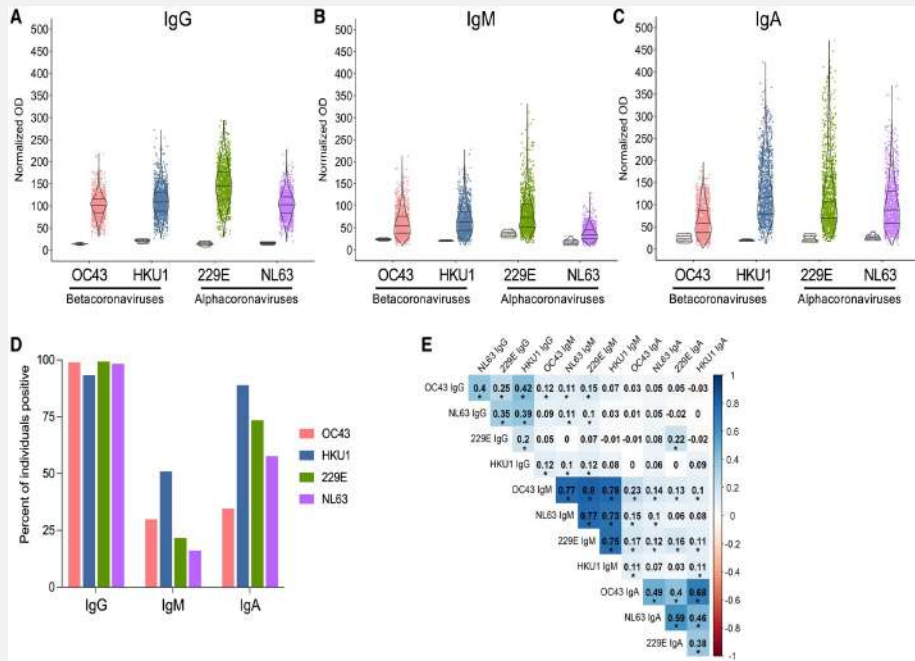
Figure 4B_Kuloğlu et al.



Pre-existing humoral immunity to human common cold coronaviruses negatively impacts the protective SARS-CoV-2 antibody response

n=1202

Enfeksiyon öncesi ve aşı sonrası antikor düzeylerini karşılaştırıyorlar

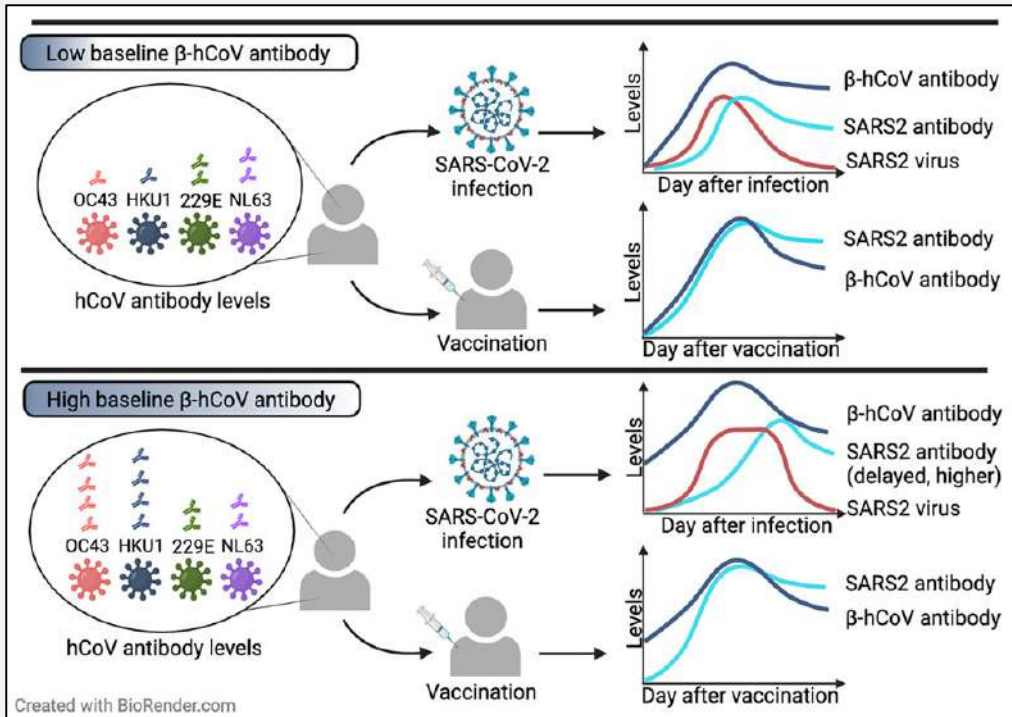


Koronavirüs antikorları yüksek oranda pozitif

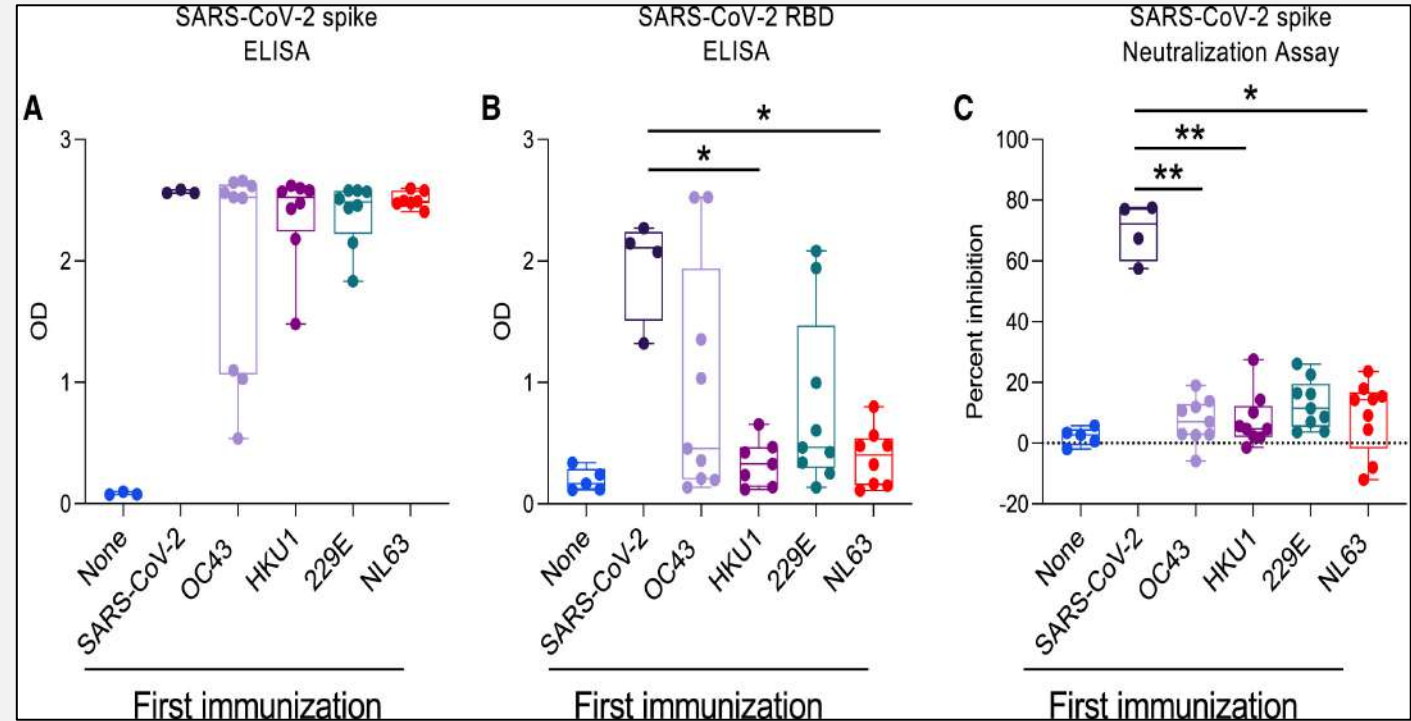
SARS-VoV-2 enfeksiyonundan ve aşıdan sonra koronavirüs antikorları artıyor



Yüksek Koronavirüs antikoru SARS-CoV-2 enfeksiyonunda koruyucu antikor yanıt oluşumunu negatif etkiliyor



Koronavirüs antikoru SARS-Cov2 enfeksiyonunda nötralizan antikor yanıtını azaltıyor



Lin et al., 2022, Cell Host & Microbe 30, 83–96
January 12, 2022 a 2021



Sonuçlar

- Laboratuvarda kullanılan antikor testlerinin PPV ve NPV değerlerinin bilinmesi önemli
- Varyantlar antikorların nötralizan aktivitesinin yorumlanmasını zorlaştırıyor
- Aşı hatırlatma dozları antikor düzeylerini artırıyor ancak omicrona etkisi takip edilmeli
- 2 doz coronaVac+1 doz biontech 3 ay koruyuculuğu yüksek ancak varyantlar dikkate alındığında ek hatırlatma dozu mutlaka gerekli
- Önceden geçirilmiş coronavirüs enfeksiyonları antikorların nötralizasyon kapasitesini düşürüyor

Teşekkürler....

