Supplementary Information

Structure of the human TRiC/CCT Subunit 5 associated with hereditary sensory neuropathy

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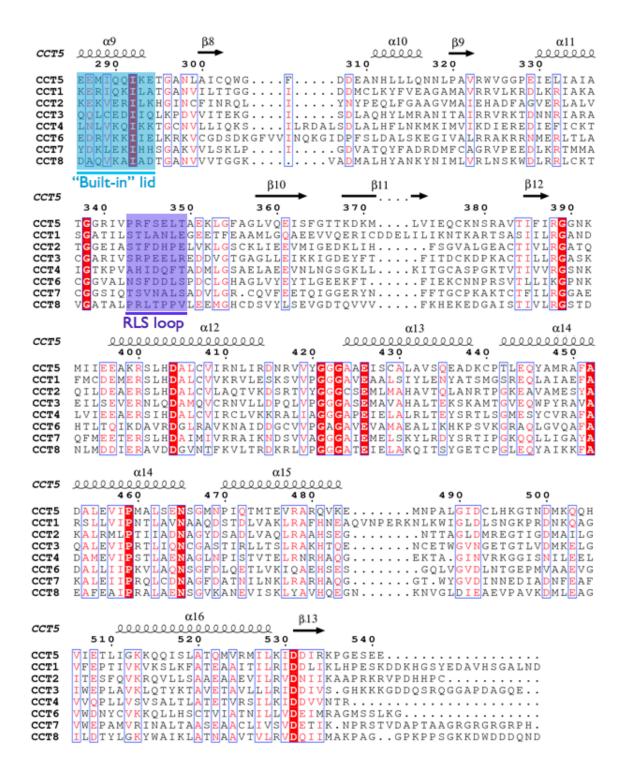
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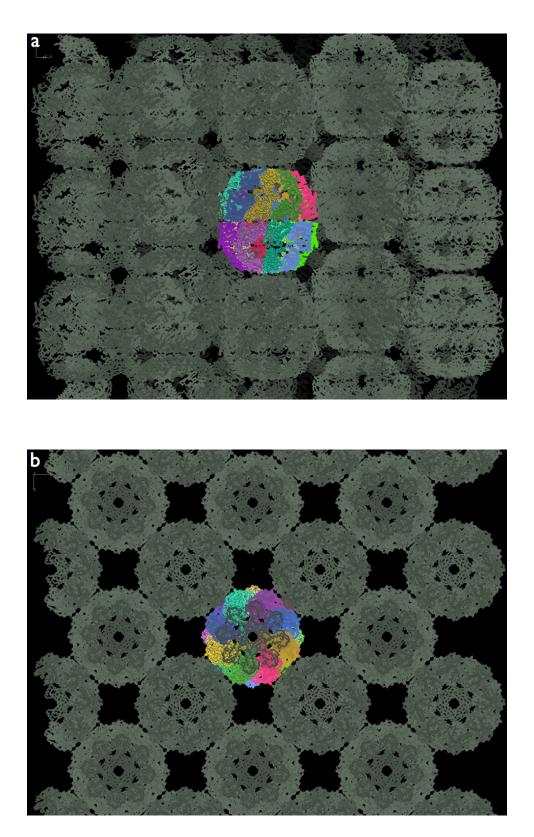
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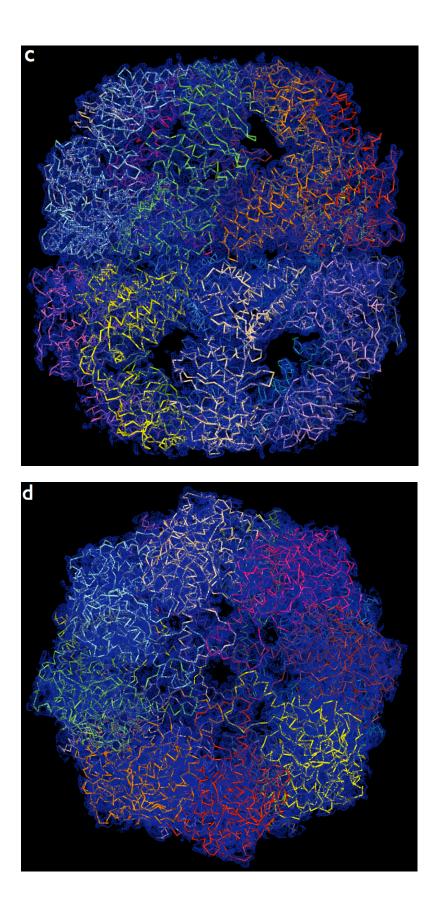
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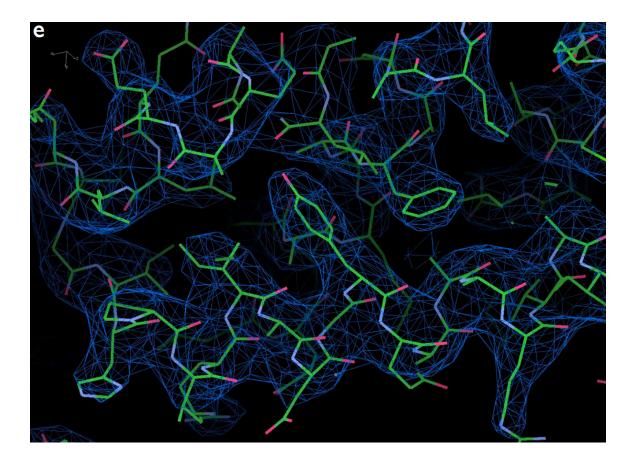
CCT5					x1 0 0 0 0 0 0 0 0 0
	i	10	20	30 40	o 50
CCT5 CCT1 CCT2 CCT3 CCT4		MASLSLAPV MMGHRPV	GPLSVFGDRS NIFKAGADEE LVLSONTKRE	TGETIRSQ <mark>NV</mark> M RAETARLTSFI SGRKVOSG <mark>NI</mark> N	AAKAVANTMRTSLGPN AAASIANIVKSSLGPV GAIAIGDLVKSTLGPK AAKTIADIIRTCLGPK AAKAVADAIRTSLGPK
CCT6 CCT7 CCT8		MA	AVKTLNPKAE ILLKEGTDSS QMLKEGAKHF	VARAQAALAVNIS QGIPQLVSNIS	AARGLQDVLRTNLGPK ACQVIAEAVRTTLGPR ACKELAQTTRTAYGPN
CCT5	60 60	→ Q	α2 00000 80	90000000000000000000000000000000000000	<u>2000000</u> 100 110
CCT5 CCT1 CCT2 CCT3 CCT4 CCT6 CCT7 CCT8	GMD <mark>K</mark> MIQDGKGD GTMKMLVSGAGD GMDKLIVDGRGK GMNKMVINHLEK	VT ITNDG ASLMVTNDG IVMTNDG VTITNDG IKLTKDG ATISNDG LFVTNDA	ATILKLLEVE ATILKNIGVD NAILREIQVQ ATILKQMQVL NVLLHEMQIQ ATILKLLDVV	HQIAKLMVELSKS HPAAKVLCELADL NPAAKVLVDMSRV HPAAKSMIEISRT HPAARMLVELSKA HPTASLIAKVATA HPAAKTLVDIAKS HPAAKMIVMASHM	DKEVGDGTTSVVIIA DDEVGDGTTSVTVLA DEEVGDGTTSVIILA DIEAGDGTTSVVIIA DDIEAGDGTTSVVIIA
	_{α4} Sensor lo		α5		loop-B α6
CCT5	<u>2000000000000000000000000000000000000</u>	130	140	150	160 <u>2222222</u>
CCT5 CCT1 CCT2 CCT3 CCT4 CCT6 CCT7 CCT8	AELLKNADELVA AELLREAESLIA GEMLSVAEHFLE GSLLDSCTKLLC GELLKQADLYIS AEFLKQVKPYVE	QKIHPTSVI AKKIHPQTII QQMHPTVVI QKGIHPTIIS EGLHPRIIT EGLHPQIII	S G Y R L A C K E A A G W R E A T K A A S A Y R K A L D D M E S F Q K A L E K G E G F E A A K E K A R A F R T A T Q L A	VRYINE.NLIVNT REALLSSAVDHGS ISTLKK.ISIPV IEILTDMSRPV. LQFLEEVKVSREM VNKIKE.IAVTV	DIKD.TEPLIQTAKTT DELG.RDCLINAAKTS DEVKFRQDLMNIAGTT DISD.SDMMLNIINSS ELSD.RETLLNSATTS DRETLIDVARTS KKAD.KVEQRKLLEKC NLRD.IDEVSSLLRTS
CCT5		α7		6.2	
	000	2000000000	00	p3	\bullet $\alpha 8 \beta 4 \beta 5$
	180	190	200	210	
CCT5 CCT1 CCT2 CCT3 CCT4 CCT6 CCT7 CCT8	180 LGSKVVNSCHRO MSSKIIGINGDE LSSKLLTHHKDE ITTKAISRWSSI LNSKVVSQYSSI LRTKVHAELADV AMTALSSKI IMSKQYGNEVFI	MAEIAVNAV FANMVVDAV FANMVVDAV HFTKLAVEAV ACNIALDAV LSPMSVNAV /LTEAVVDSI JSQQKAFFA AKLIAQACV	200 LTVAD.MERR LAIKYTDIRG LRLKGSGN KMVQFEENGR MKVIDPATAT LAIKKQDEP. KMVVDAVMML	DVDFELTKVEG QPRYPVNSVNILK LEAIHIIK KEIDIKKYARVEK SVDLRDIKIVK IDLFMIEIME DDLLQLKMIGIKK	220 KVGGRLEDTKLIKGVI AHGRSQMESMLISGYA KLGGSLADSYLDEGFL IPGGIIEDSCVLRGVM KLGGTIDDCELVEGLV MKHKSETDTSLIRGLV VQGGALEDSQLVAGVA ILGSGISSSSVLHGMV
CCT1 CCT2 CCT3 CCT4 CCT6 CCT7	180 LGSKVVNSCHRG MSSKIIGINGDE LSSKLLTHHKDE ITTKAISRWSSI LNSKVVSQYSSI LRTKVHAELADV AMTALSSKI	DODOOOOOOOO 190 DAEIAVNAV FFANMVVDAV IFTKLAVEAV ACNIALDAV LSPMSVNAV LSPMSVNAV JISOOKAFFA	200 LTVAD.MERR LAIKYTDIRG LRLKGSGN KMVQFEENGR MKVIDPATAT LAIKKQDEP. KMVVDAVMML	DVDFELTKVEG QPRYPVNSVNILK LEAIHIIK KEIDIKKYARVEK SVDLRDIKIVK IDLFMIEIME DDLLQLKMIGIKK	220 220 KVGGRLEDTKLIKGVI AHGRSQMESMLISGYA KLGGSLADSYLDEGFL IPGGIIEDSCVLRGVM KLGGTIDDCELVEGLV MKHKSETDTSLIRGLV VOGGALEDSQLVAGVA
CCT1 CCT2 CCT3 CCT4 CCT6 CCT7 CCT8 CCT5 2	180 LGSKVVNSCHRQ MSSKIIGINGDE LSSKLLTHHKDE ITTKAISRWSSI LNSKVVSQYSSI LRTKVHAELADV AMTALSSKI IMSKQYGNEVFI β5 30 240	COODOCOCO 190 CMAEIAVNAV FFANMVVDAV IFTKLAVEAV ACNIALDAV LSPMSVNAV LS	200 LTVAD.MERR LAIKYTDIRG LRLKGSGN KMVQFEENGR MKVIDPATAT LAIKKQDEP. KMVVDAVMML SIEPDSGH β7 250	DVDFELIKVEG QPRYPVNSVNILK LEAIHIIK KEIDIKKYARVEK SVDLRDIKIVK IDLFMIEIME DDLLQLKMIGIKK FNVDNIRVCK	220 KVGGRLEDTKLIKGVI AHGRSQMESMLISGYA KLGGSLADSYLDEGFL IPGGIIEDSCVLRGVM KLGGTIDDCELVEGLV WQGGALEDSQLVAGVA ILGSGISSSSVLHGMV 0 0 280
CCT1 CCT2 CCT3 CCT4 CCT6 CCT7 CCT8		Ν Ν	200 LTVAD.MERR LAIKYTDIRG LRLKGSGN KMVQFEENGR MKVIDPATAT LAIKKQDEP. KMVVDAVMML SIFPDSGH β7 250 IAILTCPFEP IACLDFSLQK ILIANTGMDT IVLLDSSLEY IGLIQFCLSA ILTCNVSLEY IALLNVELEL IAVYSCPFDG	DVDFELIKVEG QPRYPVNSVNILK LEAIHIIK KEIDIKKYARVEK SVDLRDIKIVK IDLFMIEIME DDLLQLKMIGIKK FNVDNIRVCK 260 27 PKPKT.KHKLDVT: TKMKL.GVQVVITI DKIKIFGSRVRVD: KKGES.QTDIEITI PKTDM.DNQIVVSI EKTEV.NSGFFYK: KAEKD.NAEIRVH	220 KVGGRLEDTKLIKGVI AHGRSQMESMLISGYA KLGGSLADSYLDEGFL IPGGIIEDSCVLRGVM KLGGTIDDCELVEGLV MKHKSETDTSLIRGLV VQGGALEDSQLVAGVA ILGSGISSSSVLHGMV α9 0000000000000000



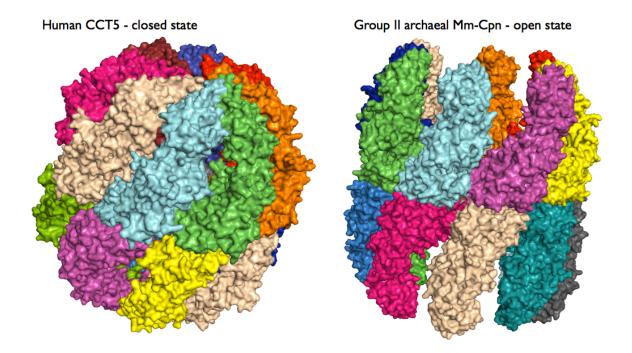
Supplementary Fig 1 – Sequence alignment of the eight human TRiC/CCT subunits. The secondary structure elements for CCT5 subunit are displayed at the top of the sequence alignment. The nucleotide-binding loop-A and loop-B, the sensor loop, rls-loop and the Apical-loop regions are indicated bellow the sequences. Figure was made using the program ESPRIPT (Robert & Gouet, 2014).



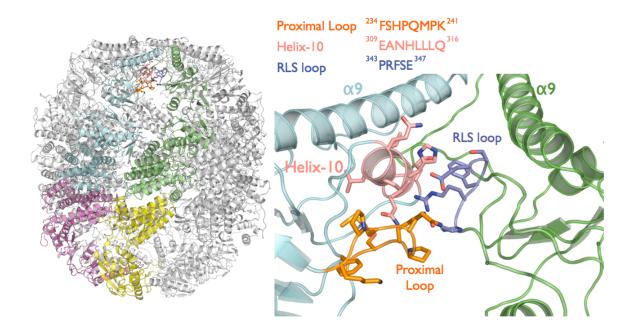




Supplementary Fig 2 – Crystal structure of the single CCT5 subunit shows the two back-to-back rings of eight subunits each, similar to the hetero-octameric human TRiC arrangement. **a,b**) Crystal packing showing the Side and Top view of CCT5 homo-octameric arrangements. **c,d,e**) Crystal structure of CCT5 solved at 3.5 Å resolution showing the experimental 2mFo-DFc electron density map contoured at 1.0 σ (blue) from the side and top view of the CCT5 double octameric rings arrangements and a zoom in at α -helices regions of equatorial domain, respectively.



Supplementary Fig 3 – Homo-octameric double ring back-to-back arrangement of the CCT5 in a closed state and the group II chaperonin from *Methanococcus maripaludis* (Mm-Cpn) in an open state (PDB ID 3KFK) (Pereira *et al.*, 2010). The open state is associated with the peptide acceptor conformation that major conformation change upon the ATP hydrolysis and the chamber is closed to fold the protein substrates.



Supplementary Fig 4 – CCT5 ring arrangement showing substrate-binding site and release loop of substrate loop (rls-loop) contacting each other on the closed state observed for CCT5 in complex with ADP. Ring picture and a zoom in showing proximal loop (orange) and helix-10 (pink) of CCT5 subunit contacting the rls-loop (blue) from adjacent subunit at apical domain region of the ring.

References

Robert, X. & Gouet, P. Deciphering key features in protein structures with the new ENDscript server. *Nucl. Acids Res.* **42**, 320-324 (2014).

Pereira J.H. *et al.* Crystal structures of a group II chaperonin reveal the open and closed states associated with the protein folding cycle. *J. Biol. Chem.* **285**, 27958-27966 (2010).