Signal integration in the (m)TORC1 growth pathway

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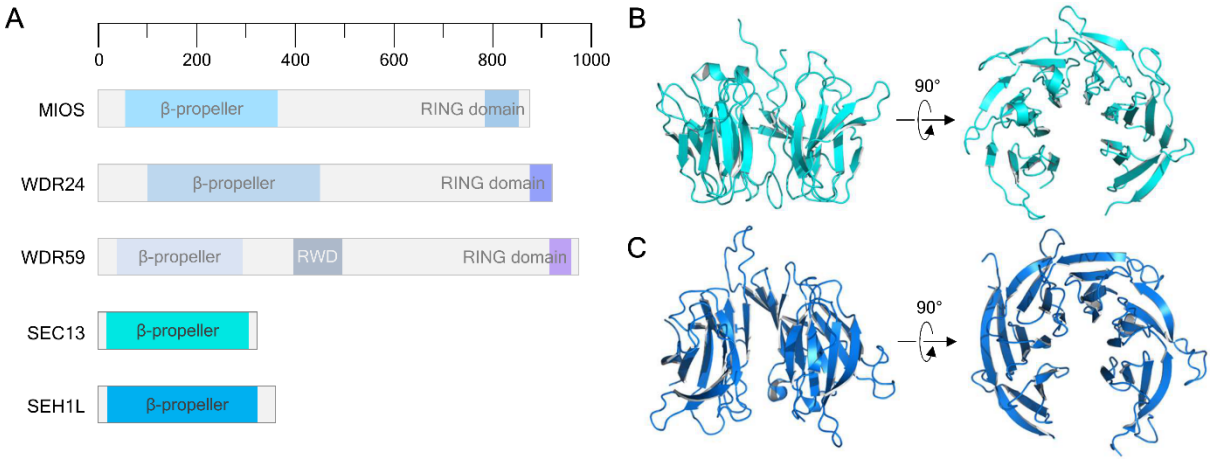
Supplementary Information

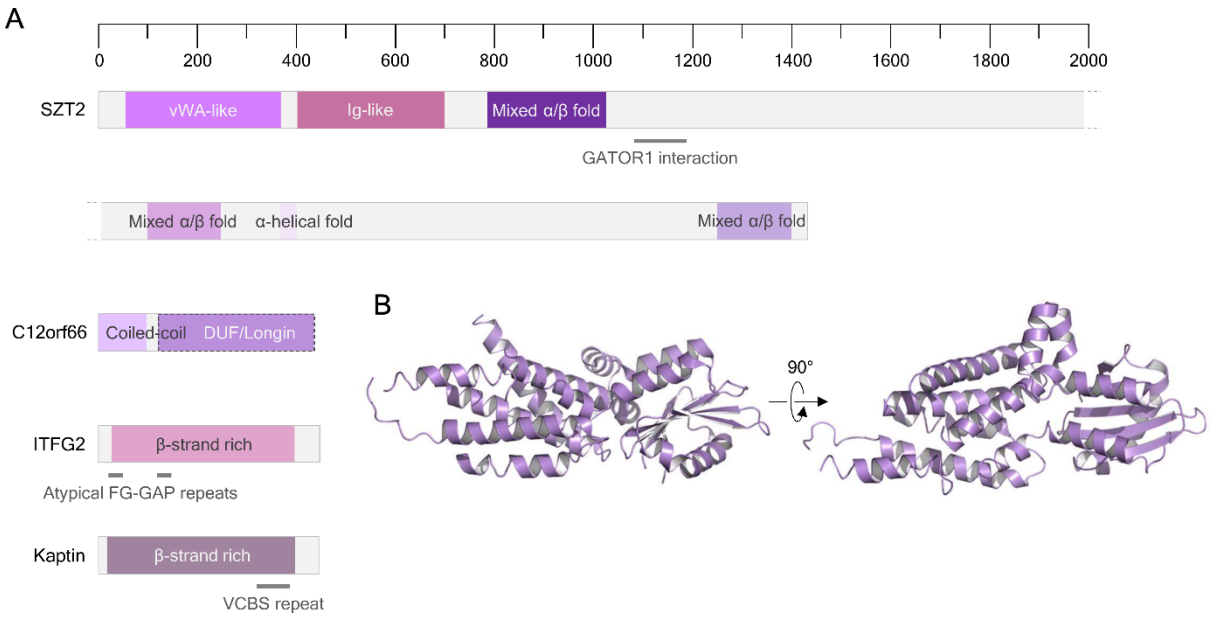
Abbreviations

ACT	Aspartate kinase, chorismate mutase and TyrA
AMPK	5’ AMP-activated protein kinase
BORC	BLOC-1 related complex
CASTOR	Cellular arginine sensor for mTORC1
CMD	Carboxymucolactone decarboxylase
COPII	Coat protein complex II
CTD	C-terminal domain
DENN	Differentially expressed in normal cells and neoplasia
DUF	Domain of unknown function
FAT	FRAP, ATM and TRAPP
FLCN	Folliculin
FNIP	Folliculin-interacting protein
FRB	FKBP12-rapamycin binding
GAP	GTPase-activating protein
GATOR	GAP activity towards Rags
GDI	Guanine nucleotide dissociation inhibitor
GEF	Guanine nucleotide exchange factor
HEAT	Huntingtin, elongation factor 3, protein phosphatase 2A and TOR
KICSTOR	KPTN, ITFG2, C12orf66, and SZT2-containing regulator of mTORC1
LAMTOR	Late endosomal/lysosomal adaptor, MAPK and mTOR activator/regulator
NTD	N-terminal domain
NPC	Nuclear pore complex
PIKK	Phosphoinositide 3-kinase-related kinase
RAPTOR	Regulatory-associated protein of mTOR
RILP	Rab34-interacting lysosomal protein
(m)TOR	(mammalian/mechanistic) Target of Rapamycin
SABA	Structural axis for binding arrangement
SAH	S-adenosylhomocysteine
SAM	S-adenosylmethionine
SAMTOR	S-adenosylmethionine sensor upstream of mTOR

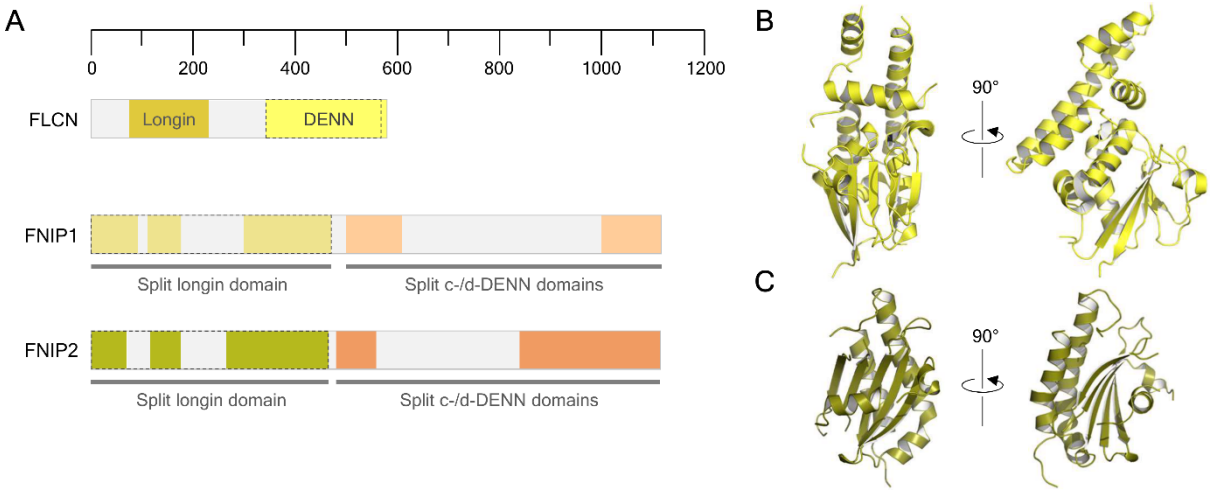
SEAC	Seh1-associated complex
SEACAT	Seh1-associated complex activating TORC1
SEACIT	Seh1-associated complex inhibiting TORC1
SESN	Sestrin
SHEN	Steric hindrance for enhancement of nucleotidase activity
TINI	Tiny interacting
TOS	TOR signalling
TSC	Tuberous sclerosis complex
vWF	von Willebrand factor



Supplementary Figure 1 | Structural biology of the integrator complex GATOR2. ***A.*** Predicted domain organisation of MIOS, WDR24 and WDR59, for which no structural data exists, and the known domain organisations of SEC13 and SEH1L. Black and grey outlines represent structurally resolved or predicted regions, respectively. ***B.*** Crystal structure of human SEC13, from a NUP145-SEC13 complex (PDB ID: 3BG0). ***C.*** Crystal structure of *S. cerevisiae* Seh1, from a Nup85-Seh1 complex (PDB ID: 3F3F).



Supplementary Figure 2 | Structural biology and predicted domains of the KICSTOR complex. ***A.*** Predicted domain organisation of SZT2, ITFG2, C12orf66 and KPTN. Black dashed boxes indicate regions whose structures have been determined, whilst grey grey bars reflect putative features. ***B.*** Crystal structure of *M. musculus* C12orf66 (PDB ID: 2GNX).



Supplementary Figure 3 | Structural biology and predicted domains of the FLCN-FNIP complex. ***A.*** Predicted domain organisation of FLCN, FNIP1 and FNIP2. Black dashed boxes indicate regions whose structures have been determined, whilst grey bars indicate predicted regions with putative functions. ***B.*** Crystal structure of the human FLCN DENN domain (PDB ID: 3V42). ***C.*** Crystal structure of the *K. lactis* Lst7 longin domain (PDB ID: 4ZY8).