



PROGRAMME
DE RECHERCHE
PSYCHIATRIE
DE PRÉCISION

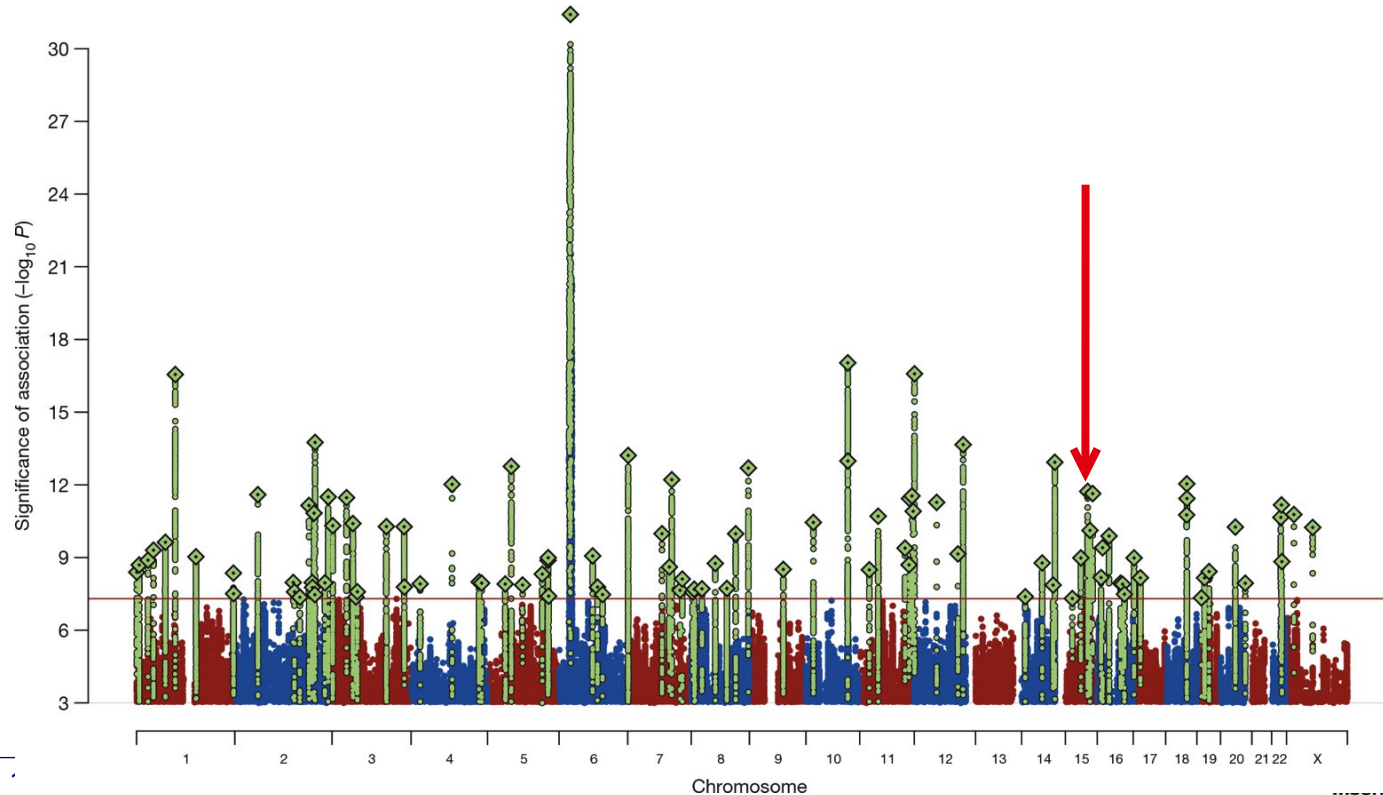
Rôle du récepteur nicotinique de *l'acétylcholine* en psychiatrie de précision

Les auto-anticorps humains contre le récepteur nicotinique et les
maladies psychiatriques

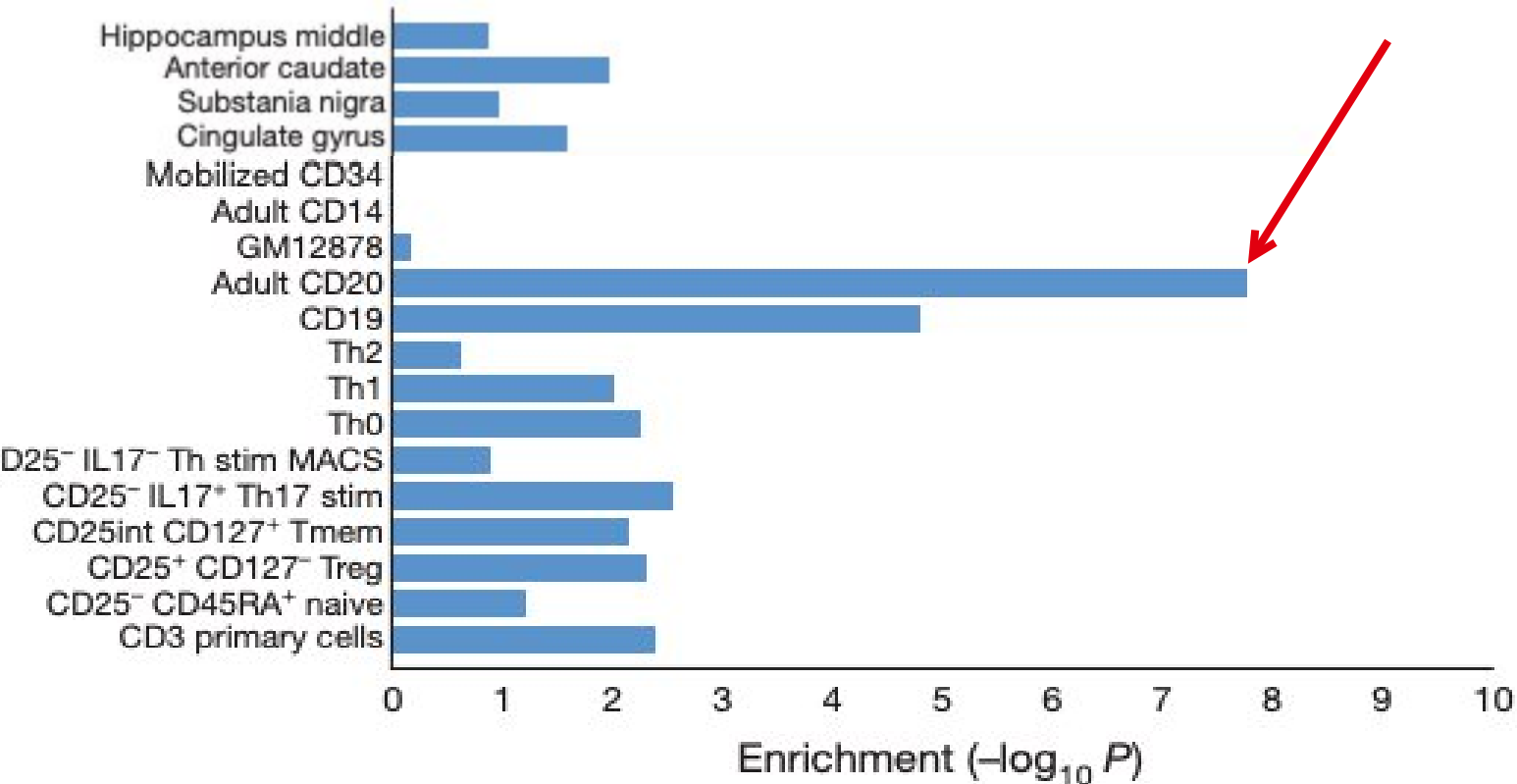
1. Intérêt du récepteur cholinergique



Génétique humaine: GWAS schizophrénie

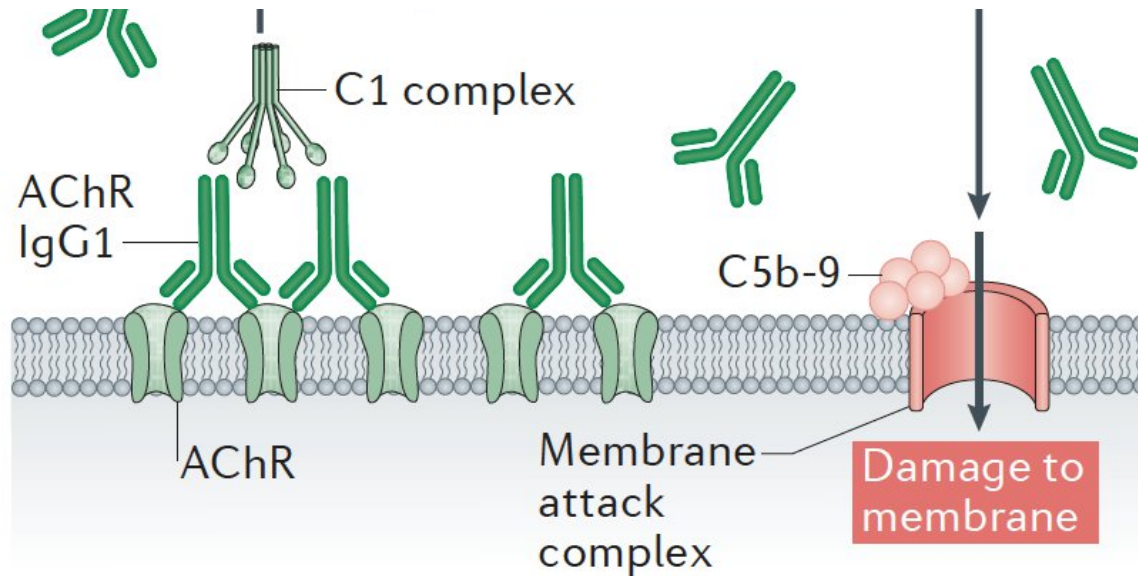


Génétique humaine: expression des SNP-clés

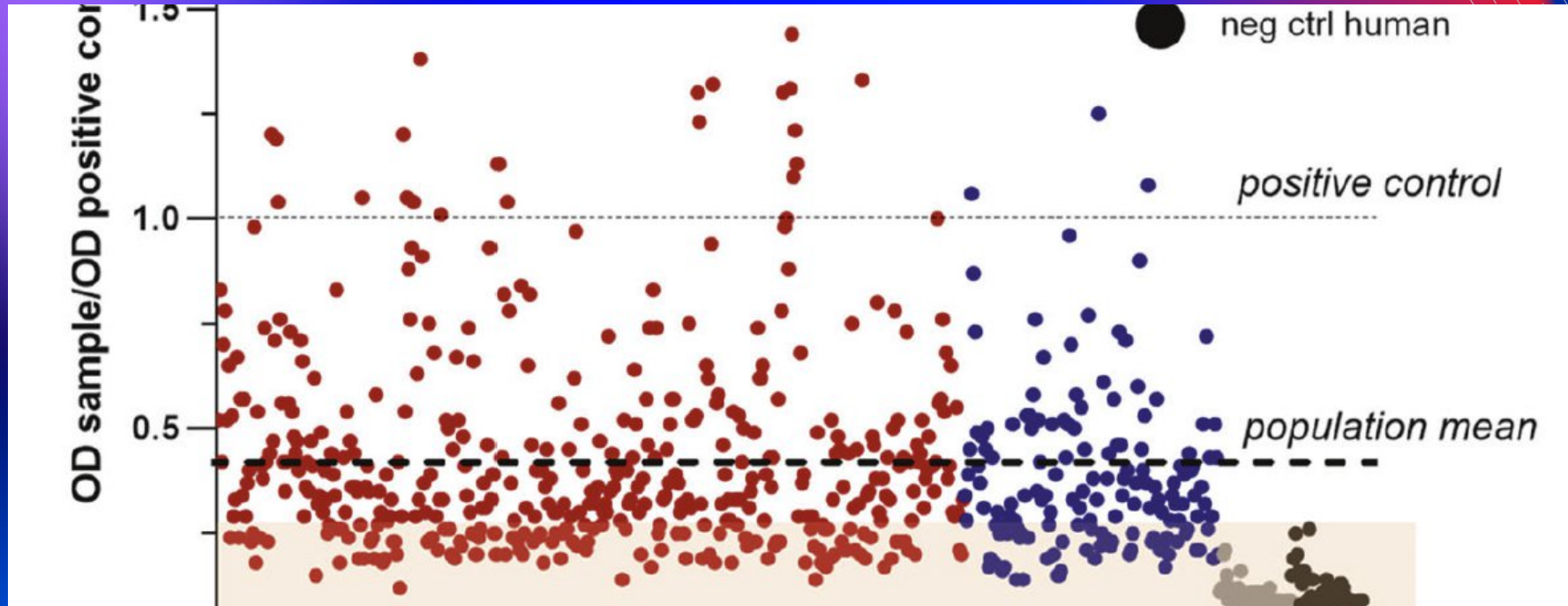


AUTOANTIBODIES TO GANGLIONIC ACETYLCHOLINE RECEPTORS IN AUTOIMMUNE AUTONOMIC NEUROPATHIES

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GIANRICO FARRUGIA, M.D., AND VANDA A. LENNON, M.D., PH.D.

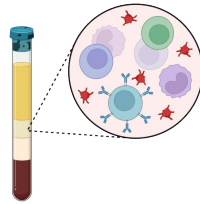


2. Analyse des auto-anticorps

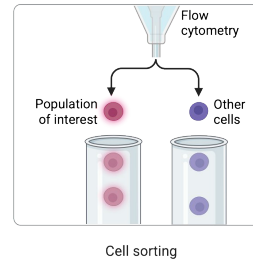


Culture des PBMC

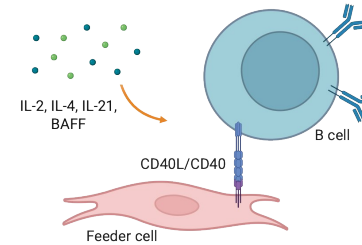
- ① PBMC from psychotic patients



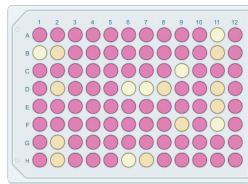
- ② Sort PBMC positive selected for CD19/CD27/nAChRα7



- ③ Co-culture B-cells with feeders cells for 25 days to induce B cell proliferation and maturation

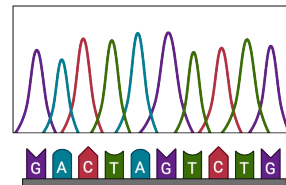


- ④ Cultured B cells are positive selected against nAChRα7 ECD.

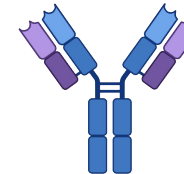


Screening

- ⑤ Sequencing of antibodies



- ⑥ Purification and recombinant expression of α7 antibodies

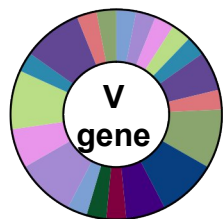


IgG/IgM antibodies

Les clonages effectués

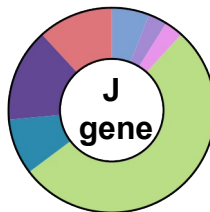
Sort	Date	Cohort	Sample	Cells in vial	Total cells sorted	Clones with a7 ECD reactivity
A	18/05/2024	I-GIVE	IG-001-681 IG-001-622	$4 \cdot 10^5$ $1 \cdot 10^6$	96 460	- 1
D	22/01/2025	I-GIVE	IG-001-137	$4,73 \cdot 10^6$	490	19
E	13/02/2025	I-GIVE	IG-001-681	$2,71 \cdot 10^6$	249	11
F	13/02/2025	I-GIVE	IG-001-325	$4,43 \cdot 10^6$	6	1
G	07/04/2025	I-GIVE	IG-001-331	$9,70 \cdot 10^6$	288	1
H	07/04/2025	I-GIVE	IG-001-628	$3,65 \cdot 10^6$	204	2

Séquençage des auto-anticorps

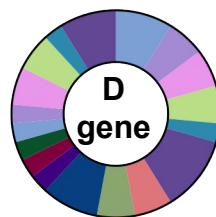


Heavy chain

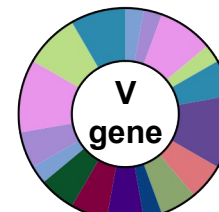
- V1-18*04 F
- V1-3*01 F, or V1-3*04 (F)
- V1-46*01 F
- V1-69*01 F, or V1-69D*01 F
- V1-69*09 F
- V3-15*01 F
- V3-21*01 F
- V3-23*01 F, or V3-23D*01 F
- V3-30*03 F, or V3-30-5*03 F
- V3-30*18 F, or V3-30-5*01 F
- V3-33*01 F, or V3-33*05 F or V3-33*08 F
- V3-49*04 F
- V3-49*05 F
- V3-74*01 F, or V3-74*03 F
- V4-30-2*07 F, or V4-30-4*01 F
- V4-34*01 F
- V4-34*02 F
- V4-39*01 F
- V4-59*02 F
- V4-61*12 F



- J1*01 F
- J2*01 F
- J3*02 F
- J4*02 F
- J5*02 F
- J6*02 F
- J6*03 F

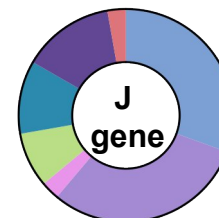


- D1-26*01 F
- D2-15*01 F
- D2-2*01 F
- D2-21*02 F
- D2-8*01 F
- D3-10*01 F
- D3-16*02 F
- D3-22*01 F
- D3-3*01 F
- D3-3*02 F
- D3-9*01 F
- D4-11*01 ORF
- D4-17*01 F
- D4-23*01 ORF
- D5-24*01 ORF
- D6-13*01 F
- D6-19*01 F
- D6-6*01 F



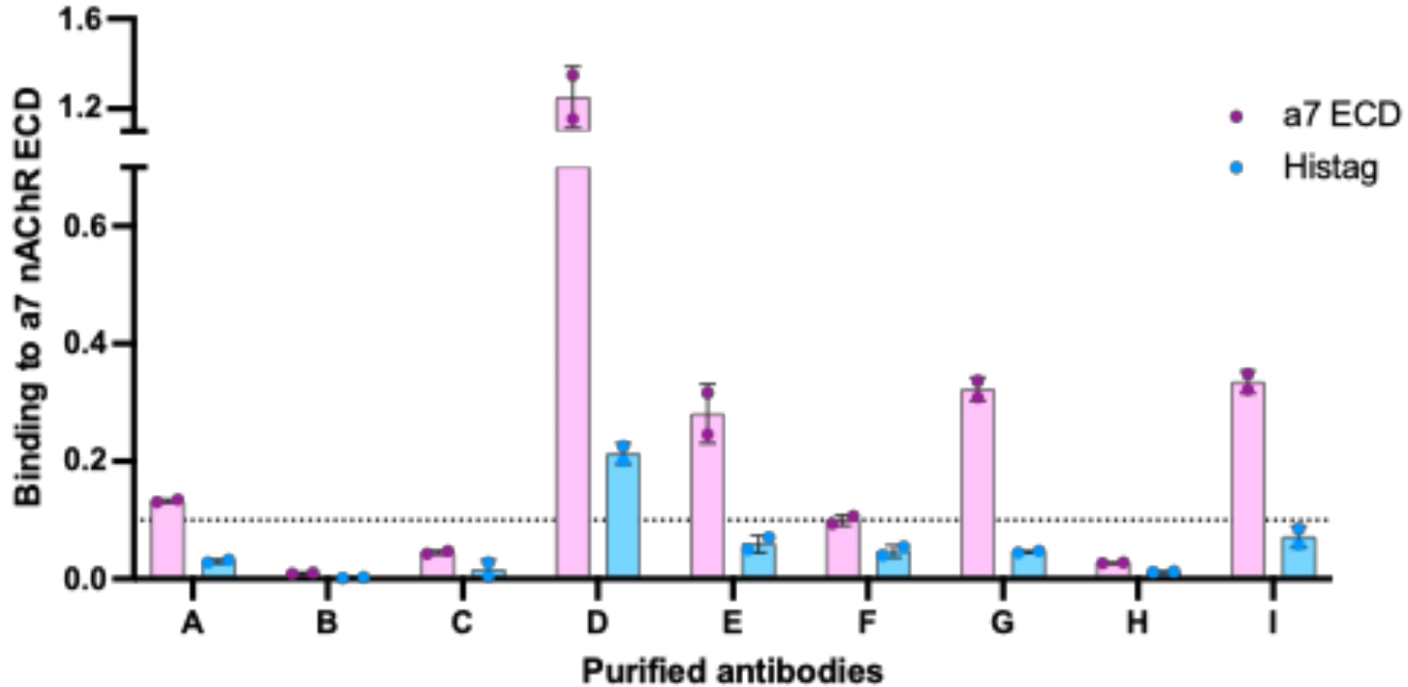
- V1-16*02 [F]
- V1-17*01 F
- V1-39*01 F, or V1D-39*01 F
- V1-44*01 F
- V1-47*01 F
- V1-5*03 F
- V1-5*04 F
- V1-51*01 F
- V1-6*02 F
- V2-23*02 F
- V2-28*01 F, or V2D-28*01 F
- V3-1*01 F
- V3-10*01 F or V3-10*03 F
- V3-11*01 F
- V3-15*01 F
- V3-20*01 F
- V4-1*01 F

Light chain

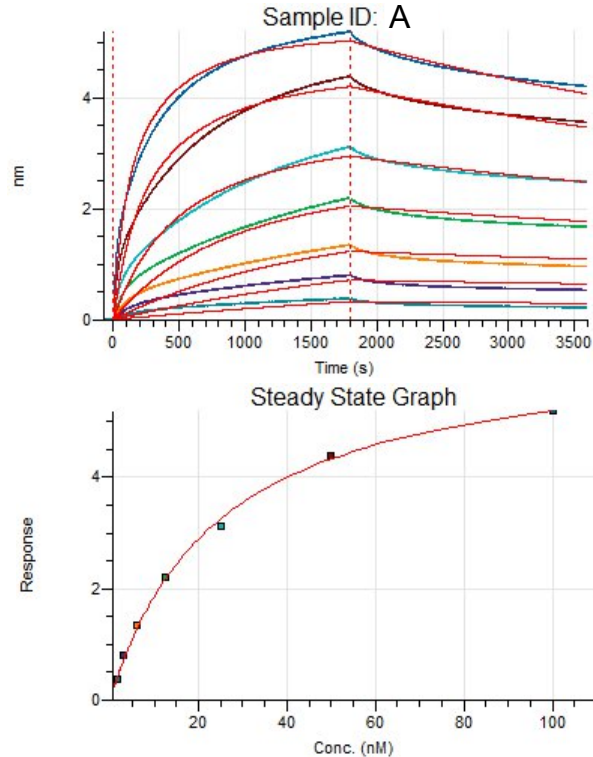


- J1*01 F
- J2*01 F
- J2*02 (F)
- J3*01 F
- J3*02 F
- J4*01 F
- J5*01 F

Caractérisation biochimique



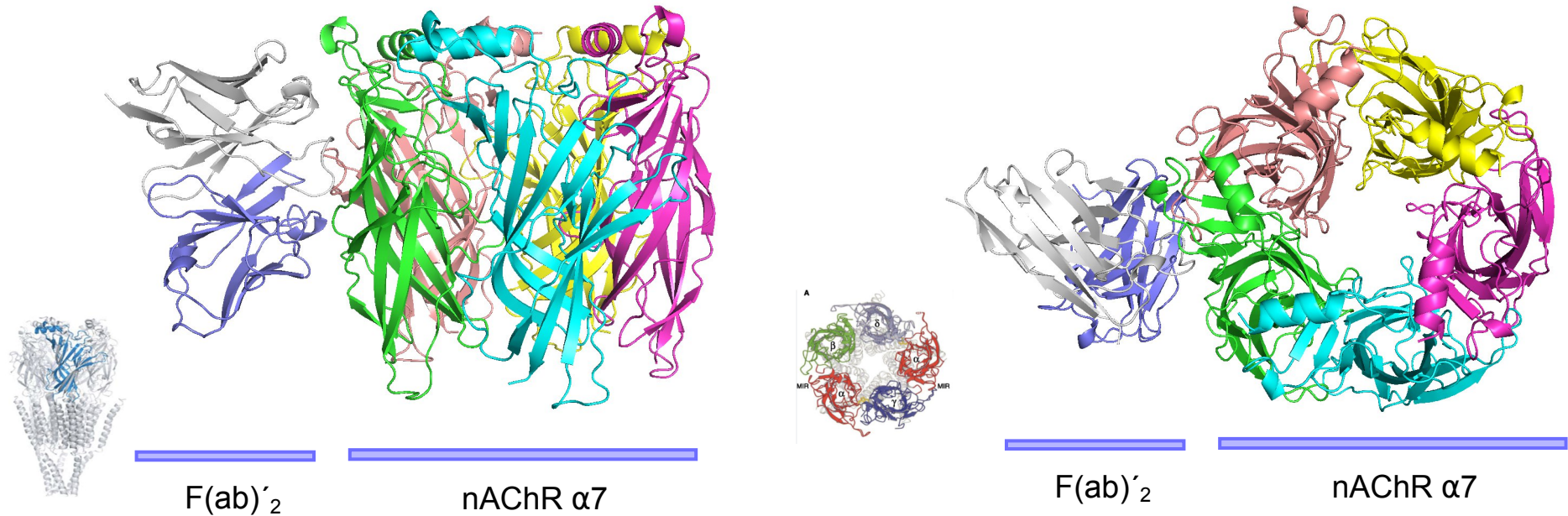
Mesures de l'affinité



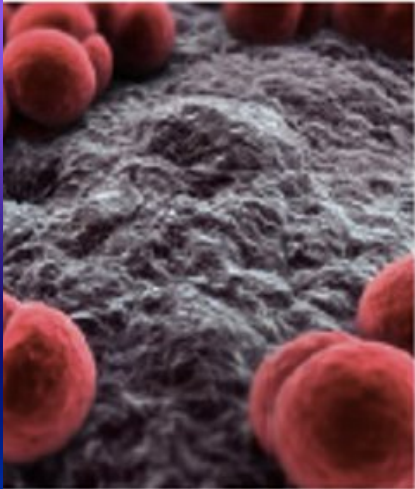
	Steady State
	Association/Dissociation
Sample	alpha 7 ECD
A	2.23E-08
B	6.55E-08
C	5.98E-08
D	1.80E-07
E	7.35E-08
F	8.27E-08
G	7.52E-08

Modélisation du site de liaison

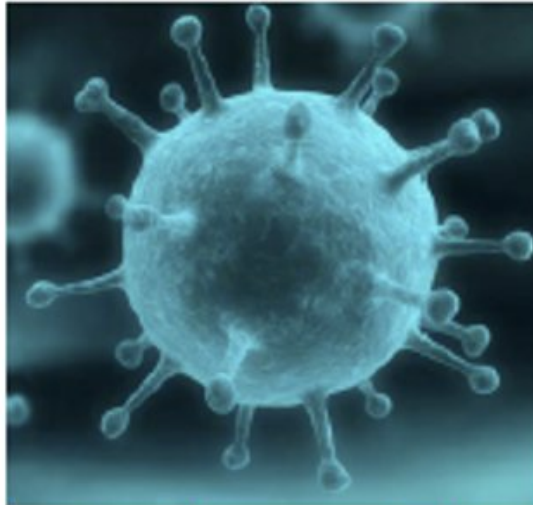
Docking alpha 7 nAChR vs Antibody A F(ab)₂



3. Prospectives: la genèse des AAb



meningitidis



Virus Influenza A (H3N2)



Streptocoque se

Prospectives: les AAb du LCR

HIGH
LIGHT

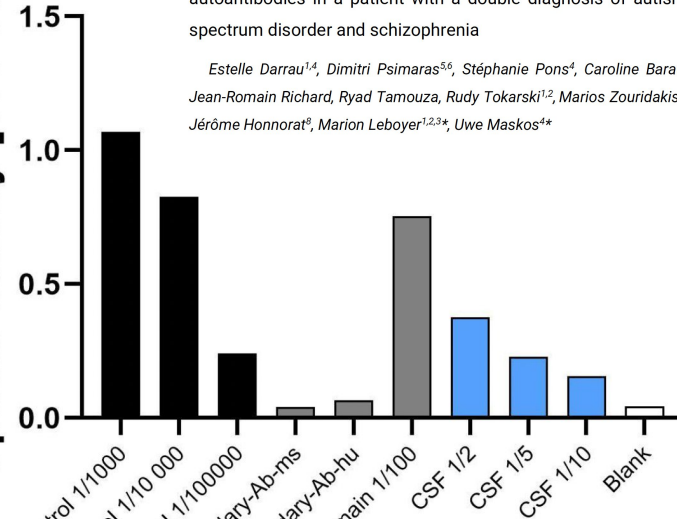
α 7-Acetylcholine receptor antibodies in two patients with Rasmussen encephalitis

Abstract—Rasmussen encephalitis (RE) sera were screened for antibodies to human α 7 nicotinic acetylcholine receptors (nAChRs) using electrophysiology, calcium imaging, and ligand binding assays. Sera from two of nine patients with RE blocked ACh-induced currents through α 7 nAChRs and the AC induced rise in intracellular free calcium ($[Ca^{2+}]_i$) and inhibited ^{125}I -bungarotoxin binding in cells expressing α 7 nAChRs. Thus, the α 7 nAChR is potential target for pathogenic antibodies in patients with RE.

NEUROLOGY 2005;65:1802–1804

R. Watson, DPhil; J.E.C. Jepson, BSc; I. Bermudez, PhD; S. Alexander, BSc; Y. Hart, MD, FRCP; K. McKnight, MRCP; A. Roubertie, MD; F. Fecto; J. Valmier, MD, PhD; D.B. Sattelle, ScD; D. Beeson, PhD; A. Vincent, FRCPath; and B. Lang, PhD

Optical density [490-415]



A case of anti- α 7-nicotinic receptors and NMDA autoantibodies in a patient with a double diagnosis of autism spectrum disorder and schizophrenia

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L'équipe: Friederike Jönsson, Stéphanie Pons, Jose Garcia, Alicia Velazquez, Sandrine



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Développer une pharmacologie ciblant ces récepteurs

Article

<https://doi.org/10.1038/s41467-023-41734-4>

An original potentiating mechanism revealed by the cryo-EM structures of the human $\alpha 7$ nicotinic receptor in complex with nanobodies

Received: 5 January 2023

Accepted: 15 September 2023

Published online: 25 September 2023

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