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Title Key role of the TM2-TM3 loop in calcium potentiation of the $\alpha 9\alpha 10$ nicotinic acetylcholine receptor

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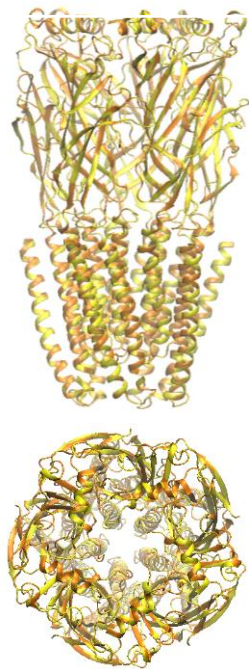
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a

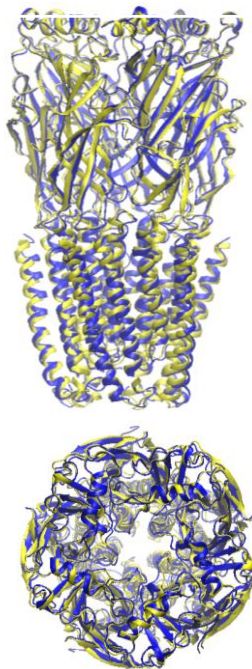
Receptors	RMSD (Å)		
	$\alpha 9$	$\alpha 9\alpha 10$	$a9\alpha 10^*$
$\alpha 9$	0.03	1.07	1.30
$\alpha 9\alpha 10$		1.10	0.98
$a9\alpha 10^*$			0.61

$a9\alpha 10^* = a9\alpha 10^{\alpha 9TM2TM3loop}$

$\alpha 9$ (r1) vs $\alpha 9$ (r2)



$\alpha 9$ (r1) vs $\alpha 9\alpha 10$ (r2)



b

Receptors	RMSD (Å)			
	$\alpha 9$	$\alpha 10$	4uy2	$\alpha 7$ (D)
$\alpha 9$		0.6	1.9	1.3
$\alpha 10$			2.0	1.4
4uy2				2.0
$\alpha 7$ (D)				

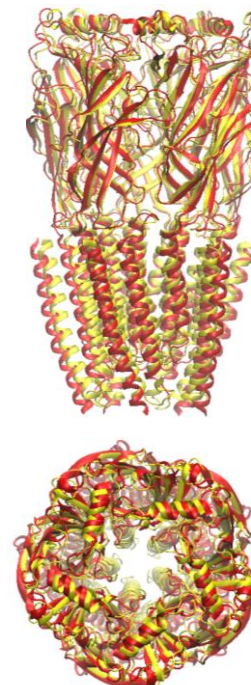


c

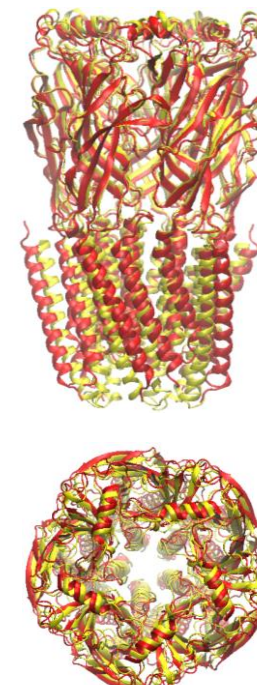
$\alpha 7$ State	RMSD (Å)		
	$\alpha 9$	$\alpha 9\alpha 10$	$a9\alpha 10^*$
D	2.2	2.6	2.7
R	2.9	3.2	3.2
A	3.6	3.7	3.7

$a9\alpha 10^* = a9\alpha 10^{\alpha 9TM2TM3loop}$

$\alpha 9$ (r1) vs $\alpha 7$ -D



$\alpha 9$ (r1) vs $\alpha 7$ -A



Structural comparison of $\alpha 9$, $\alpha 9\alpha 10$, and $a9\alpha 10^{\alpha 9TM2TM3loop}$ AlphaFold models with reference nAChR structures. Panel a: Comparison between the receptor models used in this study. The table data correspond to the average RMSD after whole structure fitting of the model replicas (r1 and r2) generated. Panel b: Comparison of the extracellular domain (ECD) of the $\alpha 9$ (yellow) and $\alpha 10$ (blue) chains of the AlphaFold models with the ECD of the human $\alpha 9$ CRX structure (PDB ID: 4UY2, green) and the cryo-EM structure of human $\alpha 7$ in the desensitized conformation (red). Panel c: Comparison between the $\alpha 9$ and $\alpha 9\alpha 10$ structural models and the cryo-EM structures of human $\alpha 7$ in the desensitized (D), resting (R), and active (A) conformations (pdb Ids= 7koq, 7koo and 7kox, respectively). The superposition of selected structures from the comparisons in Panels A, B, and C are presented.