



## M2 segment

	-5'	-3'	-1'	0	2'	6'	9'	13'	17'	20'																			
nAChR $\alpha$	238-D	S	G	-	E	K	M	T	L	S	I	S	V	L	L	S	L	T	V	F	L	L	V	I	V	E	L	I	P
nAChR $\beta$	244-D	A	G	-	E	K	M	S	L	S	I	S	A	L	L	A	V	T	V	F	L	L	L	L	A	D	K	V	P
nAChR $\gamma$	246-Q	A	G	G	Q	K	C	T	L	S	I	S	V	L	L	A	Q	T	I	F	L	F	L	I	A	Q	K	V	P
nAChR $\delta$	252-E	S	G	-	E	K	M	S	T	A	I	S	V	L	L	A	Q	A	V	F	L	L	L	T	S	Q	R	L	P
GABA <sub>A</sub> $\alpha$ 1	250-E	S	V	P	A	R	T	V	F	G	V	T	T	V	L	T	M	T	T	L	S	I	S	A	R	N	S	L	P
GABA <sub>A</sub> $\beta$ 1	245-D	A	S	A	A	R	V	A	L	G	I	T	T	V	L	T	M	T	T	I	S	T	H	L	R	E	T	L	P
GABA <sub>A</sub> $\gamma$	260-D	A	V	P	A	R	T	S	L	G	I	T	T	V	L	T	M	T	T	L	S	T	I	A	R	K	S	L	P
gly $\alpha$ 1	214-D	A	S	A	A	R	V	G	L	G	I	T	T	V	L	T	M	T	T	Q	S	S	G	S	R	A	S	L	P
gly $\beta$ 1	271-D	A	S	A	A	R	V	P	L	G	I	F	S	V	L	S	L	A	S	E	C	T	T	L	A	A	E	L	P
nAChR $\alpha$ 7	234-D	S	G	-	E	K	I	S	L	G	I	T	V	L	L	S	L	T	V	F	M	L	L	V	A	E	I	M	P

■ Water accessible, based on Cys modification

## M1 segment

nAChR $\alpha$	211-P	L	Y	F	I	V	N	V	I	I	P	C	L	L	F	S	F	L	T	G	L	V	F	Y	L	P
nAChR $\beta$	217-P	L	F	Y	L	V	N	V	I	A	P	C	I	L	I	T	L	L	A	I	F	V	F	Y	L	P
nAChR $\gamma$	219-P	L	F	Y	I	I	N	I	I	A	P	C	V	L	I	S	S	L	V	V	L	V	Y	F	L	P
nAChR $\delta$	225-P	L	F	Y	V	I	N	F	L	T	P	C	V	L	I	S	F	L	A	S	L	A	F	Y	L	P

○ Labeled by [<sup>125</sup>I]TID as protein lipid interface

■ Water accessible, based on Cys modification

**Figure 1-4 M2 and M1 segments of the nAChR**

A. Helical model of the M2 segment showing rings known to affect channel function and QX-222 interactions

B. Sequences of M1 and M2 segments of LGICs showing residues which were modified by water soluble probes (■) as well as those residues in M1 which were labeled by [<sup>125</sup>I]TID as protein-lipid interface (○).