Supplemental Information: Figure S1

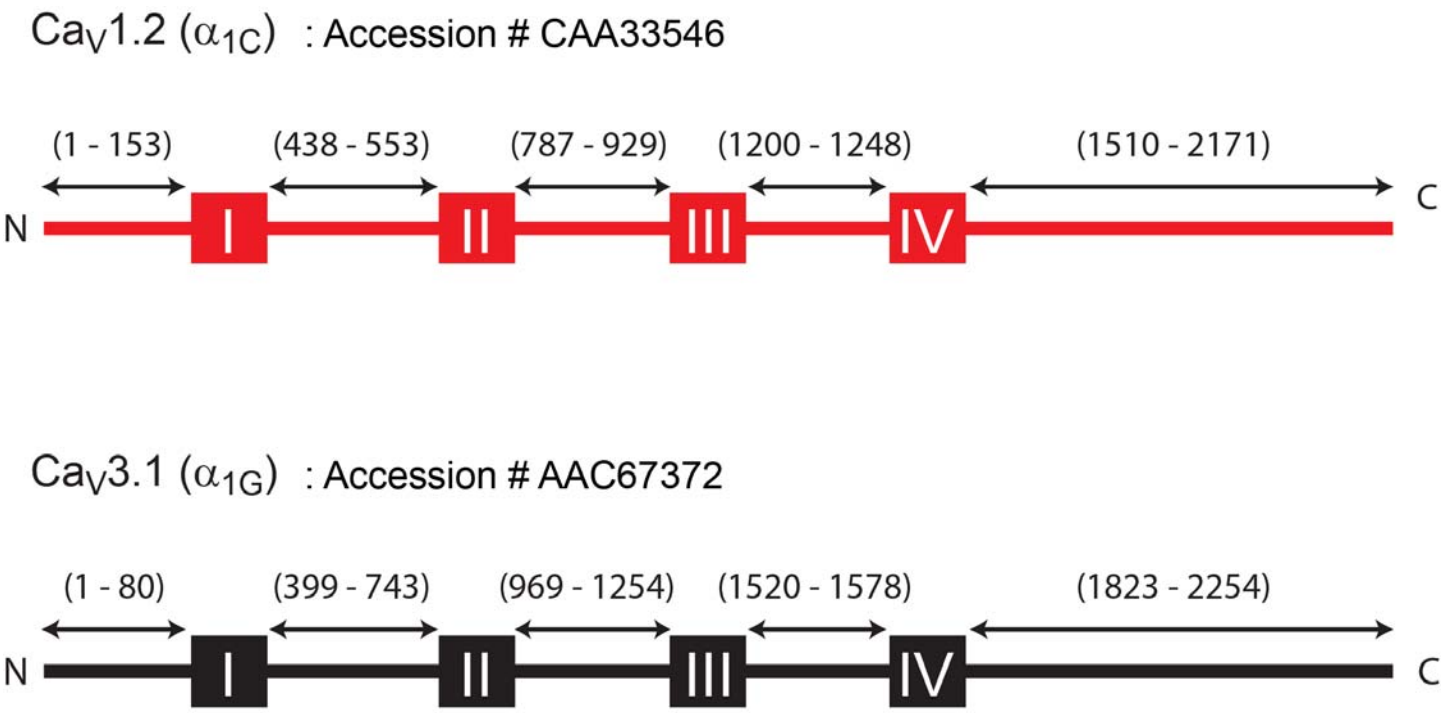

Figure S1. Schematic showing precise boundaries of the N- and C-termini, and intracellular loops of Ca$_V$1.2 (top) and Ca$_V$3.1 channels (*bottom*) used to generate chimeric channels.

Supplemental Information: Figure S2

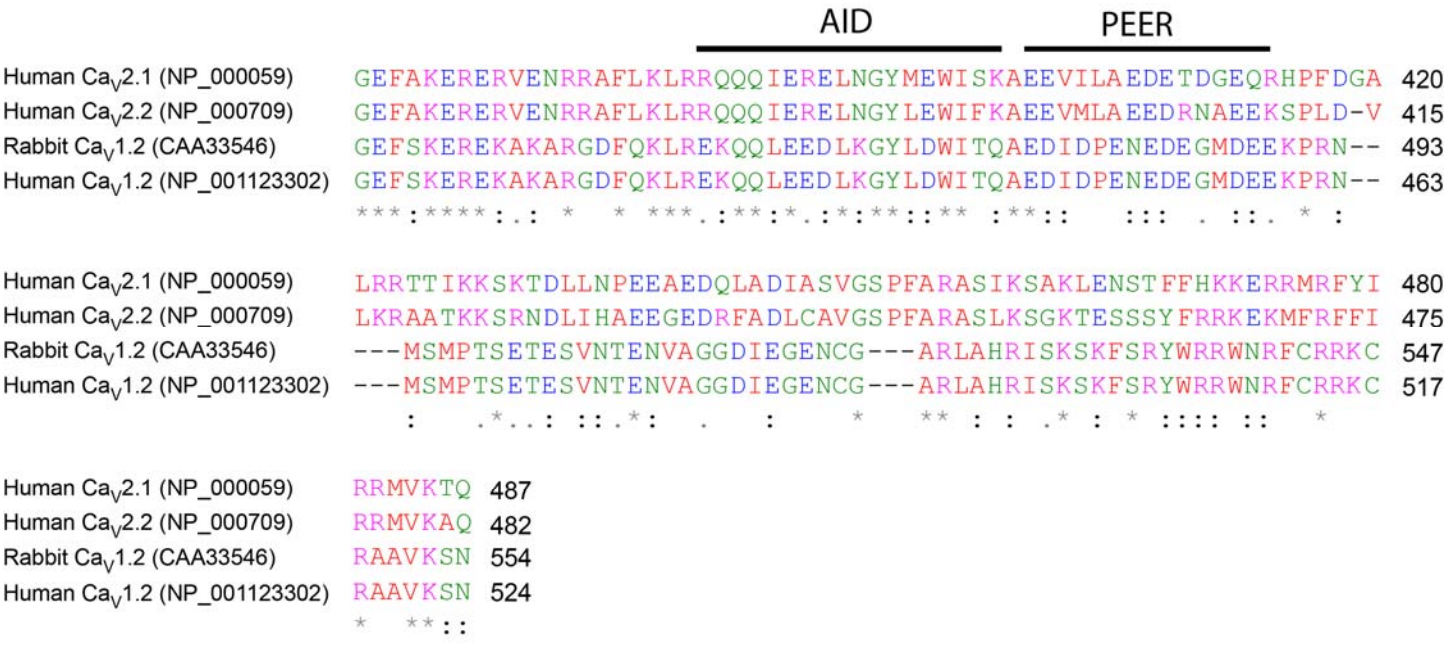

Figure S2. ClustalW alignment of the intracellular I-II loop of distinct Ca_V1 and 2 channels showing regions of sequence conservation and homology. The previously identified α interaction domain (AID) is shown. Immediately downstream of the AID is the acidic-residue-rich putative ER export region (PEER) identified in this study.

Supplemental Information: Figure S3

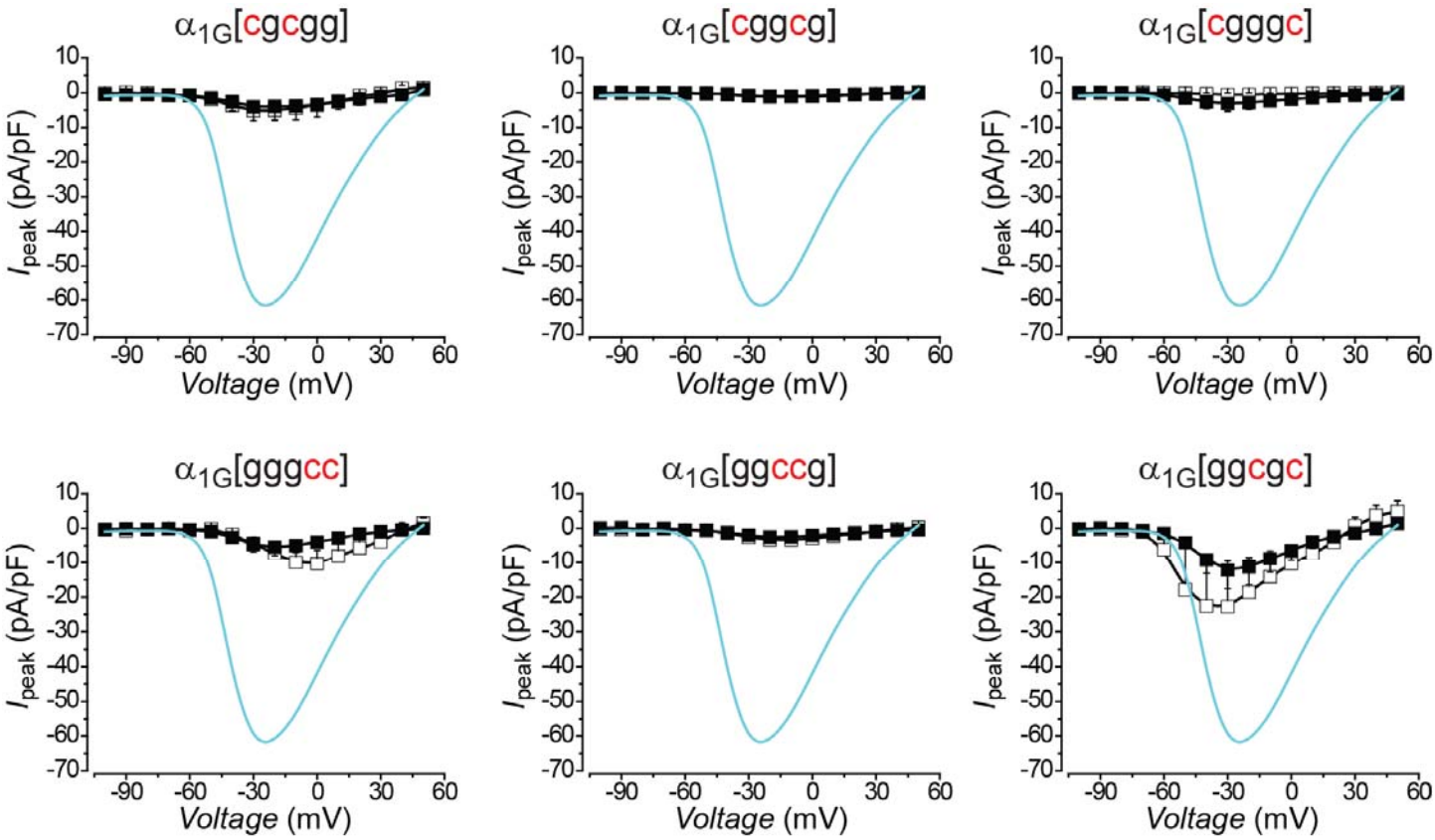

Figure S3. I_{peak}-V curves of double-intracellular-domain substituted chimeras either expressed alone (open symbols) or with β_{2a} subunits (solid symbols).

Supplemental Information: Figure S4

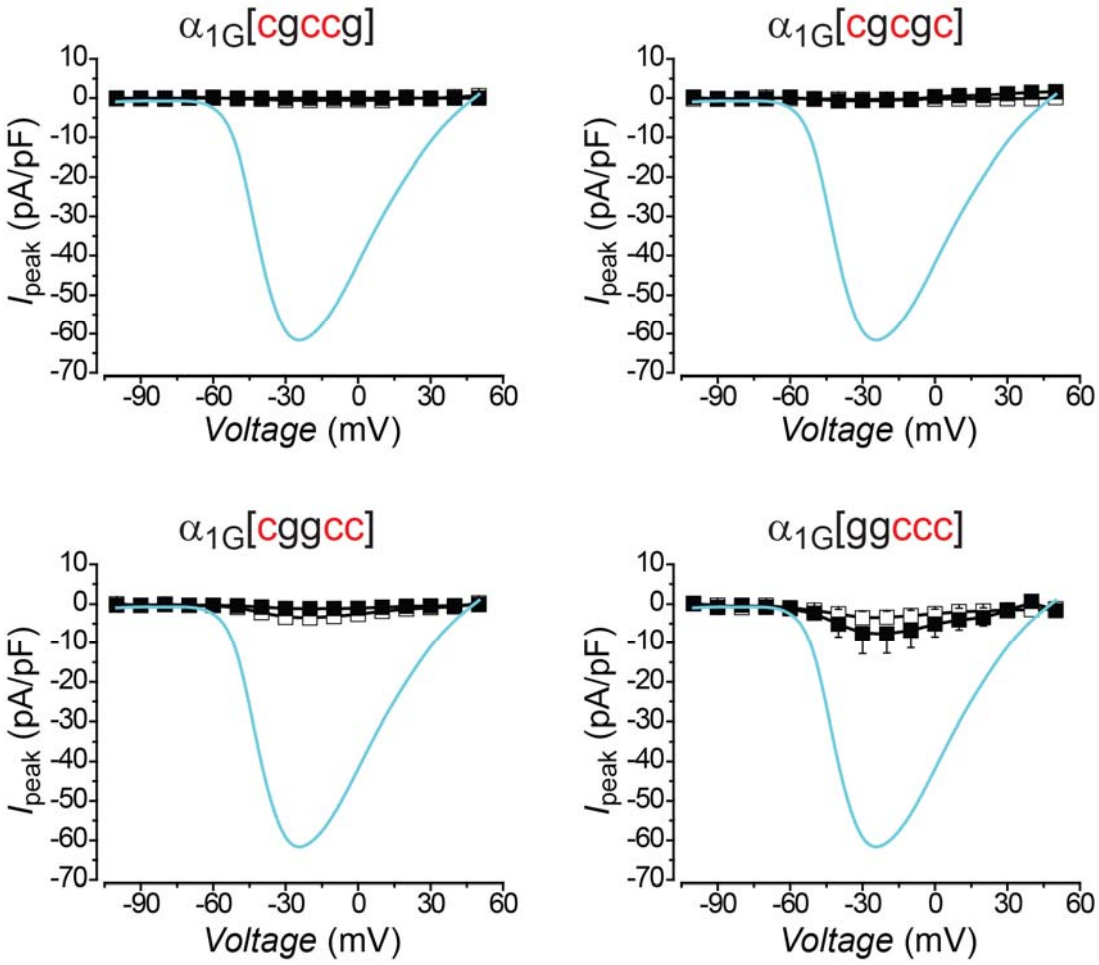

Figure S4. I_{peak}-V curves of triple-intracellular-domain substituted chimeras either expressed alone (open symbols) or with β_{2a} subunits (solid symbols).

Supplemental Information: Figure S5

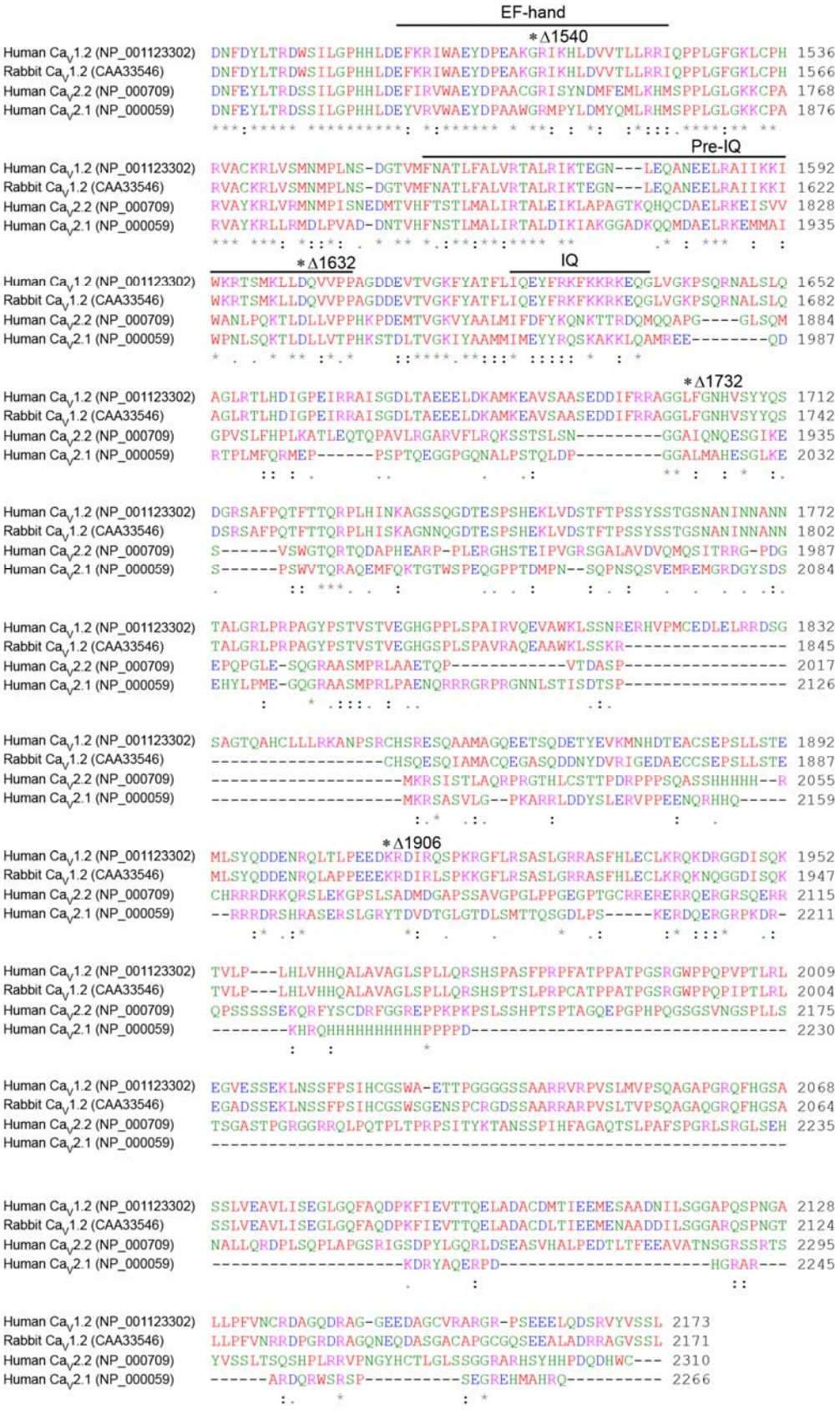

Figure S5. ClustalW alignment of the C-termini of distinct Ca_V1 and 2 α_1 subunits.

Supplemental Information: Figure S6

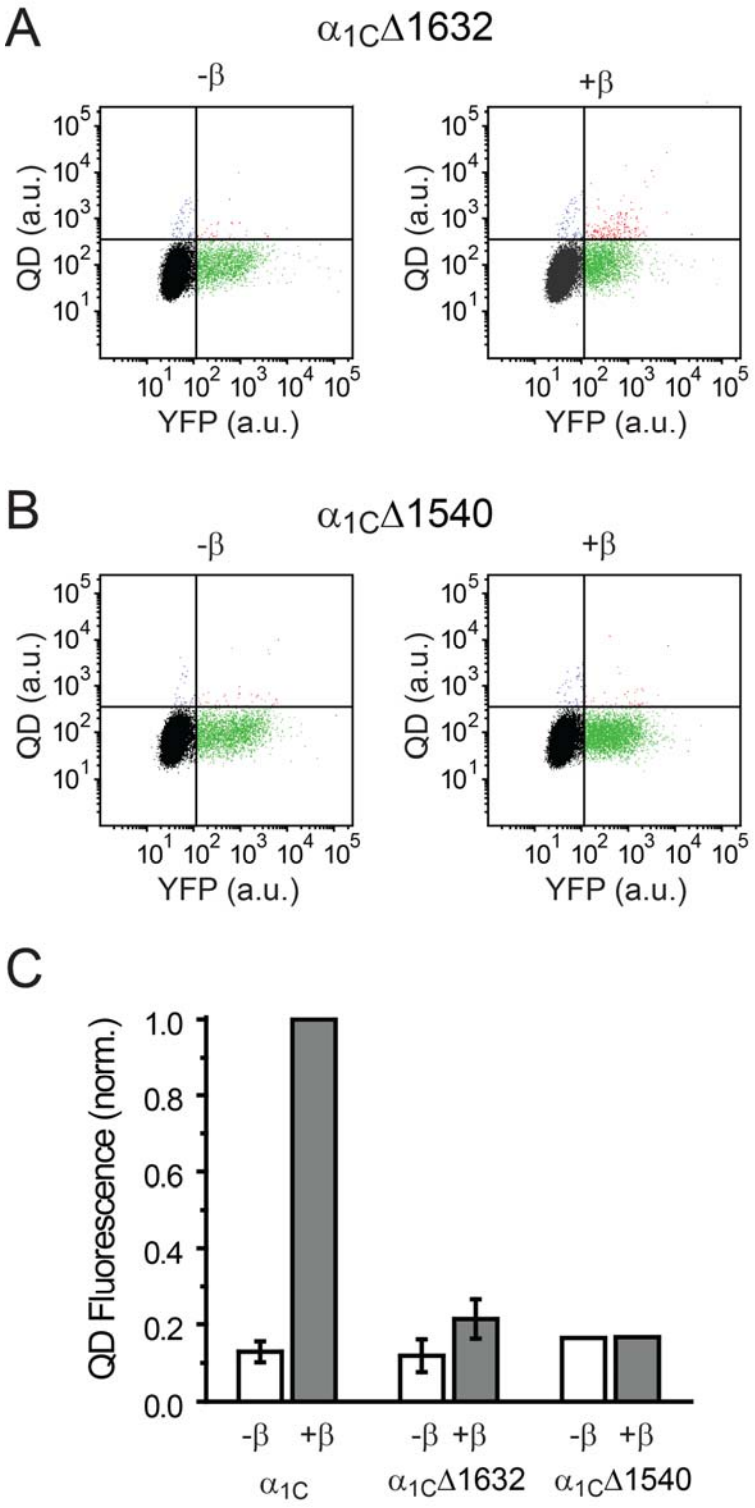

Figure S6. **Impact of C-terminus truncations on β-dependent membrane-targeting of α_{1C} subunits. (A, B)** Exemplar flow cytometry results for $\alpha_{1C}\Delta1633 \pm \beta_{2a}$ and $\alpha_{1C}\Delta1540 \pm \beta_{2a}$, respectively. **(C)** Normalized QD fluorescence intensity for truncated mutants compared to full-length α_{1C}.

Table S1. PCR primers used to generate single-intracellular-domain substituted chimeras by using in-fusion technique. For each chimera, four primers were required. The underlined 15-nucleotide segments are within the boundary of α_{1G} at the α_{1G}/α_{1C} junctions. The red 15-nucleotide segments in forward primer for insert and in reverse primer for vector, and the blue 15-nucleotide segments in forward primer for vector and in reverse primer for insert, are complementary reversal, respectively, thus the purified PCR insert and vector could be directly linked together with the consequent in-fusion reaction.

Constructs	PCR Targets	Templates	Primer 1 (Forward)	Primer 2 (Reverse)
α_{1G}[cgggg]	Insert (α_{1C} N-Terminus)	α_{1C}-YFP	GCTTCTGGCCAGAGGATGCTTCGAGCCCTTG TTCAGCCAGCTAC	TCGCTCGAACCACGGCCACTCGACGATGCTTA TGCACGCC
	Vector	α_{1G}-YFP	CCGTGGTTCGAGCGAGTCAGTATG	CCTCTGGCCAGAAGCTTAAGTTTAAAC
α_{1G}[gcggg]	Insert (α_{1C} I-II loop)	α_{1C}-YFP	ATTGCCACGCAGTTCTCCAAAGAGAGGGAGA AGGCCAAAGC	CCGGCCAAAGTATTTCGACTTGACCGCTGCGC GGCACTTTCTCCTG
	Vector	α_{1G}-YFP	AAATACTTTGGCCGGGGAATCATG	GAACTGCGTGGCAATCACCACCAGGCAC
α_{1G}[ggcgg]	Insert (α_{1C} II-III loop)	α_{1C}-YFP	CTTGTGGAAGGATTCGCTGATGCTGAGAGCC TTACTTCTGC	ATGGTCAAACATCTTGTCGTTGACGATACGGT GACACTG
	Vector	α_{1G}-YFP	AAGATGTTTGACCATGTGGTCCTCG	GAATCCTTCCACAAGAATGGCCACCAGCAGGT TAAAG
α_{1G}[gggcg]	Insert (α_{1C} III-IV loop)	α_{1C}-YFP	GTGGTGGAGAACTTCCAGGAGCAGGGGGAGC AGGAGTAC	GAGGTCCAGGTAGTGGGAGTTGACCACGTACC ACACTTTG
	Vector	α_{1G}-YFP	CACTACCTGGACCTCTTCATCACTG	GAAGTTCTCCACCACCACGCCCACAAACATG
α_{1G}[ggggc]	Insert (α_{1C} C-Terminus)	α_{1C}-YFP	CTGATGAAGCACCTGGACTACCTGACAAGGG ACTGGTCAATC	CTTGCTCACATCGATCAGGCTGCTGACGCCGG CCCTGCGGTCCGCG
	Vector	α_{1G}-YFP	ATCGATGTGAGCAAGGGCGAGGAGCTGTTC	CAGGTGCTTCATCAGCACAGCTATG