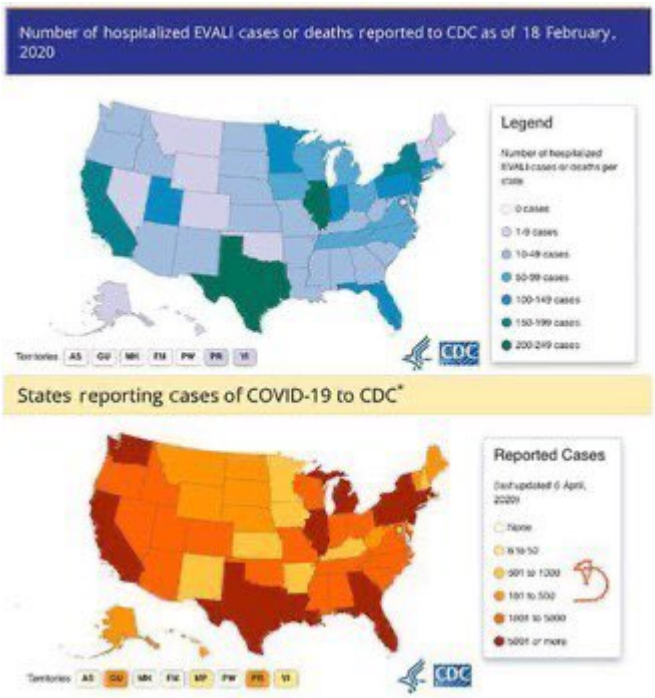
Twitter Thread by Covid Fact Check ✌■

Covid Fact Check ✌■
@2dedostesta2

■ “SARS-CoV-2 spike protein may interact with nicotinic acetylcholine receptors (nAChRs), & that such interactions may be involved in pathology & infectivity.” ■■■■ EVALI ■ COVID-19 ■https://t.co/cCdTJiZzQZ



Neuronal nicotinic acetylcholine receptors mediate ∆9-THC dependence: Mouse and human studies ■https://t.co/GseQ76q8SI

■■ CDC ■ https://t.co/zQuQe54qwp

> \u201cNo one substance has been identified in all of the samples tested. Importantly, identifying any compounds that are present in the samples will be one piece of the puzzle but will not necessarily answer questions about what is causing these illnesses.\u201d https://t.co/97UpfKIOqY
>
> — Renaissance Man (@2dedostesta) September 10, 2020

Vitamin E regulates acetylcholine receptor function of molluscan neurons ■ https://t.co/f3nT3uqXYR

“We hypothesize that the nicotinic acetylcholine receptor (nAChR) plays a key role in the pathophysiology of Covid-19 infection and might represent a target for the prevention and control of Covid-19 infection.” https://t.co/AF9IpvvUqq

https://t.co/wlaWtX2UOo

The Impact of Electronic Nicotine Delivery System (ENDS) Flavors on Nicotinic Acetylcholine Receptors and Nicotine Addiction-Related Behaviors. https://t.co/xkwA9uOzbx

E-cigarette-induced pulmonary inflammation and dysregulated repair are mediated by nAChR α7 receptor: role of nAChR α7 in SARS-CoV-2 Covid-19 ACE2 receptor regulation. https://t.co/bz38dlVDMs

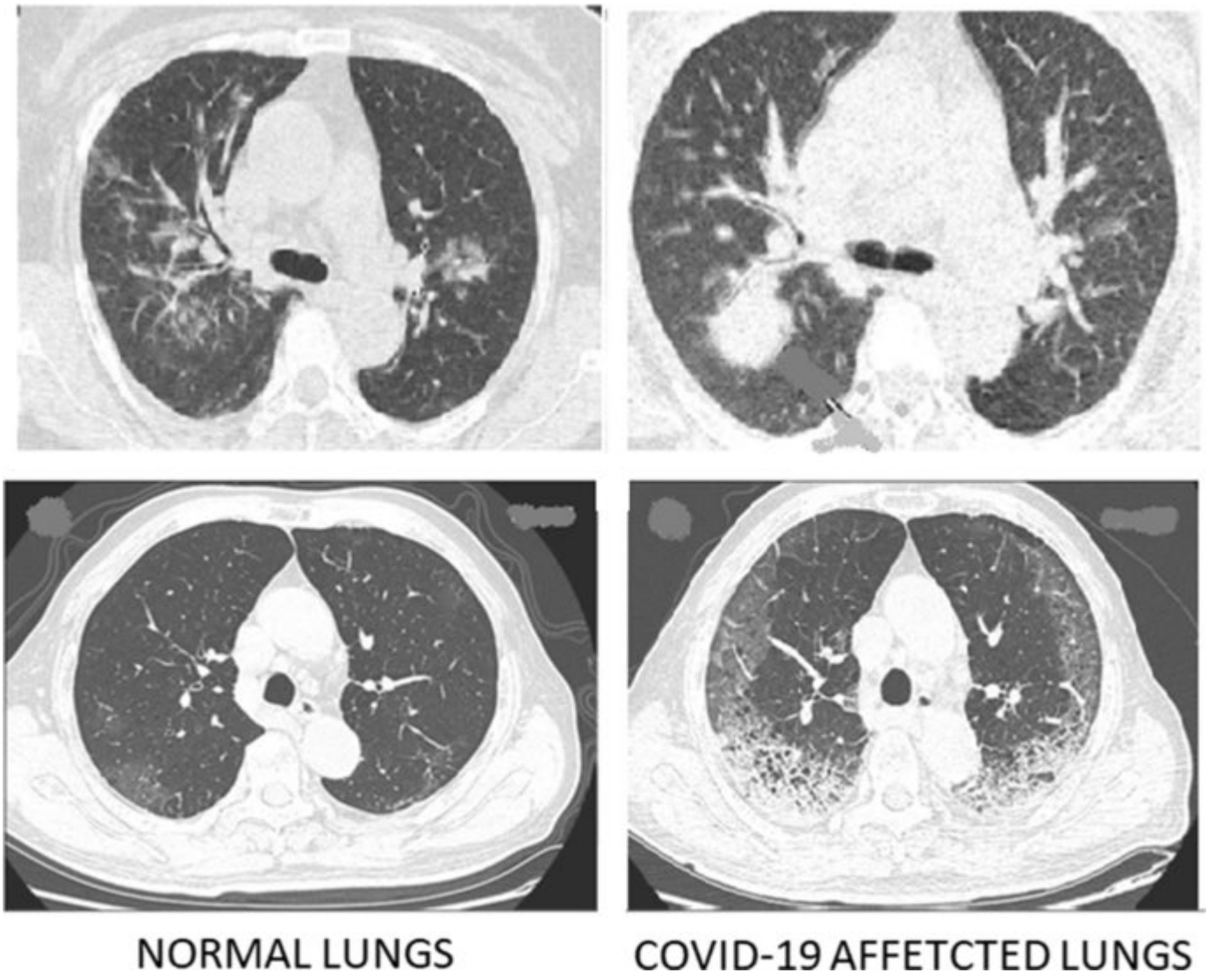
Evaluation of E-Vapor Nicotine and Nicotyrine Concentrations under Various E-Liquid Compositions, Device Settings, and Vaping Topographies. https://t.co/PpDbHcDsLX

Simulations support the interaction of the SARS-CoV-2 spike protein with nicotinic acetylcholine receptors. https://t.co/DUvljRaxfI

■ “Analyses of simulations of the glycosylated spike show that the Y674-R685 region is accessible for binding. We suggest a potential binding orientation of the spike protein with nAChRs, in which they are in a non-parallel arrangement to one another.” ■ https://t.co/cm70Drtl8G

> \U0001f449 \u201cSARS-CoV-2 spike protein may interact with nicotinic acetylcholine receptors (nAChRs), & that such interactions may be involved in pathology & infectivity.\u201d \U0001f449\U0001f449\U0001f449\U0001f449 EVALI \U0001f449 COVID-19 \U0001f447https://t.co/cCdTJiZzQZ pic.twitter.com/Vc8lwKCuH8
>
> — Covid Fact Check \u270c\ufe0f (@2dedostesta2) February 24, 2021

https://t.co/bSnbVsoOCi



2019 \U0001f449 EVALI was COVID-19 \U0001f449 Imaging of Vaping-Associated Lung Disease \U0001f449 https://t.co/zn0Er2Z3va \U0001f449 Detection of COVID-19 using CXR and CT images \U0001f449 https://t.co/w7wZBGRnvL https://t.co/nSCE1F61vP pic.twitter.com/UkMJu5iyW4

— qwert (@qwert03118543) January 27, 2021

https://t.co/Colz5bzDOL

	N tested	N reactive (% of tested)	N reactive with further testing (% of tested)	reactive with positive micro-neutralization (% of tested)	N with s neutra (% of reactiv micro-neu
All specimens	7389	106 (1.4)	90 (1.2)	84 (1.1)	23 (
All specimens from December 13-16, 2019	1912	39 (2.0)	39 (2.0)	37 (1.9)	9 (2
American Red Cross Blood Services region					
Northern California (CA)	508	12 (2.4)	12 (2.4)	11 (2.2)	7 (6
Pacific Northwest (OR, WA)	763	16 (2.1)	16 (2.1)	15 (2.0)	1 (
Southern California (CA)	641	11 (1.7)	11 (1.7)	11 (1.7)	1 (
Donor sex					
Female	859	12 (1.4)	12 (1.4)	11 (1.3)	1 (
Male	1053	27 (2.6)	27 (2.6)	26 (2.5)	8 (3
Donor age group					

\U0001f449 on Dec 13th 2019 \U0001f1fa\U0001f1f8 had > than 6 MILLION people with SARS-COV-2 antibodies \U0001f449 2%\u203c\ufe0f\U0001f447

https://t.co/mHJnt2Nnjm

— Covid Fact Check \u270c\ufe0f (@2dedostesta2) February 25, 2021

■ Conclusions:

■These findings suggest that ■SARS-CoV-2 may have been introduced into the ■■ ■prior to January 19, 2020■■

■ 2016 ■ PULITZER ■■

“We identified a main interaction between the aa 381–386 of the SARS-CoV-2 Spike Glycoprotein and the aa 189–192 of the extracellular domain of the nAChR α9 subunit, a region which forms the core of the “toxin-binding site” of the nAChRs.” https://t.co/K3D54PiPFO

examined and identified a “toxin-like” amino acid (aa) sequence in the Receptor Binding Domain of the Spike Glycoprotein of SARS-CoV-2 (aa 375–390), which is homologous to a sequence of the Neurotoxin homolog NL1, one of the many snake venom toxins that are known to interact with nicotinic acetylcholine receptors (nAChRs). We present the 3D structural location of this “toxin-like” sequence on the Spike Glycoprotein and the superposition of the modelled structure of the Neurotoxin homolog NL1 and the SARS-CoV-2 Spike Glycoprotein.

“This would establish the hypothesis that SARS-CoV-2 disrupts the cholinergic anti-inflammatory pathway and causes a variety of clinical manifestations by interacting with nAChRs.”

SARS-CoV and SARS-CoV-2 Spikes can interact with the human α7 nAChR.

SARS-CoV-2 through nAChRs may dysregulate the cholinergic anti-inflammatory pathway.

Interaction of SARS-CoV-2 Spike with nAChRs is due to a “toxin-like” sequence. https://t.co/oVGkoKIPKp

■ “Therefore, our findings demonstrated that smoking or vaping may critically exacerbate COVID-19-related inflammation or increase susceptibility to COVID-19.” ■ https://t.co/96DvISapjp

■ https://t.co/YZvHKMyzVl

■ “Interestingly, THC seems to have the opposite effect, it appears to increase the response of the α7 nicotinic receptor to ACh by a 128% (pvalue=0.44).” ■https://t.co/mDEP0XZg8r

“Colorado and Ohio banned vitamin E acetate, which is sometimes used as a thickening agent or to dilute THC oil in vape cartridges to make it go further. “ https://t.co/Kdfp6cW7Di ■ THC was the factor responsible for the susceptibility to Covid-19, not vitamin e acetate■■

nAChR subunit genes (α2–α3, α5–α7, α9–α10, β3–β4). All nAChR subtypes are activated by nicotine (with the exception of α9 and α9α10 nAChRs, which are blocked by nicotine). https://t.co/V5Zuymp8fg

“NAChRs are responsible for mediating cholinergic neurotransmission at the neuromuscular junction of striated muscles, in the autonomous peripheral ganglia and at several sites in the central nervous system.”

“12 neuronal nAChRs subunits have been identified, of these nine are α (α2 to α10) and three β (β2 to β4). Neuronal nAChRs will have distinct pharmacological and physiological properties resulting from the combination of different subunits.”

NAChRs are commonly divided into three subfamilies [20, 33]:

- **Heteromeric muscle type receptors** that are selectively labelled and blocked by the antagonist α-bungarotoxin (α-Bgt) **5** as present in snake venom of *Bungarus multicinctus* [34].
- **Heteromeric neuronal nicotinic receptors** composed of a combination of α and β subunits that are α-bungarotoxin-insensitive or resistant [20, 33].
- **Homomeric neuronal nAChRs** composed of an association of α7, α8 or α9-subunits which binds α-bungarotoxin (α-Bgt) **5** [20].

“The α10 subunit is only incorporated into a functional nAChR when co-expressed with α9. Homomeric receptors are formed by α7, α8 and α9 subunits. At least two binding sites have to be occupied for a maximal activation of nAChR.”

“nicotinic receptors go against this convention: a prolonged exposure to an agonist produces an up-regulation, with an increase in the density of nicotine binding sites in the brain tissue.”

“The α7 subunit is expressed in both para- & sympathetic neurons innervating the heart, whereby they contribute to the negative chronotropic effects, resulting in decrease in the heart rate.”

“There is growing evidence that activation of nAChRs via acetylcholine 1 can modulate some cellular functions outside the synaptic transmission in the central and peripheral nervous system.”

of auditory stimuli" (Table I/1.3).

Table I/1.3: Distribution of nAChRs in non-neuronal cells

Cell type	Subunit	Reference
Lymphocytes	α7, α4, α9 and α10	97
Vascular endothelial cells (human)	α3, α5, α7, β4, β2	99
Bronchial epithelium (human, rat)	α3, α5, α7, β4, β	95
Keratocytes	α5, α3,	94

“NAChRs, which were expressed in non-neuronal cells, have been found to be responsible for: cell lung carcinoma, respiratory disease, asthma, chronic bronchitis, tumours, skin aging, arteriosclerosis, megacystis-microcolon-intestinal hypoperistalsis syndrome and Chron’s disease.”

“Stimulation of this nAChRs subtype (α7 receptors) determines a Ca2+ influx that triggers a wide range of processes, including an increase of neurotrophic factors in the brain.”

“high propensity of the SARS-CoV-2 S TCRVβ-binding site residues potentially elicit an SAg-like response.”

“the RBD (...) interact with TCRs.”

“the same segment bears close similarity to the HIV-1 glycoprotein gp120 SAg motif F164 to V174.”
https://t.co/zqGd8m28mM

“T cells from unexposed individuals also respond to S protein epitopes from SARS-CoV-2.”

“possible that a poor initial antibody response to the virus fails to neutralize the SAg, as recently shown in MIS-C patients, leading to immune enhancement following reexposure.”

“Certain HLA types are more permissive of binding SAg, and, indeed, HLA has been shown to play a role in COVID-19 susceptibility.”

“potential genetic component to susceptibility.”

“approximately 1/3 or fewer of MIS-C patients tested positive for SARS-CoV-2, but the majority (but not all) had serologic evidence of infection or a history of exposure to COVID-19.”

“SAgs have been implicated in autoimmunity by triggering self-reactive T cells. Antibody-mediated enhancement (ADE) upon reexposure to the virus may also contribute to uncontrolled infection and inflammation.”

Can I get my Pulitzer now ■

“despite a negative nasopharyngeal PCR test, the virus may still be present in the GI tract.”

Latency ■ Pulitzer ■

“a neurotoxin-like segment (T299 to Y351) partially overlapping with the RBD exhibited a ■■ affinity to bind TCRs. Notably, this region was recently observed to elicit strong & frequent T cell reactivity mediated by CD4+ T cells in donors who have not been exposed to SARS-CoV-2.”

“TCRVβ skewing is associated with a reduction of naive CD8+ T cells & an expansion of effector CD4+ & CD8+ T cells in peripheral blood - disturbed CD4+/CD8+ T-cell ratio, reduction in naive CD8+ T cells, expansion of effector CD8+ T cells & an increase in activated CD8+ T cells.”

■ https://t.co/PAbHwnoDRr

“It can be speculated that isolated TCR Vβ perturbations may result from the partial activation of lymphocytes by HIV.” ■https://t.co/OHGcyU5yQ2

“HIV also causes specific qualitative changes to the repertoire including an altered distribution of V gene usage, depletion of public TCR sequences, and disruption of TCR networks.” ■ https://t.co/PpjsKa0Bst

“Together, our results suggest that patients with severe and hyperinflammatory COVID-19 show expansion of TCRs using distinct V genes, along with J gene/CDR3 diversity in these rearrangements.” https://t.co/PAapITB3tH

> \u201chigh propensity of the SARS-CoV-2 S TCRV\u03b2-binding site residues potentially elicit an SAg-like response.\u201d
>
> \u201cthe RBD (...) interact with TCRs.\u201d
>
> \u201cthe same segment bears close similarity to the HIV-1 glycoprotein gp120 SAg motif F164 to V174.\u201d https://t.co/zqGd8m28mM
>
> — Covid Fact Check \u270c\ufe0f (@2dedostesta2) March 6, 2021

“the major envelope protein of HIV-1, gp120, was found to exhibit SAg-like properties for B cells with potential pathological consequences for the infected host, including accelerated apoptosis and progressive loss of B cells.” https://t.co/szsp5VFxES

“Many studies have investigated TCRs in HIV-infected individuals. Flow cytometry, DNA hybridization, and quantitative PCR have shown decreased expression of certain V genes.” https://t.co/aIOhkopheV | https://t.co/nEcC7r8ymc | https://t.co/VlFmDuplld

“T-Cell Receptor Vβ Repertoire CDR3 Length Diversity Differs within CD45RA and CD45RO T-Cell Subsets in Healthy and Human Immunodeficiency Virus-Infected Children.” ■https://t.co/JmZYivuBKm

“Single-cell TCR sequencing reveals phenotypically diverse clonally expanded cells harboring inducible HIV proviruses during ART.” ■https://t.co/3bbzxa495c No Pulitzer yet ■■■■■■

“Skewed T-cell receptor repertoire: More than a marker of malignancy, a tool
to dissect the immunopathology of inflammatory diseases.” ■https://t.co/cLuJYLUUyk

Third Sequence: COVID-19: AATGGTACTAAGAGG = HIV-1 isolate 19663.24H9 from Netherlands envelope glycoprotein (env) gene, sequence ID: GU455503.1 ■https://t.co/cLuJYLUUyk

“Saturation Mutagenesis of the HIV-1 Envelope CD4 Binding Loop Reveals Residues Controlling Distinct Trimer Conformations.” ■https://t.co/kDghLe2ShF

“Conserved Vδ1 Binding Geometry in a Setting of Locus-Disparate pHLA Recognition by δ/αβ T Cell Receptors (TCRs): Insight into Recognition of HIV Peptides by TCRs.” ■https://t.co/3VRXDm0ZDm

“T■cell receptor and B■cell receptor repertoire profiling in adaptive immunity.” ■https://t.co/33UgrtqRPc

“ab T cell receptors as predictors of health and disease.” ■https://t.co/xDaq5lbpIt

Human leukocyte antigen (HLA) molecules play a central role in the immune response to HIV by presenting viral antigens to T cells. ■ https://t.co/k6SiunP2SJ https://t.co/FcNJUjimU6

“HIV and HLA Class I: an evolving relationship.” ■https://t.co/6kUnsK8Ke9

“retroviruses such as the mouse mammary tumour virus (MMTV) activate a large percentage of T cells by encoding a superantigen (SAg).” ■https://t.co/DX5KYfgrLG

■ https://t.co/UpLocWIVzL

Human immunodeficiency virus 1 reservoir in CD4$^+$ T cells is restricted to certain Vβ subsets

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Communicated by Maclyn McCarty, The Rockefeller University, New York, NY, February 9, 1995

ABSTRACT **The human immunodeficiency virus 1 (HIV-1) replicates more efficiently in T-cell lines expressing T-cell receptors derived from certain Vβ genes, Vβ12 in particular, suggesting the effects of a superantigen. The targeted Vβ12 subset was not deleted in HIV-1-infected patients. It was therefore possible that it might represent an *in vivo* viral reservoir. Viral load was assessed by quantitative PCR with *gag* primers and with an infectivity assay to measure competent virus. It was shown that the tiny Vβ12 subset (1–2% of T cells) often has a higher viral load than other Vβ subsets in infected patients. Selective HIV-1 replication in Vβ12 cells was also observed 6–8 days after *in vitro* infection of peripheral blood lymphocytes from normal, HIV-1 negative donors. Viral replication in targeted Vβ subsets may serve to promote a biologically relevant viral reservoir.**

incubating T cells (usually 3×10^6) with a Vβ-specific r clonal antibody for 45 min, followed by three washe phosphate-buffered saline (PBS) and a second incubatio goat anti-mouse Ig-coated magnetic beads (Dynal, Neck, NY) at 20 beads per target cell for 30 min on ice adherent to the beads were then separated by using a m and washed with PBS. The T cells remaining after remo the magnetic beads were stained with Vβ-specific mono antibody demonstrating 75–100% efficiency of the p selection. The positively selected subset can also be an after prolonged culture to disengage cells from the bea expand cell numbers. Such experiments have previously onstrated the high degree of specificity of this type of p selection (1). Once isolated, these subsets were immed lysed to prepare DNA for PCR, avoiding *in vitro* cell cul

“indistinguishable from the effect of known superantigens (SAGs).” ■https://t.co/VE1XCDTuY7

“existence of SARS-CoV-2 specific T cells within the CD45RA- T memory cells from the blood of convalescent donors. Memory T cells can respond quickly to the infection & provide long-term immune protection to reduce the severity of the COVID-19 symptoms.” ■https://t.co/T9n2SW91Uj https://t.co/JAg7LN1avT

Lol... https://t.co/moINQK1NOx

\U0001f449 \u201cSARS-CoV-2 spike protein may interact with nicotinic acetylcholine receptors (nAChRs), & that such interactions may be involved in pathology & infectivity.\u201d \U0001f449\U0001f449\U0001f449\U0001f449 EVALI \U0001f449 COVID-19 \U0001f447https://t.co/cCdTJiZzQZ pic.twitter.com/Vc8lwKCuH8

— Covid Fact Check \u270c\ufe0f (@2dedostesta2) February 24, 2021

“Our results predict that a viral spike protein peptide (adjacent to the furin cleavage site) exhibits favorable binding affinity to nicotinic acetylcholine receptors and suggest subtype-specific dynamics for the peptide.” https://t.co/SrCJ4TktkG