

## SUPPLEMENTAL TABLES AND REFERENCES

**Supplemental Table 1.** Residues in hCD81 and dmTSP96F backbones with critical functions.

CD81 residue	CD81 domain	Corresponding residue in dmTSP96F	Function	Reference	conserved in dmTSP96F backbone
C6	cytoplasmic N-terminus	C6	palmitoylation	[1,2]	yes
C9	cytoplasmic N-terminus	C9	palmitoylation	[1,2]	yes
N18	TM1	N18	cholesterol contact, hydrogen bonds	[3]	yes
F21	TM1	F21	cholesterol contact	[3]	yes
N43	small extracellular loop	L43	predicted beta sheet, interaction with LEL	[4]	no
L44	small extracellular loop	n.a.	predicted beta sheet, interaction with LEL	[4]	no
L45	small extracellular loop	n.a.	predicted beta sheet, interaction with LEL	[4]	no
Y46	small extracellular loop	n.a.	predicted beta sheet, interaction with LEL	[4]	no
L47	small extracellular loop	n.a.	predicted beta sheet, interaction with LEL	[4]	no
E48	small extracellular loop	n.a.	predicted beta sheet, interaction with LEL	[4]	no
I64	TM2	V58	cholesterol contact	[3]	hydrophobic
V68	TM2	I62	cholesterol contact	[3]	hydrophobic

V71	TM2	L65	cholesterol contact	[3]	hydrophobic
M72	TM2	I66	cholesterol contact	[3]	hydrophobic
V75	TM2	G69	cholesterol contact	[3]	hydrophobic
F94	TM3	F88	cholesterol contact	[3]	yes
L98	TM3	I92	cholesterol contact	[3]	hydrophobic
L101	TM3	V95	cholesterol contact	[3]	hydrophobic
K116	TM3	K110	salt bridge open conformation	[3]	yes
D117	TM3	D111	salt bridge open conformation	[3]	yes
E219	TM4	S250 (E247)	cholesterol contact, hydrogen bonds	[3]	no
C228	cytoplasmic C-terminus	C259	palmitoylation	[1,2]	yes

**Supplemental Table 2.** Critical residues in the hCD81 LEL and their function.

CD81 residue	CD81 domain	Function	Reference
Q125	LEL	predicted SEL contact	[4]
T149	LEL	predicted CDLN1 contact	[5]
E152	LEL	predicted CDLN1 contact	[5]
T153	LEL	predicted CDLN1 contact	[5]
T153	LEL	predicted SEL contact	[4]
C156	LEL	disulfite bond with C190	[3]

C157	LEL	disulfite bond with C175	[3]
L162	LEL	HCV E2 binding	[6]
T163	LEL	HCV E2 binding	[7]
L171	LEL	HCV E2 binding	[8]
L174	LEL	HCV E2 binding	[8]
C175	LEL	disulfite bond with C157	[3]
I181	LEL	HCV E2 binding	[8]
I182	LEL	HCV E2 binding	[6,8]
N184	LEL	HCV E2 binding	[6]
L185	LEL	HCV E2 binding	[8]
F186	LEL	HCV E2 binding	[7,8]
K187	LEL	HCV E2 binding	[8]
E188	LEL	HCV E2 binding	[8]
D189	LEL	HCV E2 binding	[8]
C190	LEL	disulfite bond with C156	[3]
D196	LEL	HCV E2 binding	[7]
D196	LEL	salt bridge closed conformation	[3]
K201	TM4	salt bridge closed conformation	[3]

## Bibliography

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