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Nicotinic receptors as SARS-CoV-2 Spike co-receptors?

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1 **Abstract:** Nicotinic acetylcholine receptors (nAChRs) play an important role in homeostasis
2 and respiratory diseases. Controversies regarding the association between COVID-19
3 hospitalizations and smoking suggest that nAChRs may contribute to SARS-CoV-2 respiratory
4 syndrome. We recently detailed the expression and localization of all nAChR subunits in the
5 human lung. Since virus association with nAChRs has been shown in the past, we
6 hypothesize that nAChR subunits act as SARS-CoV-2 Spike co-receptors. Based on sequence
7 alignment analysis, we report domains of high molecular similarities in nAChRs with the
8 binding domain of hACE2 for SARS-CoV-2 Spike protein. This hypothesis supported by *in*
9 *silico* pilot data provides a rational for the modelling and the *in vitro* experimental validation
10 of the interaction between SARS-CoV-2 and the nAChRs.

11 **Keywords:** Nicotinic receptors; COVID-19; SARS-CoV-2; hACE2; lung

12

13

14 **Background**

15 Severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) is responsible for the global
16 pandemic of coronavirus disease 2019 (COVID-19) [1,2]. Understanding its structure and
17 molecular interactors are crucial to explain the transmission, viral infection, and replication
18 [3]. Recent controversies regarding the impact of smoking on COVID-19 pointed to the
19 potential role of nicotinic acetylcholine receptors (nAChRs) in human angiotensin converting
20 enzyme-2 (hACE2) interaction with SARS-CoV-2 [4,5]. A similar convergence was established
21 regarding the association of nAChRs with rabies virus where the binding was ultimately
22 experimentally demonstrated a few decades ago [6–10].

23 Since it has been proposed that nAChRs may play a key role in the SARS-CoV-2-mediated
24 inflammatory syndrome [11,12], additional avenues are currently explored considering that:
25 (i) nAChRs are widely expressed in organs targeted by the virus including lung, nose, brain,
26 gastrointestinal tract, liver, and smooth muscles [13,14]; (ii) nAChRs are also present on
27 endothelial and platelet cells [15] while altered endothelial function induces vascular
28 thrombosis and microangiopathy in COVID-19 [16,17]; (iii) nAChRs are involved in
29 angiogenesis and arterial diseases [18], while significant vascular angiogenesis was found in
30 lungs from patients who died from COVID-19 [19].

31

32 **The hypothesis**

33 It was recently suggested that smoking may promote cellular uptake mechanisms of SARS-
34 CoV-2 through CHRNA7 signalling [20], and subsequently, CHRNA7 transcripts were
35 correlated with hACE2 levels [21], feeding the possible connections between hACE2 and
36 nAChR localizations in airway epithelial cells. In addition, *in silico* analysis of nAChR ligands
37 suggested an interaction between SARS-CoV-2 and nAChRs [22–24], while nicotine exposure
38 may facilitate SARS-CoV-2 infection *in vitro* [25]. Nicotinic receptors are ligand-gated ion
39 channels consisting of 5 membrane-spanning subunits selected from 16 proteins (CHRNA1-
40 A7, A9-A10, B1-B4, D, E, G) that all harbour at least one extracellular domain of
41 approximately 200 residues. Going one step further, we suggest that nAChRs may bind to
42 SARS-CoV-2-RBD (Receptor Binding Domain) similar to hACE2 and potentially act as co-
43 receptors for SARS-CoV-2-RBD at least in the airways where we documented the complete
44 atlas of pulmonary nAChR subunits in terms of transcript expression and protein localization
45 [26]. Transcripts of all 16 subunits were detected in airway epithelial cells or whole lung

46 tissues and only subunits $\alpha 1/\alpha 2/\alpha 4/\beta 3/\gamma$ were not observed via immunofluorescent
47 stainings performed on formalin-fixed paraffin-embedded lung tissues.

48

49 **Empirical data**

50 The N-terminal domain of hACE2 binding to the spike (S) glycoprotein SARS-CoV-2-RBD and
51 SARS-CoV-1-RBD has been characterized recently [27–30]. Twenty-four hACE2 residues were
52 shown to interact with 21 SARS-CoV-2-RBD residues (region K417 to Y505) and 18 SARS-CoV-
53 1-RBD residues (region R426 to Y491) organized in 4 motifs on hACE2 (**Figure 1A and B**).

54 Postulating that nAChRs may contain extracellular hACE2-like regions mimicking their
55 interactions with SARS-CoV-2, and since structural data of the 16 nAChR subunits are
56 incomplete, we performed bioinformatics analysis using the Clustal Omega program
57 (Uniprot) to align each of the 16 nAChR subunits' extracellular topological domain protein
58 sequences with the 4 motifs containing the binding residues of hACE2 with SARS-CoV-1 and
59 2. We identified identical residues in the 4 regions of interests (ROI) as well as conservations
60 between groups of similar properties with a particular focus on residues located within van
61 der Waals (vdw) contact distance between the viral ligand and the receptor (24 red residues,
62 **Figure 1 and Figure 2**).

63 Key residues to form a solid network between hACE2 and SARS-CoV-2-RBD are localized in
64 the motif-1 (S19-Q42) and the motif-4 (K355-R357). The last residue (R393) was not included
65 in the analysis since it was not in the proximity of other key residues involved in complex
66 formation (**Figure 1**). Interestingly, CHRNA2/A4/A6/A7/A10/B1 presented no overlaps for
67 the 4 motifs (**Figure 2 and Table 1**).

68 We established a score based on the percentage of matching residues either in the entire
69 proposed binding region or solely considering the residues involved in vdw contacts (**Table**
70 **1**). Each of the nAChR subunits presented on average 68.5% ([59.1-81.8]) of resemblance
71 with hACE2 binding regions to SARS-CoV-2-RBD and 64.4% ([47.8-73.9]) solely taking into
72 account vdw contacts. The best scores for the 2 parameters were obtained by CHRNA6
73 (61.4%/73.9%), and CHRNB1 (81.8%/69.5%) (**Figure 2 and Table 1**). Most of nAChRs
74 possessed mutations in the possible binding domains where a loss or a strong inhibition of

75 the interaction with SARS-CoV-1 and 2 was reported (**Table 1, [31]**). Mutagenesis might
76 favour a beneficial role of nAChRs if they were found to bind SARS-CoV-2 but their levels of
77 expression and specific localizations in various tissues weigh up the pros and cons in a
78 complex and not fully elucidated biological scale.

79 **Consequences of the hypothesis and discussion**

80 Although these findings do not demonstrate that nAChRs can function as co-receptors for
81 the ligand SARS-CoV-2-RBD, here we report a significant molecular similarity between hACE2
82 binding sites and extracellular domains of nAChRs. Structural biology to match protein
83 structures in 3D would ideally complement this bioinformatics analysis but crystallized
84 structures of all human nAChR subunits are currently not fully resolved. Notably, the protein
85 folding of nAChRs subunit should reveal the critical residues to allow the interaction with
86 SARS-CoV-2-RBD. In addition, nAChRs function as pentamers, the complexity of the
87 composition of the channel may also contribute to the potential interaction between SARS-
88 CoV-2 and one of the subunits where binding would be possible. Interestingly, CHRNA6 and
89 CHRNB1 transcripts were highly expressed in lung tissues and small airway epithelial cells,
90 and the proteins were strongly detected in bronchi strengthening the possibility of the direct
91 interaction between nAChR subunits and SARS-CoV-2 [26].

92 Although we focus here on similarities of a potential binding domain with hACE2, we do not
93 exclude the possibility that SARS-CoV-2 may interact with alternative domains on nAChRs.
94 The hypothesis of SARS-CoV-2 binding to nAChRs was originally based on the identification
95 of similar known nAChR antagonist/agonist motif sequences on SARS-CoV-2 spike protein.
96 This possible interaction has been sparsely discussed *in silico* [22,23,32]. Finally, although
97 several pentamers are functionally characterized in the nervous system or muscles, the
98 association of subunits in the airways is only partially elucidated and requires further
99 investigations in the context of COVID-19 [26]. Conversely, nAChRs may play a role in COVID-
100 19 progression beyond the respiratory system including systemic inflammation and the
101 nervous system.

102 The modulation of nAChRs in the lung may increase pro-inflammatory cytokine production, a
103 process potentially leading to the "cytokine storm" during infection [33,34]. Moreover, $\alpha 7$
104 nAChR has been involved in the control of inflammation associated with influenza virus

105 infection [35]. nAChR can also control COVID-19 physiopathology by modulating the Renin-
106 Angiotensin System (RAS) [36]. This nicotine-induced imbalance of the two arms of the RAS
107 is likely responsible for cardio-vascular dysfunction, and acute/chronic lung diseases
108 associated with severe forms of COVID-19.

109 The potential neurotropism of SARS-CoV-2 has been discussed extensively. SARS-CoV-2 has
110 been identified in the brain of patients [37]. There is by now a substantial amount of
111 literature, and cases, that link neurological and psychiatric sequelae of COVID-19 to an
112 implication of the human brain. The current state of the discussion has been reviewed [38].
113 Of specific interest is a recent description of a case of Parkinson's Disease directly linked to
114 the infection [39]. The working hypothesis is that SARS-CoV-2 infection can be a "trigger"
115 precipitating the onset of neuropathology. Nicotinic acetylcholine receptors (nAChRs) are
116 important transmembrane neurotransmitter receptors for acetylcholine in the mammalian
117 brain [40]. They modulate key neuronal functions such as excitability, synaptic transmission,
118 and plasticity. They can change neuronal network states and consequently whole-brain
119 responses to internal and external inputs and have been linked to disease [41]. They are also
120 exogenously activated by nicotine and are responsible for the events leading to nicotine
121 addiction [42]. The predominant receptors in the brain are $\alpha 4\beta 2^*$ containing hetero-, and
122 $(\alpha 7)_5$ homo-pentamers [43]. Being particularly expressed in the cortex, hippocampus, and
123 dopaminergic reward system [44], these receptors are considered to be important drug
124 targets [45]. The $\alpha 6$ and $\alpha 5$ -containing receptors are more restricted, but still very present in
125 sub-cortical "modulatory" areas. The presence of SARS-CoV-2 in the brain parenchyma can
126 therefore potentially interfere with higher cognitive function. nAChRs are potentially
127 implicated in the penetration of SARS-CoV-2 into the central nervous system, as they are
128 expressed in many nerve endings [46]. The olfactory route has been established in previous
129 types of coronaviruses able to enter nerve endings and use retrograde axonal transport [47].
130 A possibility is also the vagus nerve. It is well established that it contains most nAChR
131 subunits [48].

132 According to each individual clinical context including but not limited to respiratory diseases
133 and smoking history [49,50], nAChR binding to SARS-CoV-2-RBD may facilitate virus
134 attachment to cell surface before virus entry, or serve as a decoy either harmful as it would
135 prevent the binding of acetylcholine, or beneficial as it would dampen the virus load that

136 may infect epithelial cells [51]. Structural biology and functional analysis on SARS-CoV-2-RBD
137 in complex with nAChRs subunits alone or as pentamers is required to resolve the possible
138 interactions and unveil additional therapeutic strategies.

139

140

141 **Abbreviations**

142	ACE-2	Angiotensin converting enzyme-2
143	BR	Binding region
144	COVID-19	Coronavirus disease 2019
145	ETD	Extracellular topological domain
146	nAChRs	Nicotinic acetylcholine receptors
147	PDB	Protein data bank
148	RBD	Receptor binding domain
149	SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
150	vdw	Van der Waals
151		

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321 **Figure Legends**

322 **Figure 1. hACE2 binding motifs to SARS-CoV-1 and 2 sequences.** (A) Localizations of motifs 1
323 to 4 on hACE2 sequence (Q9BYF1) are highlighted in orange, blue, purple, and green
324 respectively. Red residues are residues involved in van der Waals contact distance between
325 hACE2 and SARS-CoV-1 and 2. Framed residues correspond to residues that are either
326 interacting with SARS-CoV-2-RBD only (E35) or SARS-CoV-1-RBD only (Q325, E329). The
327 residue highlighted in yellow corresponds to the 24th residue involved in van der Waals
328 contact distance but not in the immediate proximity of other residues involved in the
329 binding, therefore it was not included in the analysis. (B) The crystal structure (Protein Data
330 Bank: 6M0J) shows the 4 motifs highlighted in (A) with similar colour codes. The crystal
331 structure of SARS-CoV-2 spike receptor-binding domain bound with hACE2 (PDB ID: 6M0J
332 [52]) was highlighted and exported from the viewer of the Research Collaboratory for
333 Structural Bioinformatics (RCSB; www.rcsb.org).

334

335 **Figure 2. Clustal alignment of nAChRs with hACE2 binding motifs.** Data from the UniProt
336 Knowledgebase (UniProtKB, [53]) were used to perform a sequence alignment study of
337 matching residues between hACE2/SARS-CoV-2 binding sites and nAChR protein sequences.
338 The UniProtKB/Swiss-Prot accession numbers of the sequences used for analyzing the
339 similarities are the following: ACE2 (Q9BYF1), CHRNA1 (P02708), CHRNA2 (Q15822), CHRNA3
340 (P32297), CHRNA4 (P43681), CHRNA5 (P30532), CHRNA6 (Q15825), CHRNA7 (P36544),
341 CHRNA9 (Q9UGM1), CHRNA10 (Q9GZZ6), CHRNB1 (P11230), CHRNB2 (P17787), CHRNB3
342 (Q05901), CHRNB4 (P30926), CHRNG (P07510), CHRNE (Q04844), CHRND (Q07001). Motifs 1
343 to 4 were aligned with the 16 nAChR sequences to identify molecular similarities. The nAChR
344 extracellular topological domains' subunit sequences are represented with the partial
345 alignment obtained with Clustal for the 4 motifs. *, position with a single fully conserved
346 residue; :, position with a residue showing conservation between groups of strongly similar
347 properties (scoring >0.5 in the Gonnet PAM 250 matrix); ., position with a residue showing
348 conservation between groups of weakly similar properties (scoring =<0.5 in the Gonnet PAM
349 250 matrix).

350

351 **Table 1. Table presenting the sequence similarities with SARS-CoV-hACE2 binding motifs**
 352 **for all nAChRs**

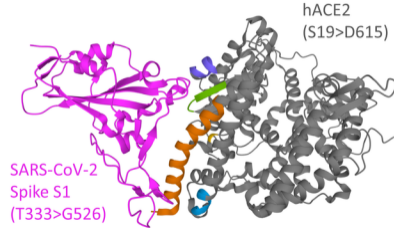
CHRN	ETDL	BRO	BR in ETD (44 R)			vdw contacts in ETD (23 R)			Mutagenesis
			Id (R, (%))	Sim (R, (%))	Tot (R, (%))	Id (R, (%))	Sim (R, (%))	Tot (R, (%))	
A1	21-255	Y	11 (25)	17 (38.6)	28 (63.6)	4 (17.4)	9 (39.1)	13 (56.5)	353 K>D 357 R>A
A2	27-264	N	14 (31.8)	16 (36.4)	30 (68.2)	5 (21.7)	8 (34.8)	13 (56.5)	353 K>D 357 R>A
A3	32-240	Y	12 (27.3)	20 (45.4)	32 (72.7)	6 (26.1)	10 (43.4)	16 (69.5)	31 K>D
A4	29-242	N	14 (31.8)	17 (38.6)	31 (70.4)	5 (21.7)	8 (34.8)	13 (56.5)	353 K>D 357 R>A
A5	23-254	Y	13 (29.6)	18 (40.9)	31 (70.5)	6 (26.1)	11 (47.8)	17 (73.9)	31 K>D 353 K>D
A6	26-239	N	16 (36.4)	11 (25)	27 (61.4)	9 (39.1)	8 (34.8)	17 (73.9)	
A7	23-230	N	12 (27.3)	14 (31.8)	26 (59.1)	5 (21.7)	9 (39.1)	14 (60.8)	
A9	26-237	Y	10 (22.7)	22 (50)	32 (72.7)	5 (21.7)	12 (52.2)	17 (73.9)	
A10	25-237	N	12 (27.3)	17 (38.6)	29 (65.9)	6 (26.1)	7 (30.4)	13 (56.5)	353 K>D 355 D>A
B1	24-244	N	16 (36.4)	20 (45.4)	36 (81.8)	6 (26.1)	10 (43.4)	16 (69.5)	353 K>D
B2	26-233	Y	15 (34.1)	16 (36.4)	31 (70.5)	7 (30.4)	9 (39.1)	16 (69.5)	
B3	25-232	Y	13 (29.6)	20 (45.4)	33 (75)	4 (17.4)	13 (56.5)	17 (73.9)	353 K>D
B4	22-236	Y	14 (31.8)	15 (34.1)	29 (65.9)	5 (21.7)	11 (47.8)	16 (69.5)	31 K>D
G	23-240	Y	14 (31.8)	14 (31.8)	28 (63.6)	5 (21.7)	7 (30.4)	12 (52.1)	353 K>D
E	21-239	Y	12 (27.3)	17 (38.6)	29 (65.9)	2 (8.7)	9 (39.1)	11 (47.8)	
D	22-245	Y	13 (29.6)	17 (38.6)	30 (68.2)	6 (26.1)	10 (43.4)	16 (69.5)	353 K>D

353 Highlighted nAChRs in grey present overlap in binding regions (BR) in Extracellular topological domains (ETD).
 354 The binding regions correspond to the 4 motifs containing a total of 44 residues (R). The van der Waals (vdw)
 355 contacts include 23 residues. ETDL, ETD position on protein sequence; BRO, BR overlaps; Id, fully conserved
 356 residues (Number, % of total); Sim, residues with similar properties (Number, % of total); Tot, sums of the fully
 357 conserved and similar residues (Number, % of total). Bold numbers indicate the best two hits. Mutagenesis
 358 indicates the positions of the residues that were shown to be involved in a loss of SARS-CoV interaction and
 359 that are also present on nAChR sequences.

360

A

	10	20	30	40	50
motif1	MSSSSWLLLS	LVAVTAAQ ST	IEE QAKTFLD	KFNHE AEDLF	YQSSL ASWNY
	60	70	80	90	100
motif2	NTNITEENVQ	NMNNAGDKWS	AFLKEQST LA	QMY PLQEIQN	LTVKLQLQAL
	310	320	330	340	350
motif3	AWDAQRIFKE	AEKFFVSVGL	PNMT Q GFW EN	SMLTDPGNVQ	KAVCHPTAWD
	360	370	380	390	400
motif4	LG KGDFR ILM	CTKVTMDDFL	TAHHEMGHIQ	YDMAYAAQPF	LL R NGANEGF

B

10 20 30 40 50
MKNPFLPLL SLCSAGLVV SEHETRLAK LFKDYSSVR PVEDHVVQ
60 70 80 90 100
VTGVLQIQL INVDVEVQV TTNVRLKGD MVLDFPSPCV TGLVPLFSLH
110 120 130 140 150
DNKWDVQV KRNFDYDGVV KKHIFSRKI WFDLVAIKN AGDFATVAFK
160 170 180 190 200
TKVLQYQTH IWTWPAIFK SYCEIIVTHF PFDQNCNSK LGTMVYDGVV
210 220 230 240 250
VAINPESQDF DLGNMSESG VKWESRQWK HSTVYDQDF TPLDYIIVHF
VMKRL

CHRNA1

10 20 30 40 50
MGSPCVPLFS FTKLISMLL LTPAGGERAK RFPFRAGDP LSSPSPALP
60 70 80 90 100
QSGSHTRKQ RLKPKLFRYK NWRAPRVVMT SDVIVRSLQ SIAGLIDVDR
110 120 130 140 150
KNQMTTWW LKQWESDKL RWRPTFQSI TSLAVFESMI WIPDIVLNN
160 170 180 190 200
ADGFVAIKN TKAHLESTDT VHWVPAIFK SSCSITIVY FFDQNCNSK
210 220 230 240 250
FGSMYDQAK IDLEGMQVY DLKDWESGE MAAVNAVYI NSKDYDCAE
260 270 280 290 300
IYPTVYATV IERL

CHRNA2

10 20 30 40 50
MGSGLLPL ALSPPRLLL LLLSLPVAR ASEARHLEF RLFEDVNEII
60 70 80 90 100
RPAVNSVDV IIEHFVMSQ LKRVDEVQI METNMLKQI WNDYKLVNP
110 120 130 140 150
SYGGASRQV VPACTWQDF ILYVNAWQV FQVDFKRAL KYATGEVVI
160 170 180 190 200
PFAIKGSKQ IDVTFPFYV QNCTMKEQV SYDAKAKLV LIGSMQVQ
210 220 230 240 250
YWSGEMALI KAPYKHDIK YNCEIIVPD ITYSLYIRL
WVW

CHRNA3

10 20 30 40 50
MELGGPQAF LPLPLLLLL TGLLRASSHV ETRAHAERL LKLFQSYNK
60 70 80 90 100
KSRFVANSIS VVIVRFLSI AGLIDVDRN QMNTTWWK QSHWYIKLV
110 120 130 140 150
PDAFVYNSI IRPSELIRK PDIVLYNAD GDFATVAFK AHLFDGVR
160 170 180 190 200
MTPFAIYKSC CSIVITFFFV DQNCNTRKQ SWYDQAKI LNMNSRVQ
210 220 230 240 250
LDWMSGEMV IVDWVYNT RYKCEARLY PDITVAFVR RL
WVW

CHRNA4

10 20 30 40 50
MAARSGPRA LKLLLLQMD AGRCOLAGAA GGAORGLSEP SSIKHEHSL
60 70 80 90 100
LKLQFDQYR WVRVPEHLD KIKIKFGLT SOLVDVDRKN QMNTTWWK
110 120 130 140 150
QEWIVKLRK NFDQDGGIV IRVPSVDFV PDIVLYNAD GFEQSTSTK
160 170 180 190 200
VIRYQWYVM TPFMAYKSC TIDVTFPDQ LQNCMSKVI MYSYDGVQ
210 220 230 240 250
ILEDDQVKN DDFIWESEI VSAVTSQNRK TQCCVYTVY TYSYFIRKL
LWVW

CHRNA5

10 20 30 40 50
MLTSGQKGLI HGLGLMLCVL FTFPFGKGVQ CATEERLFIK LFSHYQFIR
60 70 80 90 100
PVENSYVPT VHEFAVITQL ANVDVEMKI ETNMLKSHIV NDKYLRWQV
110 120 130 140 150
EYDGIETLVR PAKIKKVDI VLYNNAWQV OVQRTKALL KYNMKITWP
160 170 180 190 200
PAIFRSMQV DITTFPFIRH NMLKSPGVS YKAEKIDALI IGSQVDFDQ
210 220 230 240 250
HNSWSEIID ASDYKHDIK NCEIIVYDI TYSYFIRL
WVW

CHRNA6

10 20 30 40 50
MRCSPGVWL ALAALLVVS LQGFQPKLY KELVYVNPFL ERPFVANDQ
60 70 80 90 100
LTVFSLLEL QIMQVDRQV VLTNVLWQV SWDGHYQLWV VSEYGVPTV
110 120 130 140 150
RFPDQIQWF DILLNVAE RFDATHTVY LVNWSGQV LPFQIFKSC
160 170 180 190 200
YLDVWFFPD VQWCKLFSV SYWGSMLDL QMADRSIT IPNWSGQV
210 220 230 240 250
IPGRSEREY ECKCPYFVW TPFVIMRBT
WVW

CHRNA7

10 20 30 40 50
MNSWSCISF CMYIPASRL RAETATQKY AQKLNFLDFE DYSNMLAV
60 70 80 90 100
DTQVYVLIQ QITLQIQIKM DERQULITAY IHTQYDQRA YLTKWQDQ
110 120 130 140 150
SLDSTRIDR LHMDFQVLY NKAQDSQEP WTVWVLYAD GLITWDAPK
160 170 180 190 200
TKSGCVVIT YFFPDQCNK LTVSGMYNG KQVDFINALD SDDSDSEID
210 220 230 240 250
VENWYRMPA VHWVSYGCC SEPYVDTVT LLKRRS
WVW

CHRNA9

10 20 30 40 50
MGLRSHLSL GLLLLFLPA ECLGAEGRLA LKLFIRDFAN YTSALRPVAD
60 70 80 90 100
TQDTLVITL VLSQIIMDM ERQVULIYL WIQEWDYAD LKWQNPYGG
110 120 130 140 150
LDATRIFSL WSRPDIIVLN KADAQFPGA STNVLRSGE AWSDAFATP
160 170 180 190 200
RSCSRVIAW FFDQAQGLQ TFGSTHGGH QLVDFRGA AASLADVENV
210 220 230 240 250
SRVLRQAFR RRVLTGQCC EPTFYVFTL LLRRRAA
WVW

CHRNA10

10 20 30 40 50
MTPGALLML GALGAPLAF VRSQEAERL REKLFSSYDS SVRPAEVDV
60 70 80 90 100
RVRSVGLIL AGLISLNEK EMSTKYVLD LKWTDYRQV DPAHQDIDS
110 120 130 140 150
DRITASEYV FQVLLNND QNFVALDIS VVSDYDGRV WQPFYSSR
160 170 180 190 200
CSIQYTFYF DWQNTWYFS SYDYSQVS LQVLDQGV QGHEIHBSG
210 220 230 240 250
TFIENQDEI IHRPSELQK PGGDFGREG QROEVIFTL IRK
WVW

CHRNA11

10 20 30 40 50
MARQOPVAL LGLFLLRCL SGWWTQVTE FLVSHLQFS RYKYLIPAT
60 70 80 90 100
NSELVTVQL MVSIAQLIYS HREQIMTIN VMLTQSEMY RMLTKRFPD
110 120 130 140 150
NNKRVLRSK HMLFVAVLY NNAQYHYSV FYSNVAVSD GSIWFLPAI
160 170 180 190 200
YSAKCIKVE HFPFDQMT MFRSNTYDR TEIDLKSKS VASLDITFS
210 220 230 240 250
QENDVALAG RNNENPDST YVDIYDFLI RIK
WVW

CHRNA12

10 20 30 40 50
MLPDMMLYLI VLGPSSATT GPNEDANED ALLRHLPQY QRWVRFVH
60 70 80 90 100
NDTRIFQV KISQLVQVDE KQMLTMMWV LKQETKQL RANFDYDGI
110 120 130 140 150
HSIKVSESL WLDIVLFRN ADGRFESGLM TKVYKSNQT VVWFPYASK
160 170 180 190 200
SCTMVTYF PFRQNCMSK FGSMTYDGM VDLILINMY DRKFFESG
210 220 230 240 250
WEILNARQK GNRQDGVSY FFITYSFLVR RL
WVW

CHRNA13

10 20 30 40 50
MRAPSLVLF FVALQDQNR CRVANAERL MDLNLKNTYV NNLIRPATS
60 70 80 90 100
SOLISIKQL SIAGLVSNK REQIMTNNW LQEWTDYPL TNSRSYGVV
110 120 130 140 150
NILKPAKRI WLDIVLYNAD ADGTYEVYV TNLVNSKVS VMLPFPALYK
160 170 180 190 200
SACKIEVYF PFDQNTCLK FRKWTQVTE IDMLVPTTA SMDQTFES
210 220 230 240 250
MDVALQGR TVNPDQSYV DVTYDFIR KELYT
WVW

CHRNA14

10 20 30 40 50
MGGQGLPLL LLLLVACVLA QGNQERLLL ADLQNTQYN LRPASREVD
60 70 80 90 100
VWVSKLTLI NLIISNERE ALTNWVEM QWQVDRQLK FDFYQVETL
110 120 130 140 150
RVSPWWRP DIVLENNDQ VFEVALYCVR LVSPQCIYM LPAFIFASC
160 170 180 190 200
SISVYTFPD WQNCSLPQS QYTSNREIL QLSQEDQTI KWIFIDPAF
210 220 230 240 250
TENGEWQTH RPARMLDFA APAQEAQRK VYVFLIQRK
WVW

CHRNA15

10 20 30 40 50
MARAPLVL LGLLGRGVQ KNEELRYLHV LFNNYDQGR PVREPVETI
60 70 80 90 100
ISLKYVTLIN ISLNEKPEL TFEVWIGIIV QVRYNRSQ DQFQIETLV
110 120 130 140 150
PSELWLFEE VLENNIDQF QVAYDANLY YEGSYVTLV PAIRSVCAV
160 170 180 190 200
EYVTFPQVW NCSLIFQDF YNAREVTFV AVUNDQRTIN KIDDITAVY
210 220 230 240 250
ENCAWATQC FQVIRHBSG ATDQGETDV IYSLIRK
WVW

CHRNA16

10 20 30 40 50
MSEPVITGL LAALQGVGQ GMEERKLR LHFQEQYKQ ELRVAEYK
60 70 80 90 100
SVVDAALIL SNLISKQVE ETLITWVTE HWNTANLAK MAREFQIV
110 120 130 140 150
LGLPFWQV FEVLNNDQ SPQISQYCN VLVHYVYV MLFPAIRSS
160 170 180 190 200
CFISVYTF DWQNCLSKS SLKYAREIT LSLQADQNR RYTFVEMII
210 220 230 240 250
DEPSTEGE MELVHWYR VQDFAPLDS FERGQITYL IRK
WVW

CHRNA17