

Identification of a TNF-TNFR-like system in malaria vectors (*Anopheles stephensi*) likely to influence *Plasmodium* resistance

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Supplementary figure 1 : Photomap showing the standard form of the 3Li region in the IndInt strain, supporting 52% homozygous for the standard form of 3Li.

78 bp :

Database: IndInt_chr2R.fasta			
1 sequences; 55,427,671 total letters			
Query= IndCh_Astel_HiC_Chr2R			
Length=55103326			
Sequences producing significant alignments:		Score	E
		(Bits)	Value
chr2R		331	1e-90
>chr2R			
Length=55427671			
Score = 331 bits (179), Expect = 1e-90			
Identities = 179/179 (100%), Gaps = 0/179 (0%)			
Strand=Plus/Minus			
Query	38082990	GGCAGAAGTGAGTGAATGACTTAAATCTTTGAAATGAATTAGATGATTTAAATCATCACG	38083049
Sbjct	17244809		17244750
Query	38083050	CAGCGTTATTTAGCTCACTTTTGATTTAATTCGCCATGCCGATTAACCACTCACTCACT	38083109
Sbjct	17244749		17244690
Query	38083110	ACTTTTAACTCACTCACTATGAATGGCTCTCTCGTGAATTAACGAGTGAGTTAAAGG	38083168
Sbjct	17244689		17244631

78 bp Reverse Complement :

Database: indint_rev_chr2R.fasta
1 sequences; 55,427,671 total letters

Query= IndCh_Astel_HiC_Chr2R

Length=55103326

Sequences producing significant alignments:	Score (Bits)	E Value
chr2R	331	1e-90

>chr2R

Length=55427671

Score = 331 bits (179), Expect = 1e-90
Identities = 179/179 (100%), Gaps = 0/179 (0%)
Strand=Plus/Plus

Query	38082990	GGCAGAAGTGAGTGAATGACTTAAATCTTTGAAATGAATTAGATGATTTAAATCATCACG	38083049
Sbjct	38182863	GGCAGAAGTGAGTGAATGACTTAAATCTTTGAAATGAATTAGATGATTTAAATCATCACG	38182922
Query	38083050	CAGCGTTATTTGAGCTCACTTTTGATTTAATTCGCCATGCCGATTAACCACTCACTCACT	38083109
Sbjct	38182923	CAGCGTTATTTGAGCTCACTTTTGATTTAATTCGCCATGCCGATTAACCACTCACTCACT	38182982
Query	38083110	ACTTTTTAACTCACTCACTATGAATGGCTCTCTCGTGAATTAACGAGTGAGTTAAAGG	38083168
Sbjct	38182983	ACTTTTTAACTCACTCACTATGAATGGCTCTCTCGTGAATTAACGAGTGAGTTAAAGG	38183041

8 bp :

Database: IndInt_chr2R.fasta
1 sequences; 55,427,671 total letters

Query= IndCh_Astel_HiC_Chr2R

Length=55103326

Sequences producing significant alignments:	Score (Bits)	E Value
chr2R	202	6e-52

>chr2R

Length=55427671

Score = 202 bits (109), Expect = 6e-52
Identities = 109/109 (100%), Gaps = 0/109 (0%)
Strand=Plus/Minus

Query	21514292	ATTTAAGGTTGACCAATTCCTGAGAAACACGGGTAAGAATATAATCCAATCATATCTTTA	21514351
Sbjct	33742489	ATTTAAGGTTGACCAATTCCTGAGAAACACGGGTAAGAATATAATCCAATCATATCTTTA	33742430
Query	21514352	GCGAGCTGCAAATTAGTGATTTTCCTAGAACACTGGCAACACCGCCAAC	21514400
Sbjct	33742429	GCGAGCTGCAAATTAGTGATTTTCCTAGAACACTGGCAACACCGCCAAC	33742381

8bp Reverse Complement :

Database: indint_rev_chr2R.fasta
1 sequences; 55,427,671 total letters

Query= IndCh_Astel_HiC_Chr2R

Length=55103326

Sequences producing significant alignments:	Score (Bits)	E Value
chr2R	202	6e-52

>chr2R

Length=55427671

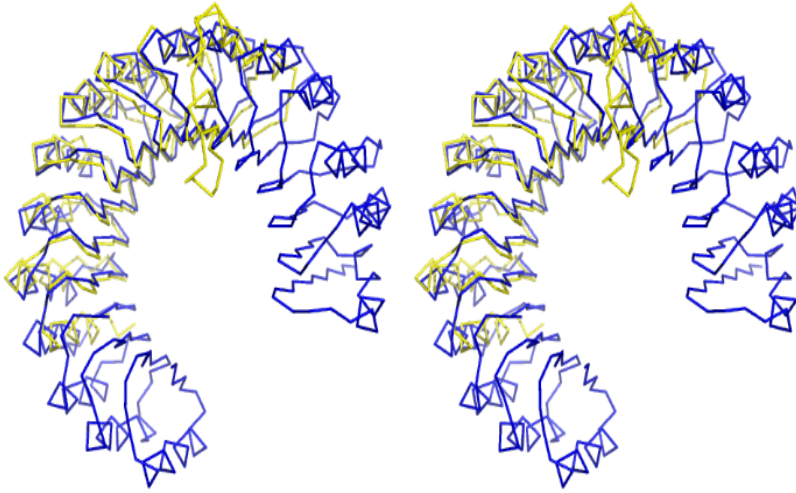
Score = 202 bits (109), Expect = 6e-52
Identities = 109/109 (100%), Gaps = 0/109 (0%)
Strand=Plus/Plus

```
Query 21514292 ATTTAAGGTTGACCAATTCCTGAGAAACACGGGTAAGAATATAATCCAATCATATCTTTA 21514351
          |||
Sbjct 21685183 ATTTAAGGTTGACCAATTCCTGAGAAACACGGGTAAGAATATAATCCAATCATATCTTTA 21685242

Query 21514352 GCGAGCTGCAAATTAGTGATTTTCCTAGAACACTGGCAACACCGCCAAC 21514400
          |||
Sbjct 21685243 GCGAGCTGCAAATTAGTGATTTTCCTAGAACACTGGCAACACCGCCAAC 21685291
```

Supplementary figure 2 : Pairwise alignment using BLASTN showing the validation of 2Rb breakpoints between the IndCh and IndInt strains.

g22432.t1



BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - 1z7x-W

DOMAIN LENGTH- 226-477 (251)

DALI TEMPLATE LENGTH- 460

The number of structurally equivalent residues (LALI) - 227 aa

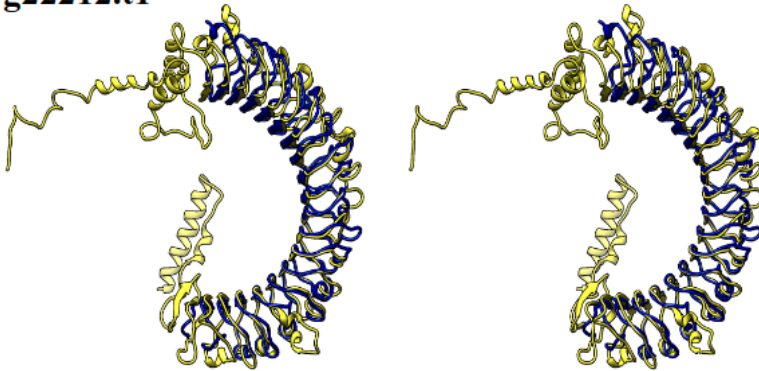
RMSD (DALI) - 2.3

ANNOTATION - **LRR - Ribonuclease Inhibitor**

A leucine-rich repeat (LRR) is a protein structural motif that forms an α/β horseshoe fold. Leucine-rich repeats are frequently involved in the formation of protein-protein interactions. Leucine-rich repeat motifs have been identified in a large number of functionally unrelated proteins. Ribonuclease inhibitors (RI) or Ribonuclease/angiogenin inhibitor are a family of large proteins that bind to and inhibit ribonucleases.

Supplementary figure 3a : Conserved domain structure of IndInt g22432

g22212.t1



DOMAIN 1 389-1021
(635 amino acid)

BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - 4li1-B

DOMAIN LENGTH- 635 AA

LALI - 418 AA

DALI TEMPLATE LENGTH- 425

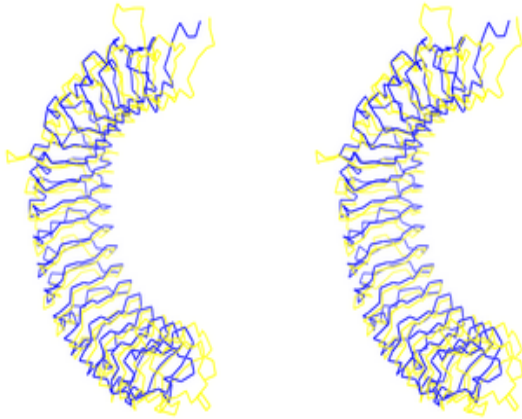
RMSD (DALI) - 2.6

Function :

LEUCINE-RICH REPEAT-
CONTAINING G-PROTEIN COUPLED

g22212.t1

DOMAIN 2 → 435-932
(497 amino acid)



BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - **4li1-B**

DOMAIN LENGTH- **497 AA**

LALI - **414 AA**

DALI TEMPLATE LENGTH- **425**

RMSD (DALI) - **2.5**

Function :

LEUCINE-RICH REPEAT-CONTAINING G-PROTEIN COUPLED

Supplementary figure 3b : Conserved domain structure of IndInt g22212

g22118.t1

BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY DOMAIN

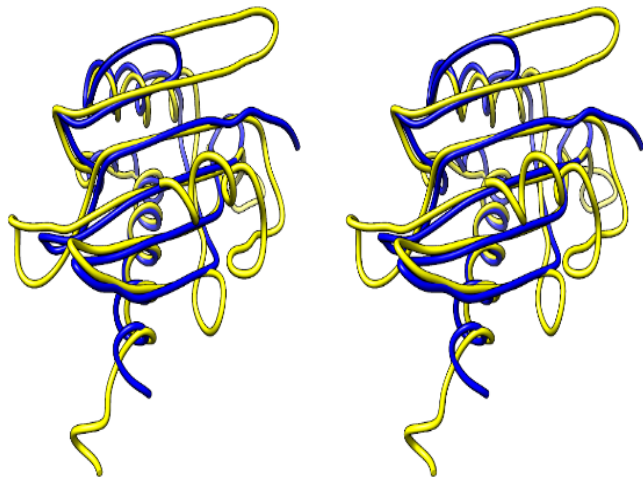
DALI TEMPLATE ID - **1JB4-B**
DOMAIN LENGTH- 181-347 (167 AA)
DALI TEMPLATE LENGTH-123 AA

The number of structurally equivalent residues (LALI) - 120 AA

RMSD (DALI) - 2.2

ANNOTATION - **NTF2**

[**NTF2** is a cytosolic protein responsible for nuclear import of Ran, a small Ras-like GTPase involved in a number of critical cellular processes, including cell cycle regulation, chromatin organization during mitosis, reformation of the nuclear envelope following mitosis, and controlling the directionality of nucleocytoplasmic transport]



Supplementary figure 3c : Conserved domain structure of IndInt g22118

g22089.t1

BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - **5MBX-A**
DOMAIN LENGTH- 1-508 (508 AA)
DALI TEMPLATE LENGTH- 472 AA

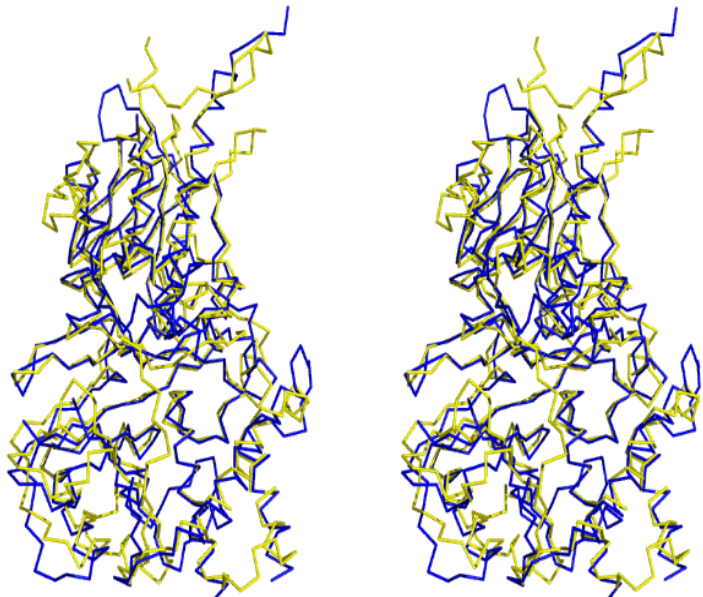
The number of structurally equivalent residues(LALI)- 433 AA

RMSD (DALI) - 2.4

ANNOTATION-

PEROXISOMAL

**N1-(ACETYL)-SPERMINE/SPERMIDINE
OXIDASE**



Supplementary figure 3d : Conserved domain structure of IndInt g22089

g22220.t1
(Domain 3)

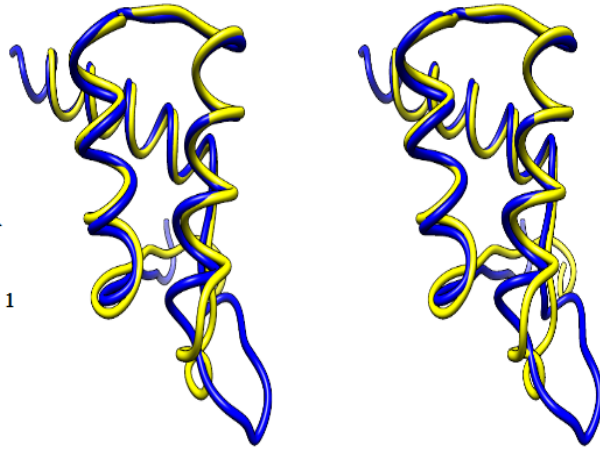
BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - **4J19-B**
DOMAIN LENGTH- 975-1042(68 AA)
DALI TEMPLATE LENGTH- 76 AA

The number of structurally equivalent residues(LALI) - 65 AA
RMSD (DALI) - 2.5

ANNOTATION - **HOMEBOX-CONTAINING PROTEIN 1**
[Binding to double-stranded telomere-associated DNA]



Supplementary figure 3e : Conserved domain structure of IndInt g22220

g22349.t1

DOMAIN →153-405
(252 AMINO ACIDS)

BLUE COLOUR →DALI TEMPLATE

YELLOW COLOUR → QUERY DOMAIN

DALI TEMPLATE ID - **3I0P**

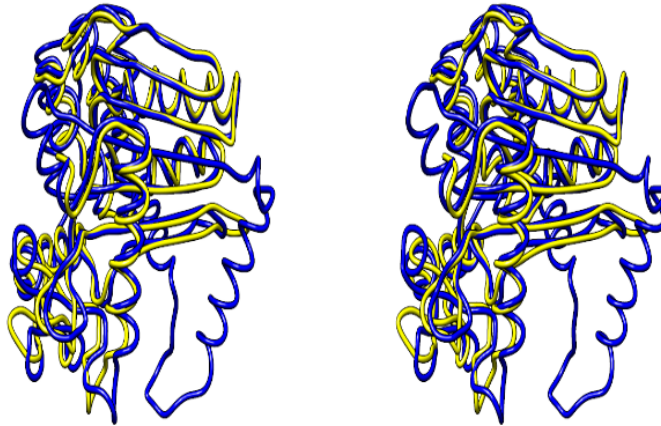
DOMAIN LENGTH- 252 AA

LALI - 253 AA

DALI TEMPLATE LENGTH- 361 AA

RMSD (DALI) - 1.7

FUNCTION - MALATE DEHYDROGENASE



Supplementary figure 3f : Conserved domain structure of IndInt g22349

g23051.t1

DOMAIN →189-468
(279 AMINO ACIDS)

BLUE COLOUR →DALI TEMPLATE

YELLOW COLOUR → QUERY DOMAIN

DALI TEMPLATE ID - 3SZ4

DOMAIN LENGTH- 279 AA

LALI - 180 AA

DALI TEMPLATE LENGTH- 195 AA

RMSD (DALI) - 2.6

FUNCTION - EXONUCLEASE



Supplementary figure 3g : Conserved domain structure of IndInt g23051

g22565.t1

BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY
DOMAIN

DALI TEMPLATE NAME - TUMOR
NECROSIS FACTOR-INDUCIBLE
GENE 6 PROTEIN

DALI TEMPLATE ID - 2wno-A

DOMAIN LENGTH - 128 aa

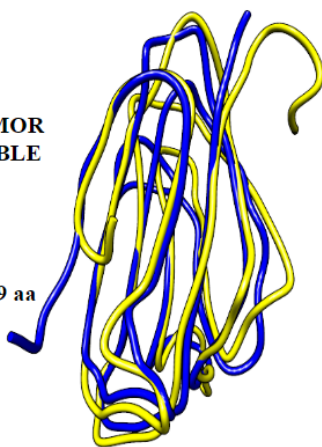
DALI TEMPLATE LENGTH- 119 aa

LALI - 110

RMSD (DALI) - 2.0

Percentage Coverage - 92.4%

Sequence identity - 20%



g22565.t1

BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY
DOMAIN

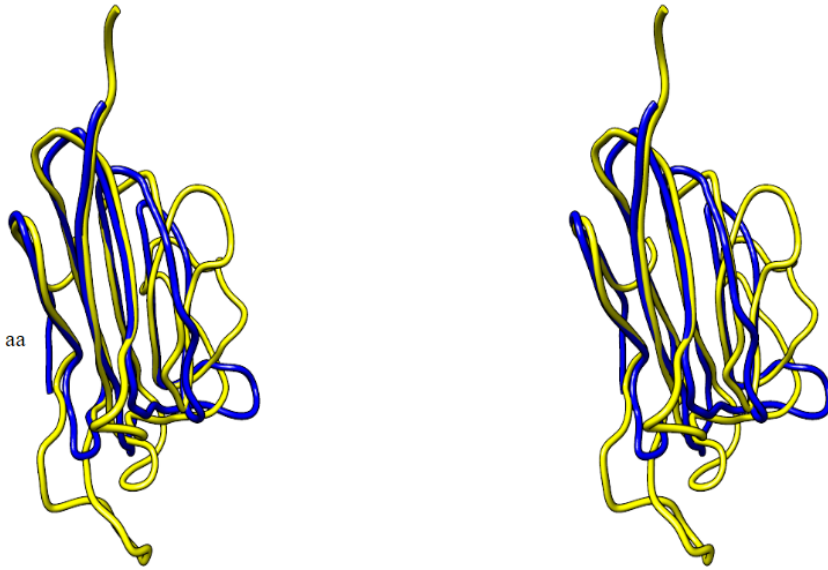
DALI TEMPLATE NAME -
COMPLEMENT C1R
SUBCOMPONENT

DALI TEMPLATE ID - 6f1d-A
DOMAIN LENGTH - 158
DALI TEMPLATE LENGTH- 117 aa

LALI - 112

RMSD (DALI) - 2.5

Percentage Coverage ~ 71%
Sequence identity - 24%



Supplementary figure 3h : Conserved domain structure of IndInt g22565

g21982.t1

BLUE COLOR - DALI TEMPLATE

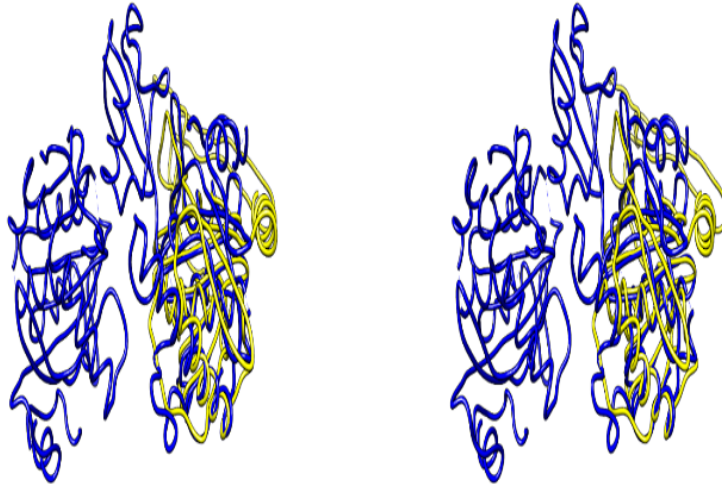
YELLOW COLOR-QUERY DOMAIN
DALI TEMPLATE NAME -
UBIQUITIN

DALI TEMPLATE ID - 2j7q-A
DOMAIN LENGTH - 248
DALI TEMPLATE LENGTH- 232

LALI - 177

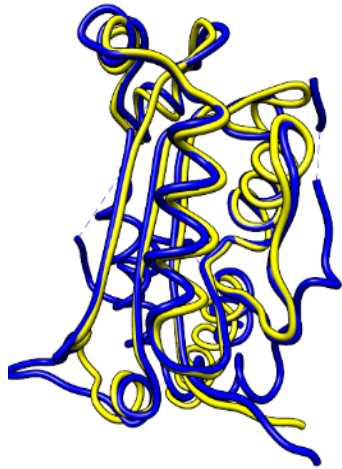
RMSD (DALI) - 3.1

Percentage Coverage ~ 71.4%
Sequence identity - 24%



Supplementary figure 3i : Conserved domain structure of IndInt g21982

g22147.t1



BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - 1y97-B
DOMAIN LENGTH- 1-156 (156)
DALI TEMPLATE LENGTH- 211

The number of structurally equivalent residues (LALI) - 145 aa

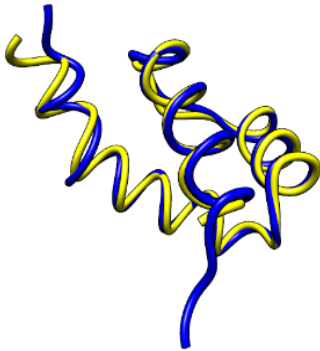
RMSD (DALI) - 1.4

ANNOTATION - **TREX2**

Exonuclease with a preference for double-stranded DNA with mismatched 3' termini. May play a role in DNA repair. Exonucleolytic cleavage in the 3'- to 5'-direction to yield nucleoside 5'-phosphates.

Supplementary figure 3j : Conserved domain structure of IndInt g22147

g22088.t1



BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - 6FQQ-B
DOMAIN LENGTH- 240-297 (57)
DALI TEMPLATE LENGTH- 61

The number of structurally equivalent residues (LALI) - 57 aa

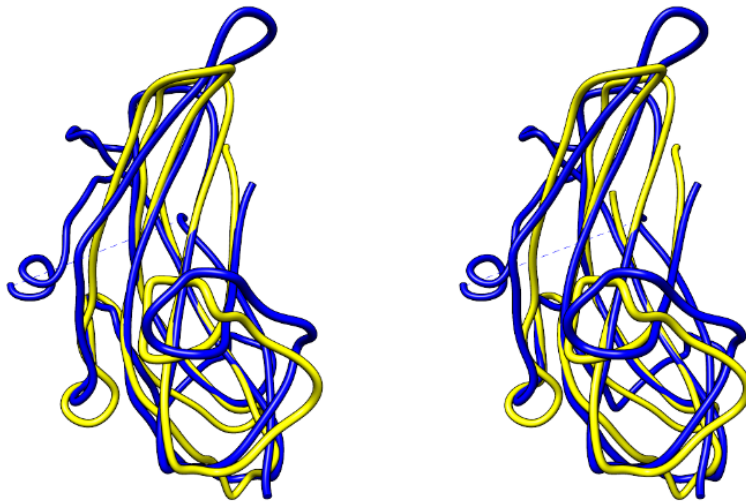
RMSD (DALI) - 1.4

ANNOTATION-**HOMEBOX PROTEIN TGIF1**

A member of the three-amino acid loop extension (TALE) superclass of atypical homeodomains. TALE homeobox proteins are highly conserved transcription regulators. Both TGIF1 and TGIF2 act as transcription factors repressing TGF- β signalling.

Supplementary figure 3k : Conserved domain structure of IndInt g22088

g22941.t1



BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - 4ajv-A
 DOMAIN LENGTH- 404-517 (113)
 DALI TEMPLATE LENGTH- 152

The number of structurally equivalent residues (LALI) - 106 aa

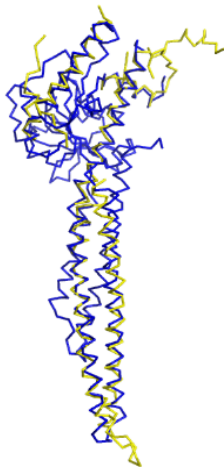
RMSD (DALI) - 2.1

ANNOTATION - **TRANSFORMING GROWTH FACTOR BETA RECEPTOR TYPE 3**

Transforming growth factor beta (TGFβ) receptors are single pass serine/threonine kinase receptors that belong to TGFβ receptor family. TGFβ is a growth factor and cytokine involved in paracrine signalling and can be found in many different tissue types.

Supplementary figure 3l : Conserved domain structure of IndInt g22941

g22536.t1



BLUE COLOR - DALI TEMPLATE

YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - 6jfm-A
 DOMAIN LENGTH- 1-219 (219)
 DALI TEMPLATE LENGTH- 422

The number of structurally equivalent residues (LALI) - 121

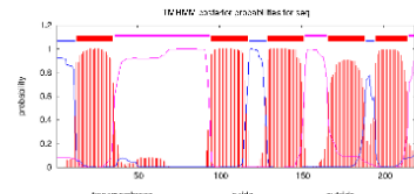
RMSD (DALI) - 3.1

ANNOTATION - **Mitofusin**

MFN2, an outer mitochondrial membrane GTPase, is critical for mitochondrial fusion, which in turn affects mitochondrial dynamics, distribution, quality control, and function. MFN2 modulates ER-mitochondria tethering.

TMHMM result

```
# seq Length: 239
# seq Number of predicted TMs: 5
# seq Exp number of AA in TMs: 111, 62975
# seq Exp number, first 69 AA: 23, 58, 84
# seq local score of TM1: 0.82884
# seq POSSIBLE N term signal sequence
seq TMHMM:0 inside 1 12
seq TMHMM:0 TMHELX 13 25
seq TMHMM:0 outside 26 40
seq TMHMM:0 TMHELX 45 117
seq TMHMM:0 inside 126 126
seq TMHMM:0 TMHELX 129 153
seq TMHMM:0 outside 157 165
seq TMHMM:0 TMHELX 166 188
seq TMHMM:0 inside 189 191
seq TMHMM:0 TMHELX 225 244
seq TMHMM:0 outside 275 279
```

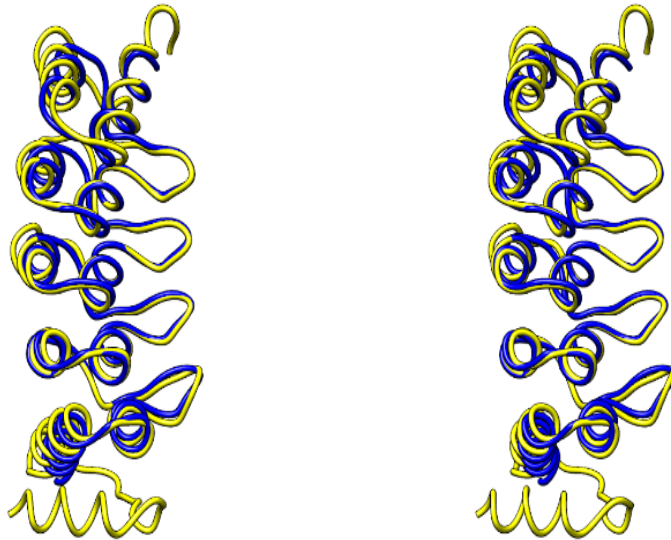


Supplementary figure 3m : Conserved domain structure of IndInt g22536

G22843

BLUE COLOR - DALI TEMPLATE
YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - 6FP9
DOMAIN LENGTH- 209 AA
DALI TEMPLATE LENGTH-171 AA
The number of structurally equivalent residues (LALI) - 168 AA
RMSD (Chimera) - 1.897
ANNOTATION - DARPin



Supplementary figure 3n : Conserved domain structure of IndInt g22843

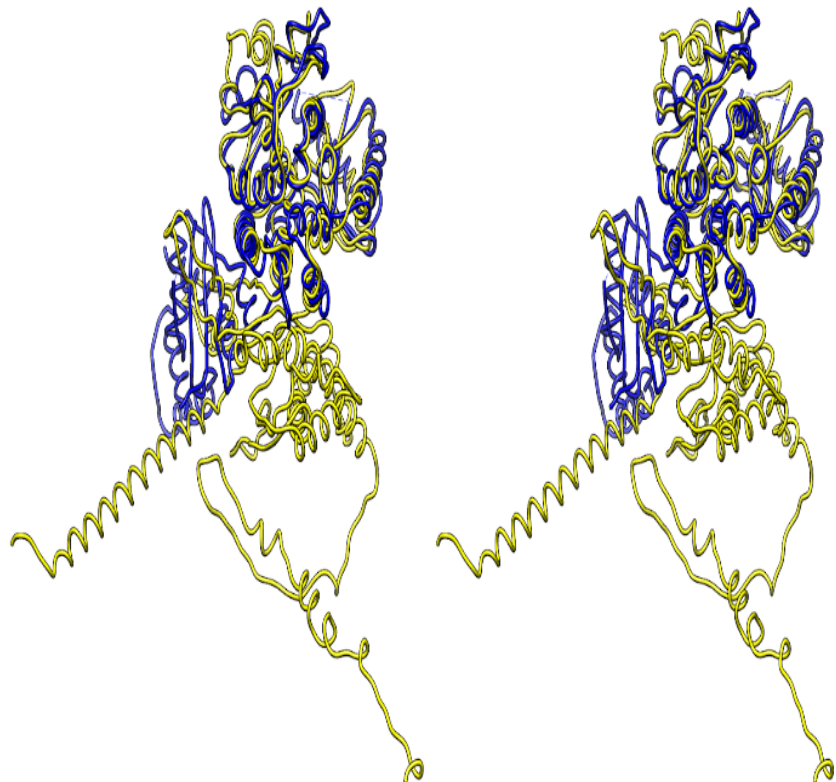
G22150

BLUE COLOR - DALI TEMPLATE
YELLOW COLOR-QUERY DOMAIN

DALI TEMPLATE ID - 5WU1
DOMAIN LENGTH- 727 AA
DALI TEMPLATE LENGTH-493 AA
The number of structurally equivalent residues (LALI) - 353 AA
RMSD (Chimera) - 2.5

ANNOTATION -

SPECKLE TARGETED
PIP5K1A-REGULATED POLY(A)
POLYMERASE.
Poly(A) polymerase that creates the
3'-poly(A) tail of specific pre-mRNAs



Supplementary figure 3o : Conserved domain structure of IndInt g22150

**DOMAINS WHICH DID NOT SUPERIMPOSE
WELL BUT HAVE A FUNCTIONAL
ANNOTATION IN DALI**

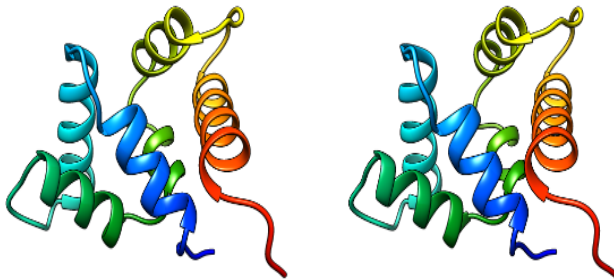
GENE ID - **g22118.t1**
DOMAIN LENGTH - 1-109(109 AA)

FIRST HIT DALI TEMPLATE PDB ID - **7K3R-A**
DALI TEMPLATE LENGTH- **95 AA**

The number of structurally equivalent
residues(LALI) - **80 AA**

RMSD (DALI) - **3.5**

ANNOTATION - **INTERFERON INDUCIBLE
PROTEIN AIM2**



Supplementary figure 3p : DALI functional annotation of IndInt g22118

G22810.t1 (not superimposed well with template)

DOMAIN 1
246-561
(315 amino acid)

DALI TEMPLATE ID - **7lw7-A (only one hit)**

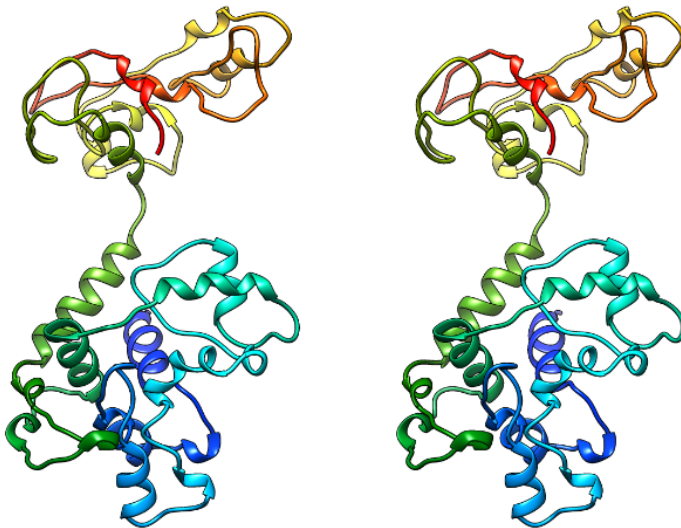
DOMAIN LENGTH- **315 AA**

LALI - **80 AA**

DALI TEMPLATE LENGTH- **277**

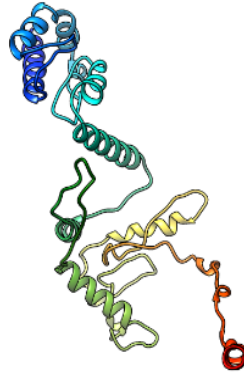
RMSD (DALI) - **5.7**

Function :
EXONUCLEASE V
The Exonuclease V enzyme is an
ATP-dependent, double-strand DNA
exonuclease.



Supplementary figure 3q : DALI functional annotation of IndInt g22810

g22301.t1 (not superimposed well with template)



DOMAIN 1
21-306
(285 amino acid)

DALI TEMPLATE ID - 2v71-A
DOMAIN LENGTH- 285 AA

LALI - 156 AA

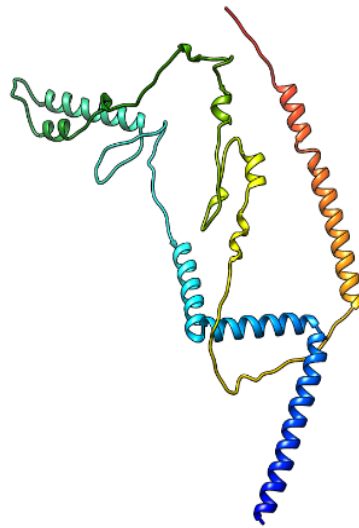
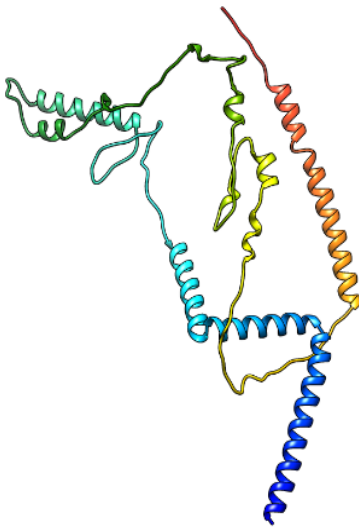
DALI TEMPLATE LENGTH- 160

RMSD (DALI) - 5.2

Function :
NUCLEAR DISTRIBUTION PROTEIN
NUDE-LIKE 1
It plays a role in multiple processes
including cytoskeletal organization,
cell signaling and neuron migration,
outgrowth and maintenance

Supplementary figure 3r : DALI functional annotation of IndInt g22301

g23001 (not superimposed properly)



DOMAIN
115-395
(280 amino acid)

DALI TEMPLATE ID - 1xpj-D
DOMAIN LENGTH- 280 AA

LALI - 106 AA

DALI TEMPLATE LENGTH- 123

RMSD (DALI) - 2.6

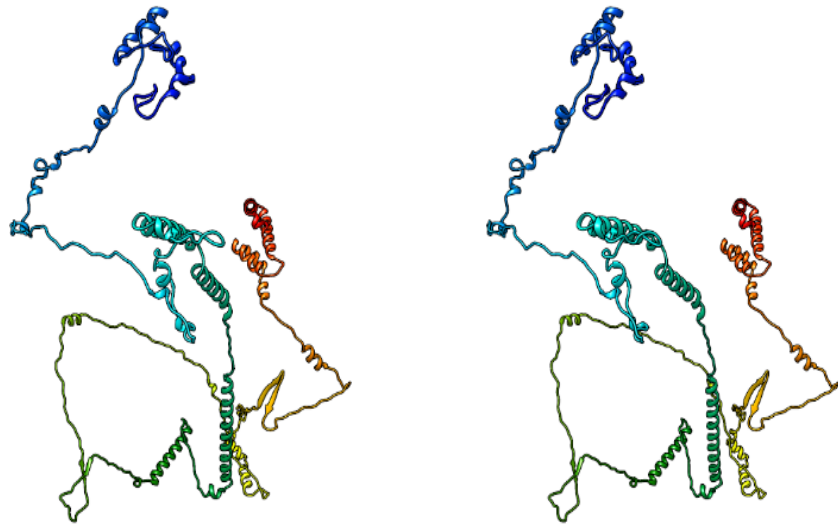
The Hit template is a
HYPOTHETICAL
PROTEIN;

Supplementary figure 3s : DALI functional annotation of IndInt g23001

MODELS WHICH DID NOT FOLD WELL-

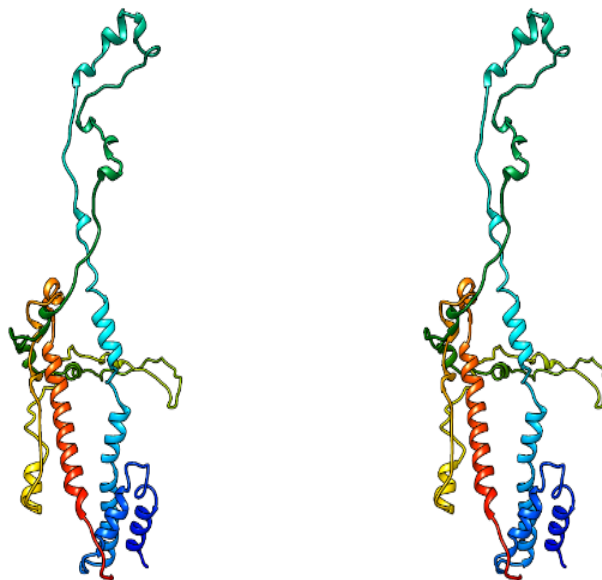
MODELS WHICH DID NOT FOLD WELL

g22846.t1(length - 701 AA)



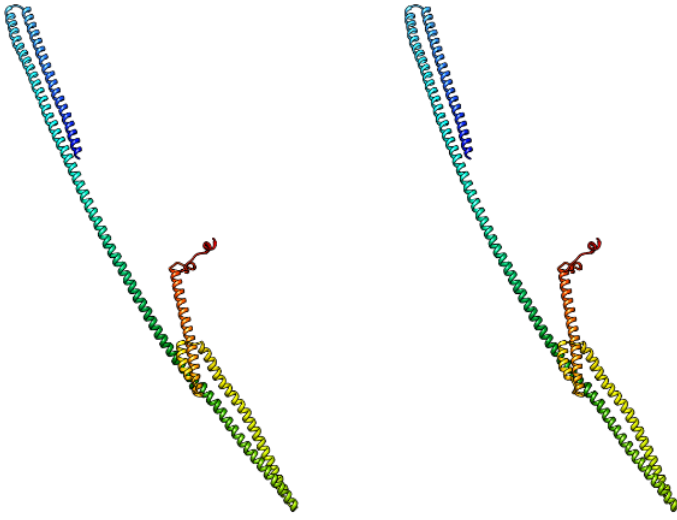
Supplementary figure 3t : Alpha fold predicted structure of IndInt g22846

g22224.t1 (LENGTH - 343 AA)



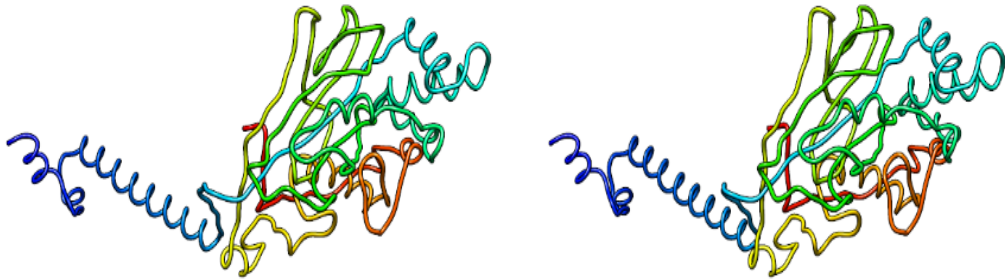
Supplementary figure 3u : Alpha fold predicted structure of IndInt g22224

g22323 450 amino acids - very high error plot



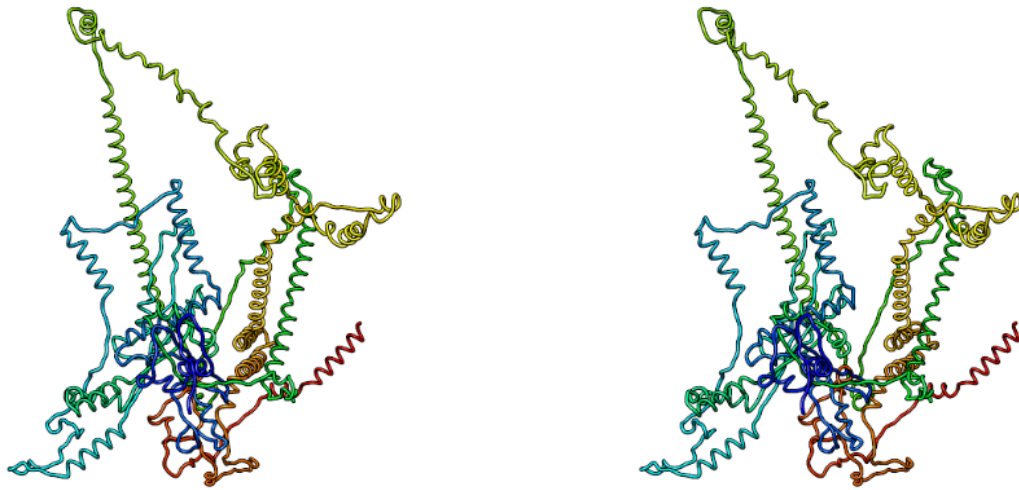
Supplementary figure 3v : Alpha fold predicted structure of IndInt g22323

g21978.t1



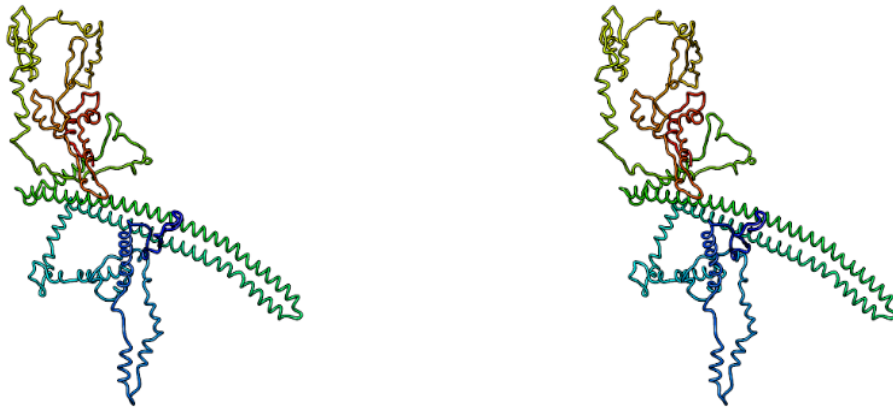
Supplementary figure 3w : Alpha fold predicted structure of IndInt g21978

g22197.t1



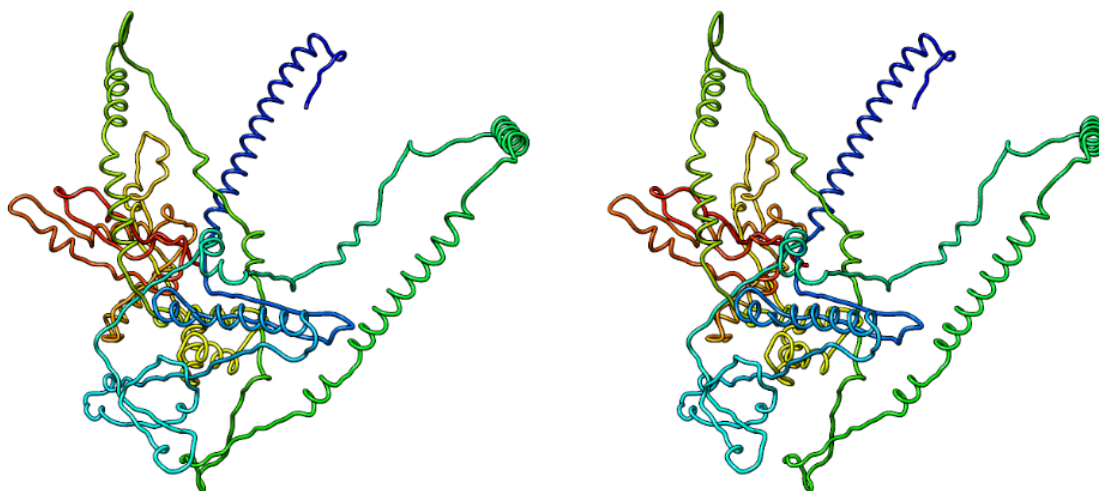
Supplementary figure 3x : Alpha fold predicted structure of IndInt g22197

g22416.t1



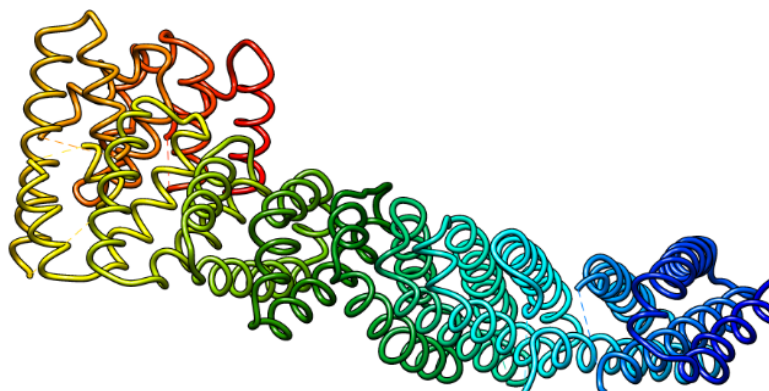
Supplementary figure 3y : Alpha fold predicted structure of IndInt g22416

g22689.t1



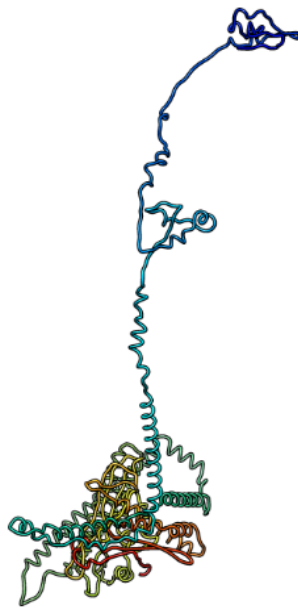
Supplementary figure 3z : Alpha fold predicted structure of IndInt g22689

g21989.t1



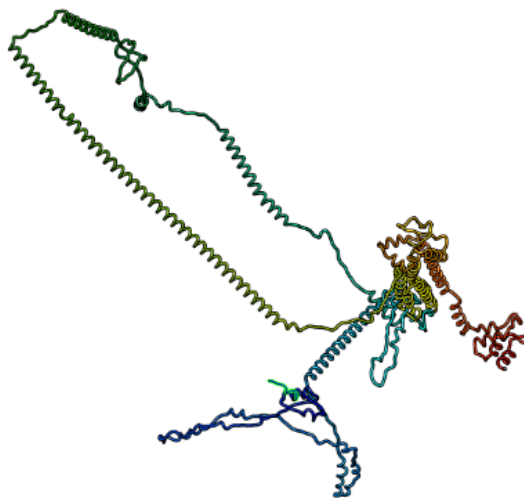
Supplementary figure 3a1 : Alpha fold predicted structure of IndInt g21989

g22713.t1



Supplementary figure 3a2 : Alpha fold predicted structure of IndInt g22713

g23157.t1

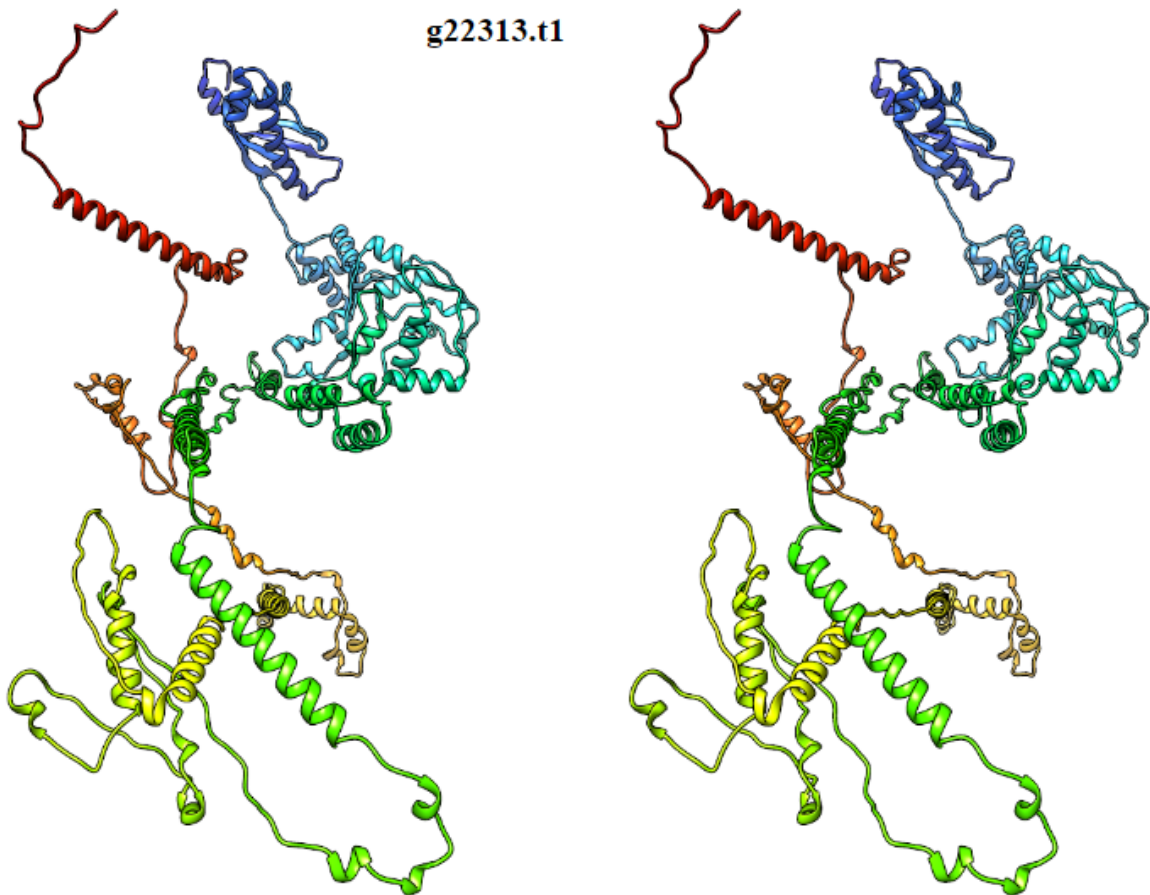


Supplementary figure 3a3 : Alpha fold predicted structure of IndInt g23157

g22302.t1



Supplementary figure 3a4 : Alpha fold predicted structure of IndInt g22302



Supplementary figure 3a5 : Alpha fold predicted structure of IndInt g22313


```

AnColuzzii_XP040229266          LDKLNL SYNPIGEAGVLILGGAIKGRAQLSELHFTGCPMGVEGSFRVIQLLSFHETLRKV 433
AnArabiensis_XP040157989       LDKLNL SYNPIGEAGVLILGGAIKGRAQLSELHFTGCPMGVEGSFRVIQLLSFHETLRKV 433
AnGambiae_AGAP005805          LDKLNL SYNPIGQAGVLILGGAIKGRAQLSELNFTGCPLGVEGSFRVIQLLSFHETLRKV 433
IndInt_g22432                   VDRDL SYNPIGEAGVLILGGAIKGR TQLSELNFTGCQMGVEGSFRL--LSFHVTLRKV 428
AnStephensi_XP035917226       VDRDL SYNPIGEAGVLILGGAIKGR TQLSELNFTGCQMGVEGSFRVIQLLSFHVTLRKI 478
: * : ***** : ***** : ***** : ***** : ***** : ***** :
AnColuzzii_XP040229266          SLNCVPISPEGGDKLQVLENNRIEEVQVRDCGLTERVRSKIGKILRKNASTRHQSRRS 493
AnArabiensis_XP040157989       SLNCVPISPEGGDKLQVLENNRIEEVQVRDCGLTERVRARIGKILRKNANARHRSRRS 493
AnGambiae_AGAP005805          SLNCVPISPEGGDKLQVLENNRIEEVHVRDCGLTERVVRIGKILRKNANARHRSRRS 493
IndInt_g22432                   SLNCVPISLEGGAKLVQLQENIRIEDVQVRQCGLPDELLVKPHIIFANPDYRASSSGDT 488
AnStephensi_XP035917226       SLNCVPISLEGGAKLVQLQENIRIEDVQVRQCGLPDELLVKVRKILRKNAKIRDQLR-S 537
***** ** * ***** ** * : * : * : * : * : * : * :
AnColuzzii_XP040229266          DGKVATPPMVRSPAT-----MFQLERQVFPVQS----- 521
AnArabiensis_XP040157989       DGKVATPPMVRSPAS-----MFQLERQVFPVQS----- 521
AnGambiae_AGAP005805          AGKVATPPMVRSPAS-----MFQLERQVFPVQS----- 521
IndInt_g22432                   ALLTAPKEIRHCPPVDRQAEPVPGRTIIHYANKSHFPFPVRILVKVLRPVAFIGPRTK 548
AnStephensi_XP035917226       VRMSSEQPMDKCHTSERSLGS-----MFLLERQ-----VFSE----- 569
: : : : : * : :
AnColuzzii_XP040229266          ----- 521
AnArabiensis_XP040157989       ----- 521
AnGambiae_AGAP005805          ----- 521
IndInt_g22432                   CRVAPGPTFASASDSEQTLALWSECNTRADRSSTADRPIRSRSIGGLIVKWECLWHGPEH 608
AnStephensi_XP035917226       ----- 569
AnColuzzii_XP040229266          ----- 521
AnArabiensis_XP040157989       ----- 521
AnGambiae_AGAP005805          ----- 521
IndInt_g22432                   KRMCACASVCLCMWAPRFGRHFDSMTLKTSTGNIIYQTGYRLSGTSGRITSACFTRVHP 668
AnStephensi_XP035917226       ----- 569
AnColuzzii_XP040229266          ----- 521
AnArabiensis_XP040157989       ----- 521
AnGambiae_AGAP005805          ----- 521
IndInt_g22432                   GTICSGFMATGERHHAHIPPTRK 693
AnStephensi_XP035917226       ----- 569

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Supplementary figure 4a : MSA for IndInt gene g22432.t1 across other Anopheles species shows high conserved homology.

CLUSTAL O(1.2.4) multiple sequence alignment

```

AnColuzzii_XP040230463 ----- 0
AnArabiensis_XP040158968 ----- 0
AnGambiae_AGAP006645 ----- 0
AnStephensi_XP035917013 ----- 0
IndInt_g22212 MRGLTRSVDPARLQDHETERVVCAYGYIGIPDISFWQLVNAPLRESEMASEPYTVPDS 60

AnColuzzii_XP040230463 -----MVSVHTMRCQ 10
AnArabiensis_XP040158968 -----MVSVHTMRCQ 10
AnGambiae_AGAP006645 -----MRCQ 4
AnStephensi_XP035917013 -----MSRQ 4
IndInt_g22212 GCMAMHSRKSVEECRVQSRNDGGFSPARMQTPPWYNICSNLTVPLIFFTQQGSIHMSRQ 120
* *

AnColuzzii_XP040230463 YLLVLTVVLCALTVN---SLKPDLPKAKDPLFNKMLAESNKGVDADPRYNKMLPDLEE 67
AnArabiensis_XP040158968 YLLVLTVVLCALTVN---SLKPDLPKAKDPLFNKMLAESSTKGVQDPRYNKMLPDLEE 67
AnGambiae_AGAP006645 YLLVLTVVLCALTVN---SLKPDLPKAKDPLFNKMLAESSTKGVDAQDPRYNKMLPDLEE 61
AnStephensi_XP035917013 YLLVLAVALCALAVHSSPALKPDLPKADPLYNKILAETTRSVMDAHRHYNKMLPQPDE 64
IndInt_g22212 YLLVLAVALCALAVNSSPALKPDLPKADPLYNKILAETTRSVMDAHRHYNKMLPQPDE 180
*****.*.....* :*****.*.....* :*:* :*****:*

AnColuzzii_XP040230463 NLIDDDDDDDEEEEDDV---APPTKKAADLNPMYALRGKQ-VKPEVSTVGSVAINKVK 122
AnArabiensis_XP040158968 NLIDDDDDDDEEEEDDV---APPTKKAADLNPMYALRGKQ-VKPEVSTVGSVAINKVK 122
AnGambiae_AGAP006645 NLIDDDDDDDEEEEDDV---APPTKKAADLNPMYALRGKQ-VKPEVSTVGSVAINKVK 116
AnStephensi_XP035917013 NLINSDISEDEDGEDDAMANDDILPKKAADLNPMYAQRGKQPAKPEVSTVGSVAINKVK 124
IndInt_g22212 NLINSDISEDEDADDDEAMANDDILPKKAADLNPMYAQRGKQPAKPEVSTVGSVAINKVK 240
*****.* :*:* :*:* :*****.*

AnColuzzii_XP040230463 INEDIDSYEEVLLKGNKGSV-----KPSKSTTAKPVAKPATEDNYDEYDDD 168
AnArabiensis_XP040158968 INEDIDSYEEVLLKGNKGSV-----KPSKSTTAKPVAKPATEDNYDEYDDD 168
AnGambiae_AGAP006645 INEDIDSYEEVLLKGNKGSVDIDDSYQVEDLSGEEKPSKSTTAKPVAKPATEDNYDEYDDD 176
AnStephensi_XP035917013 INEDIDSYEEVLLKGNKGSV-----KPSKPTTSKPAAKTEGED--DE-YDD 167
IndInt_g22212 INEDIDSYEEVLLKGNKGSV-----KPSKPTTSKPAAKTEGED--DE-YDD 283
*****.* :*:* :*:* :*****.*

AnColuzzii_XP040230463 ESDEQIDFSGVQKVLAKPLKQVPAEKSAKPAVPSTTAKPKAVTTGKQNVIELDQYDDDA 228
AnArabiensis_XP040158968 ESDEQIDFSGVQKVLAKPLKQVPAEKSAKPAVPSTTAKPKAVTTGKQNVIELDQYDDDA 228
AnGambiae_AGAP006645 ESDEQIDFSGVQKVLAKPLKQVPAEKSAKPAVPSTTAKPKAVTTGKQNVIELDQYDDDA 236
AnStephensi_XP035917013 ESDEKIDFSGVQKVLAKPLKQVPAEKSVKTSPPSTTLKPKSTTTGKQNVIELDQYDEDA 226
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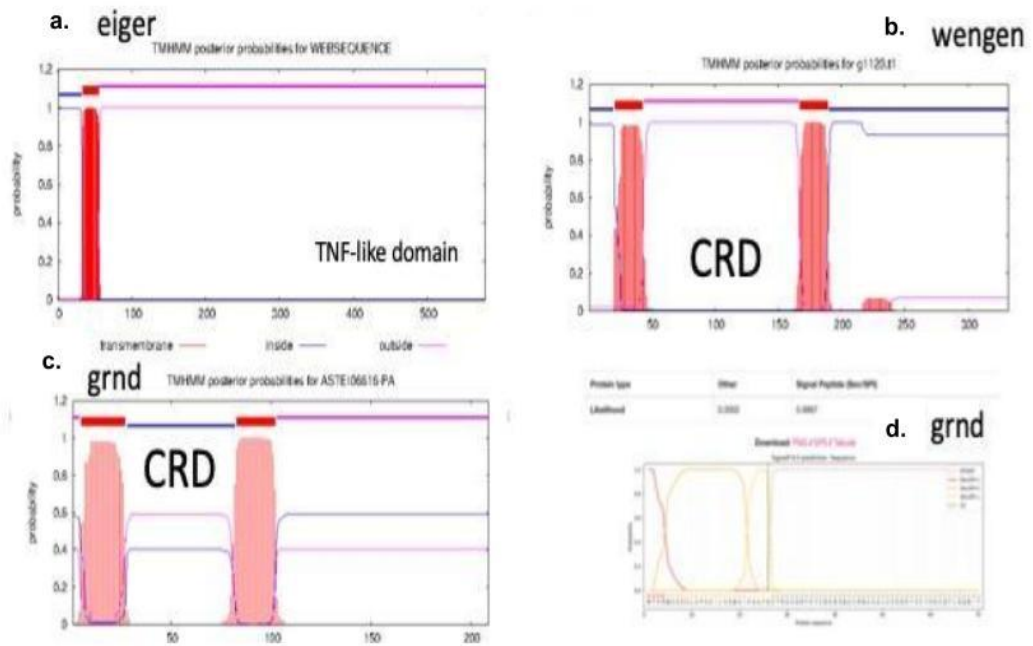
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AnArabiensis_XP040158968 DM DYQYNYDDDEDNDDDDDEDDDDDEEEDAETLPAQKITNKVNKEVAKKQTNPVKTKDQ 288
AnGambiae_AGAP006645 DM DYQYNYDDDEDNDDDDDEDDDDDEEEDAETLPAQKITNKVNKEVAKKQTNPVKTKDQ 296
AnStephensi_XP035917013 DM DYQYTYDDDEDNDDDDDEDDDD- DDEDAAEELPPQKAGKNVNSE- AKKQTKPVKKTKEQ 284
IndInt_g22212 DM DYQYTYDDDEDNDDDDDEDDDD- DDEDAAEELPPQKAGKNVNSE- AKKQTKPVKKTKEQ 400
*****.* :*:* :*:* :*****.*

```


AnColuzzii_XP040230463	NKAAGKDNAEDYYDDDEYDD--DDNAEPSNSSYCPRGICERNMHAYMVATCSRLDLETQ	346
AnArabiensis_XP040158968	NKAAGKDNAEDYYDDDEYDD--DDNAEPSNSSYCPRGICERNMHAYMVATCSRLDLETQ	346
AnGambiae_AGAP006645	NKAAGKDNAEDYYDDDEYDD--DDNAEPSNSSYCPRGICERNMHAYMVATCSRLDLETQ	354
AnStephensi_XP035917013	NKTAAGKGTDESYYYDDEDDDDDDYNVDSSNSTYCPRGICERNMHSYMVATCSRLDLETQ	344
IndInt_g22212	NKTAAGKSTDESYYYDDEDDDDDDYNVDSSNSTYCPRGICERNMHSYMVATCSRLDLETQ	460
	:*. *.. *.* ** ** * *.: **.*:**.*****	
AnColuzzii_XP040230463	KFTSHITDLQVLDVGPKYPIELGPEFFKKIGLSHVVISIKITNCTIVYISPOAFAGLDLEY	406
AnArabiensis_XP040158968	KFTSHITDLQVLDVGPKYPIELGPEFFKKIGLSHVVISIKITNCTIVYISPOAFAGLDLEY	406
AnGambiae_AGAP006645	KFTSHITDLQVLDVGPKYPIELGPEFFKKIGLSHVVISIKITNCTIVYISPOAFAGLDLEY	414
AnStephensi_XP035917013	KFTSAITDLQVLDVGPKYPIELGPEFFKKIGLSHVVISIKITNCTIVYISPOAFAGLDVLY	404
IndInt_g22212	KFTSAITDLQVLDVGPKYPIELGPEFFKKIGLSHVVISIKITNCTIVYISPOAFAGLDVLY	520
	****.*****.*****	
AnColuzzii_XP040230463	SVNLTNSGIDIIHPDTFANNTKLRLLTSLSGNDLSAMQSVNHNTPYMDYMLKAPTVEELDI	466
AnArabiensis_XP040158968	SVNLTNSGIDIIHPDTFANNTKLRLLTSLSGNDLSAMQSVNHNTPYMDYMLKAPTVEELDI	466
AnGambiae_AGAP006645	SVNLTNSGIDIIHPDTFANNTKLRLLTSLSGNDLSAMQSVNHNTPYMDYMLKAPTVEELDI	474
AnStephensi_XP035917013	SVNLTNSGIDIMHPDTFANNTKLRLLTSLSGNDLSAMQSVNHNTPYMDYMLKAPTVEELDI	464
IndInt_g22212	SVNLTNSGIDIMHPDTFANNTKLRLLTSLSGNDLSAMQSVNHNTPYMDYMLKAPTVEELDI	580
	*****.*****.*****	
AnColuzzii_XP040230463	SRCKLQELQPNAFNELKNIYINLSENNLSNLPEGIFDNVETIEELDLSMNNIVELPKNI	526
AnArabiensis_XP040158968	SRCKLQELQPNAFNELKNIYINLSENNLSNLPEGIFDNVETIEELDLSMNNIVELPKNI	526
AnGambiae_AGAP006645	SRCKLQELQPNAFNELKNIYINLSENNLSNLPEGIFDNVETIEELDLSMNNIVELPKNI	534
AnStephensi_XP035917013	SRCKLQELQPNAFNELKNIYINLSENNLSNLPEGIFDNVETIEELDLSANNIAELPKNI	524
IndInt_g22212	SRCKLQELQPNAFNELKNIYINLSENNLSNLPEGIFDNVETIEELDLSANNIAELPKNI	640
	*****.*****.*****	
AnColuzzii_XP040230463	FAKTSLAILHLKHNKITNNVDFVTADLQKLDLSFCQIRTVHNTMFKGMDGLTNLILKGNH	586
AnArabiensis_XP040158968	FAKTSLAILHLKHNKITNNVDFVTADLQKLDLSFCQIRTVHNTMFKGMDGLTNLILKGNH	586
AnGambiae_AGAP006645	FAKTSLAILHLKHNKITNNVDFVTADLQKLDLSFCQIRTVHNTMFKGMDGLTNLILKGNH	594
AnStephensi_XP035917013	FAKTSLAILHLKHNKISNNVDFVTADLQKLDVDFCQIRTVHNTMFKGMEGLTNLILKGNH	584
IndInt_g22212	FAKTSLAILHLKHNKISNNVDFVTADLQKLDVDFCQIRTVHNTMFKGMEGLTNLILKGNH	700
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AnArabiensis_XP040158968	IEKIKPMAFISLKNLRQIDLSYNNLEQISAQTFIGNKMLDIIRLNNNPRKRLPNEGFEI	646
AnGambiae_AGAP006645	IEKIKPMAFISLKNLRQIDLSYNNLEQISAQTFIGNKMLDIIRLNNNPRKRLPNEGFEI	654
AnStephensi_XP035917013	IEKIKPMAFISLSSLRQIDLSYNNLEQISAQTFIGNKMLDIIRMMNNPRKRLPNEGFEI	644
IndInt_g22212	IEKIKPMAFISLSSLRQIDLSYNNLEQISAQTFIGNKMLDIIRMMNNPRKRLPNEGFEI	760
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AnArabiensis_XP040158968	SFNGFTVYFMDVSNCDISELADNTFKTMPHLTRLNLAWNNLQIRSTYFAHLNKLMDLD	706
AnGambiae_AGAP006645	SFNGFTVYFMDVSNCDISELADNTFKTMPHLTRLNLAWNNLQIRSTYFAHLNKLMDLD	714
AnStephensi_XP035917013	SYNGTFNVYLMDISNCDISELADNTFKTMPQLTRLNLAWNNLQIRPPVMAHLSKLMDD	704
IndInt_g22212	SYNGTFNVYLMDISNCDISELADNTFKTMPQLTRLNLAWNNLQIRPPVMAHLSKLMDD	820
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AnColuzzii_XP040230463	LSNNMIINMDEKTFQNNRNLNLTNLAGNQIATLTSKLFHPLQYLSELDVSDCDLRTIWD	766
AnArabiensis_XP040158968	LSNNMIINMDEKTFQNNRNLNLTNLAGNQIATLTSKLFHPLQYLSELDVSDCDLRTIWD	766
AnGambiae_AGAP006645	LSNNMIINMDEKTFQNNRNLNLTNLAGNQIATLTSKLFHPLQYLSELDVSDCDLRTIWD	774
AnStephensi_XP035917013	LSNNMITELDEKTFQNNRNLNLTNLAGNQIATLTSKLFHPLQYLSELDVSDCDLRTIWD	764
IndInt_g22212	LSNNMITELDEKTFQNNRNLNLTNLAGNQIATLTSKLFHPLQYLSELDVSDCDLRTIWD	880
	***** :*****:***:***:***:*****:*****:*	
AnColuzzii_XP040230463	SAAGTKREEVLPNPKRLNVSYNEIMEVFVSDLESMGKLRVLDIRNNTLTCNERLPTLIDW	826
AnArabiensis_XP040158968	SAAGTKREEVLPNPKRLNVSYNEIMEVFVSDLESMGKLRVLDIRNNTLTCNERLPTLIDW	826
AnGambiae_AGAP006645	SAAGTKREEVLPNPKRLNVSYNEIMEVFVSDLESMGKLRVLDIRNNTLTCNERLPTLIDW	834
AnStephensi_XP035917013	SAVKAKREEVLPNPKRLNASYNEISEVFVSDLASMAKLRVLDIRNNSLSCNGRFPRTLIDW	824
IndInt_g22212	SAVKTKREEVLPNPKRLNASYNEISEVFVSDLASMAKLRVLDIRNNSLSCNGRFPRTLIDW	940
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AnColuzzii_XP040230463	LQKKQISMGLGDTHDHTHAEMTTELRTDNSATLKQWGFQFAWEICQGGGSDSPNQRTYS	886
AnArabiensis_XP040158968	LQKKQISMGLGDTHDHTHAEMTTELRTDNSATLKQWGFQFAWEICQGGGSDSPNQRTYS	886
AnGambiae_AGAP006645	LQKKQISMGLGDTHDHTHAEMTTELRTDNSATLKQWGFQFAWEICQGGGSDSPNQRTYS	894
AnStephensi_XP035917013	LQKKQISMAD-NSHDHTHAEMN-VLRTDNSVSLKQWGFQFAWEICQGGSG-DPNTLSYS	881
IndInt_g22212	LQKKQISMGD-NSHDHTHAEMN-VLRTDNSVSLKQWGFQFAWEICQGGSG-DPNTLSYS	997
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AnColuzzii_XP040230463	ESDEEYNIIEDEDDVSEAADADVMAEAKNAKSNKIVDSKNELDDYSDDSVSDSSEDEDSA	946
AnArabiensis_XP040158968	ESDEEYNIIEDEDDVSEAADADVMAEAKNAKSNKIVDSKNELDDYSDDSVSDSSEDEDSA	946
AnGambiae_AGAP006645	ESDEEYNIIEDEDDVDAADADVMAEAKNAKSNKIVDSKNELDEYSDSVSDSSEDEDSA	954
AnStephensi_XP035917013	ETEEDYDEDEDDSED-ADAEV-TADTNAKSNKIVDSKNELDEYSDSETADSDSDNDNAD	939
IndInt_g22212	ETEEDYDEDEDDSED-ADAEV-TAGTNAKSNKIVDSKNELDEYSDSETADS--DDNDNAD	1053
	.*::***:*****:*****:*****:*****:***:***:***:***	
AnColuzzii_XP040230463	--DEDD--EEDDEEDDDDDDDDEEEQERENILDAANGIQKIEQGILTGKQADED--DDG	999
AnArabiensis_XP040158968	--DEDD--EEDDEEDDDDDDDDEEEQERENILDAANGIQKIEQGILTGKQADED--DDG	999
AnGambiae_AGAP006645	--DEDD--EEDDEEDDDDDDDDEEEQERENILDAANGIQKIEQGILTGKQADED--DDG	1007
AnStephensi_XP035917013	ADSEDEDEDEDADDDDDDEEEEEEDDVQERENILDAANGIQQIEQDILTGKLNNAADDDDD	999
IndInt_g22212	ADSEDEDEDEDADDDDDDEEEEEEDDVQERENILDAANGIQQIEQDILTGKLNNAADDDDD	1113
	*** * :*****:*****:*****:*****:*****:*****:***:***	
AnColuzzii_XP040230463	EYE--DDGASVDDVVILENGSMFAVSSVWIVVACILFGISMLLL VVVKVLT EVMKRRGER	1057
AnArabiensis_XP040158968	EYE--DDGASVDDVVILENGSMFAVSSVWIVVACILFGISMLLL VVVKVLT EVMKRRGER	1057
AnGambiae_AGAP006645	EYE--DDGASVDDVVILENGSMFAVSSVWIVVACILFGISMLLL VVVKVLT EVMKRRGER	1065
AnStephensi_XP035917013	EYEDDSEGTNVDDVVILENASMFALSTVALMVSCIVIGSLIMVLLVAKIVGLIFKRRGER	1059
IndInt_g22212	EYEDDSEGTNVDDVVILENASMFALSTVALMVSCIVIGSLIMVLLVAKIVGLIFKRRGER	1173
	*** :*:*****:*****:* :*:***:* :*:***:* :*:*****	
AnColuzzii_XP040230463	YRQALLASKNSFVYQKLTEDIVPSKVPKIHRYEPINQV	1095
AnArabiensis_XP040158968	YRQALLASKNSFVYQKLTEDIVPSKVPKIHRYEPINQV	1095
AnGambiae_AGAP006645	YRQALLASKNSFVYQKLTEDIVPSKVPKIHRYEPINQV	1103
AnStephensi_XP035917013	YRQALLASKNSFVYQKLTEDIVAPKVPKVHRYEPINQV	1097
IndInt_g22212	YRQALLASKNSFVYQKLTEDIVAPKVPKVHRYEPINQV	1211
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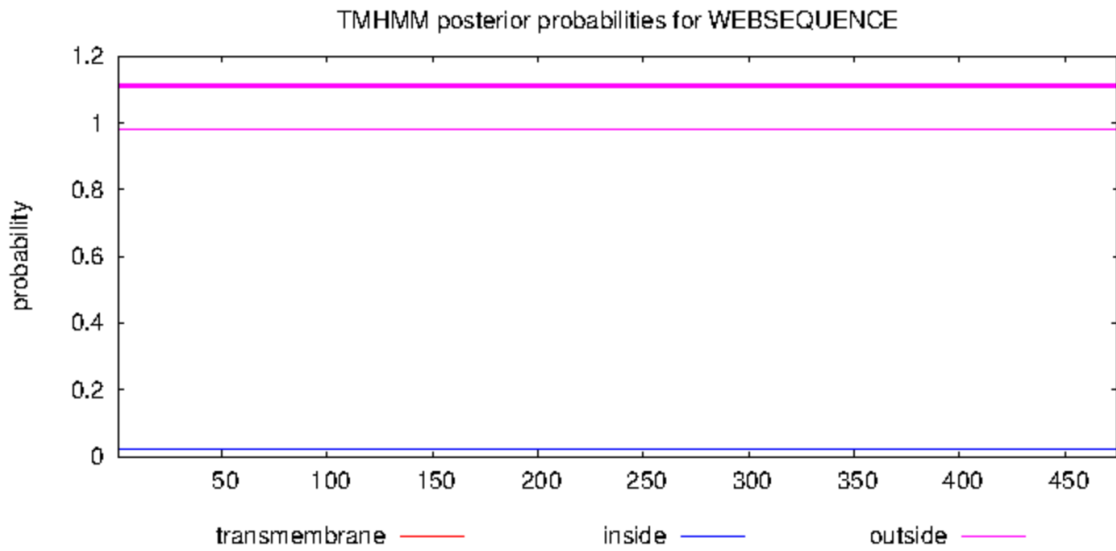
Supplementary figure 4b : MSA for IndInt gene g22212.t1 across other Anopheles species shows high conserved homology.



Supplementary figure 5: (a) transmembrane prediction for eiger (b) transmembrane domain prediction for wengen (c) transmembrane prediction of grnd (d) signal peptide prediction for grnd.

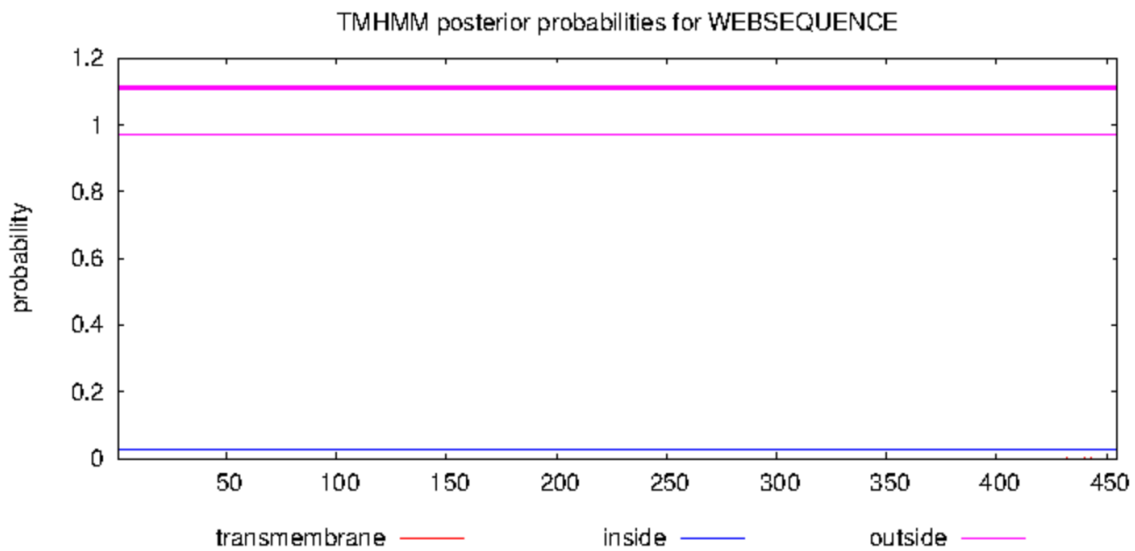
UCI

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# WEBSEQUENCE Length: 475
# WEBSEQUENCE Number of predicted TMHs: 0
# WEBSEQUENCE Exp number of AAs in TMHs: 0.00271
# WEBSEQUENCE Exp number, first 60 AAs: 0
# WEBSEQUENCE Total prob of N-in: 0.02124
WEBSEQUENCE TMHMM2.0 outside 1 475
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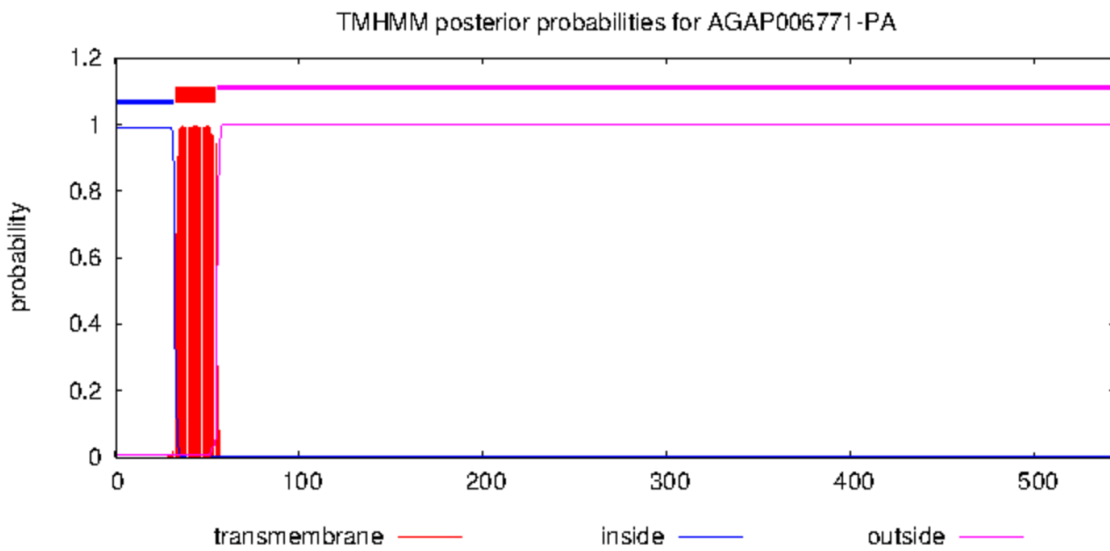
STE2

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# WEBSEQUENCE Length: 455
# WEBSEQUENCE Number of predicted TMHs: 0
# WEBSEQUENCE Exp number of AAs in TMHs: 0.00349
# WEBSEQUENCE Exp number, first 60 AAs: 0
# WEBSEQUENCE Total prob of N-in: 0.02710
WEBSEQUENCE TMHMM2.0 outside 1 455
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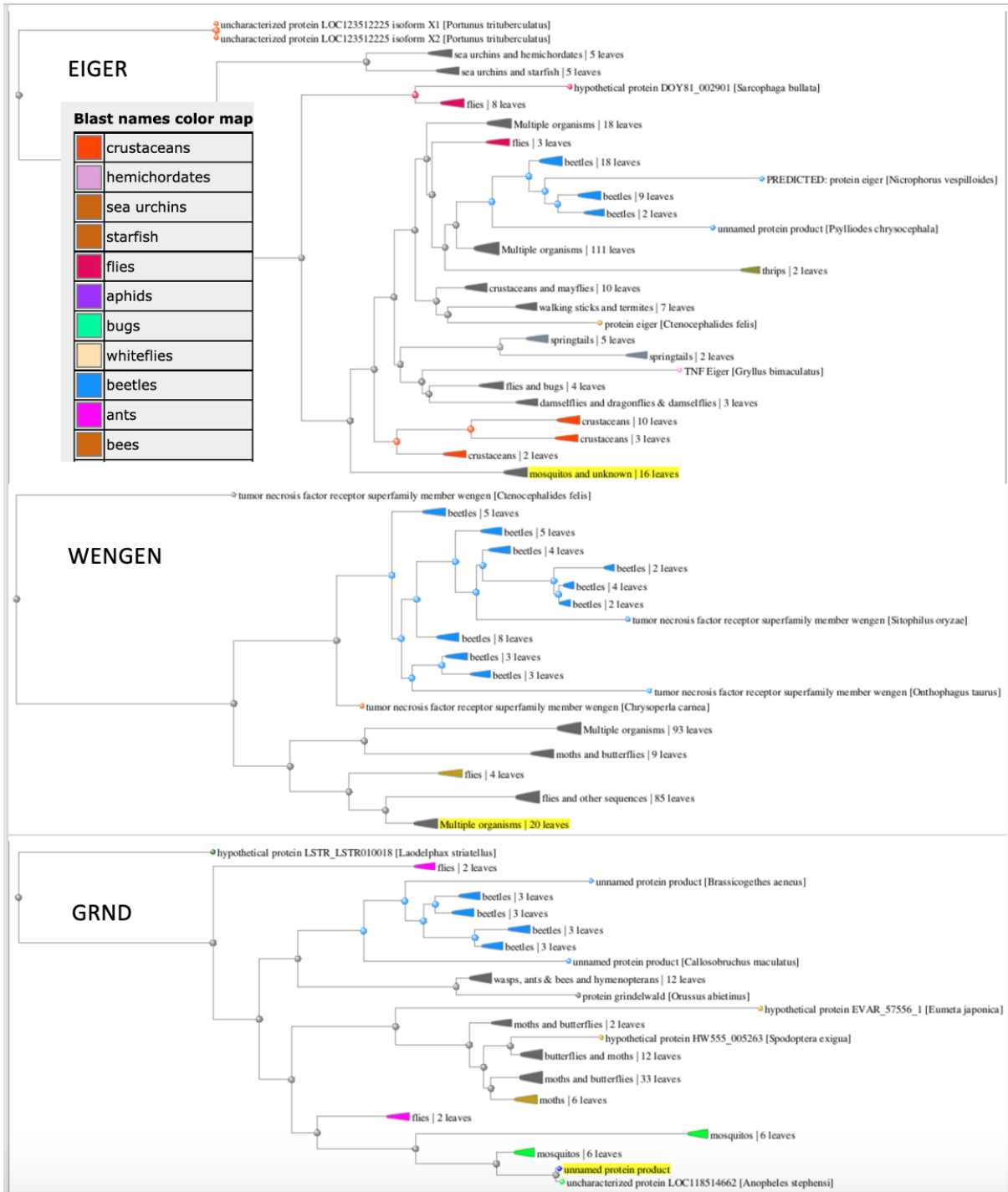


An. gambiae:

```
# AGAP006771-PA Length: 544
# AGAP006771-PA Number of predicted TMHs: 1
# AGAP006771-PA Exp number of AAs in TMHs: 22.71772
# AGAP006771-PA Exp number, first 60 AAs: 22.71771
# AGAP006771-PA Total prob of N-in: 0.99203
# AGAP006771-PA POSSIBLE N-term signal sequence
AGAP006771-PA TMHMM2.0 inside 1 32
AGAP006771-PA TMHMM2.0 TMhelix 33 55
AGAP006771-PA TMHMM2.0 outside 56 544
```



Supplementary figure 6: TmHMM analysis of the *eiger* gene in the UCI and STE2 strains and the *An. gambiae* PEST strain, respectively.



Supplementary figure 7: BLAST result of eiger-wengen-grnd proteins from IndInt against NR-protein database at NCBI suggesting diversity in eiger gene across vectors across arthropods.

>ANSTEP-UCI_TRAN_00009302-RA protein Name:"Similar to Litaf Lipopolysaccharide-induced tumor necrosis factor-alpha factor homolog (Xenopus tropicalis OX=8364)" AED:0.00 eAED:0.00 QI:437|1|1|1|0|0.33|3|1007|126
MTKDGPPPYGFVAPPSAPPSYAQAQVGGVPPSSPFTPPQQPVLTSAQIVTTVVPPIGPQSTHMVCPSCH
SEVVTKTTTTSPGMIAIVVSGFLIALFGCWLGCCLIPCCIDECMDVHHTCPHCKAYLGRHRR

>ANSTEP-UCI_TRAN_00010133-RB protein Name:"Similar to Litaf Lipopolysaccharide-induced tumor necrosis factor-alpha factor homolog (Mus musculus OX=10090)" AED:0.14 eAED:0.14 QI:206|1|1|1|0.66|0.5|4|598|158
MNPSPGKSGSGPEGFQAQPLNQPPYPAQSPPYPGQMPAATGGYPHPSANVFNIAHPPPPPPYDANSNV
IPPPQNAGTTYVQVVTSPQVGPDPASMVCPSCTKHVITRLDYETSTKTHIAAGLLCLFICWPCFWI
PYIIDSKNANHYCPNCGAYIGTYRG

>ANSTEP-UCI_TRAN_00010132-RB protein Name:"Similar to Litaf Lipopolysaccharide-induced tumor necrosis factor-alpha factor homolog (Mus musculus OX=10090)" AED:0.01 eAED:0.01 QI:206|0.5|0.66|1|1|1|3|787|124
MDPPPYDQINRPVPAAYPHQQTPTADPFKSASLHTQEPPSLQTTVIVTSPQVGPDPPTTIICPSCRA
TVVTRLEYETTTHKTHLCAGLLCLFLCWPCAFVVPYCSTACRDANHYCPNCGSFIGTYRK

>ANSTEP-UCI_TRAN_00010131-RA protein Name:"Similar to FV3-075L Uncharacterized protein 075L (Frog virus 3 (isolate Goorha) OX=654924)" AED:0.00 eAED:0.00 QI:483|1|1|1|1|1|1|2|936|82
MTTIIIVTNPQVGPDPMTITCPSCRATVVRTKVKHESTTSTHACALLLWIVCWPCCLCLPYCC
NSCRDANHYCPRCNTFLGSYKH

Supplementary text 1: FASTA sequences of the LITAF genes from the UCI strain

>g6300_ADAM17_TACE_IndInt
MSLPSIMLTVVLVVSFAVLIVPLQGQLHKNLKYETLHAKDLSHRIEKRGTKHSTHPFNTIKEVEF
KVLGRKFRLILPHASVLHSNFRAYSVDGNGSESIVHLDRSNFFKGRVFGEMESHVNAHIDDGVM
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>g17575_NIK_Brun_IndInt

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SMFLNGNGPGEGTHVSVYIKVLPGEYDALLKWPFSHSVTFTLFEQGTLGSGGGGGQGGVAESFVDPD
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>g488_FOS_kayak_IndInt

MRSVRGSTLYGLGIIAFAWLAPATHHNIHKAVQGACPLAVAWWRFASFDDGIGVHSGVPTRTTPTLT
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DDHDSKSSASLEQPSSGTRRRSATGTDENAKNETVTFAIGTGGSGTGARTGGRNVGGRRPHKPS
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LETHREHCRLQARRSPIDLKPVLDLDTGGFENTGTFVLPKIKTEPEDEFAAAAAAAAAATQQHHQPP
PPNQLQEQLAIEAAEHGTISKKLKLSHAHSDSLETPTPTSSAFAPLAGVGLAGNSGNKLSATPAGS
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NPLELITPTSTEPSKLC SL

>g17088_IKKB_IndInt

MSGLHSATFIVRGC AVNRLNIAQPAAFFRYIKTQLSVL CALLQESNRGV SLLVNVLANMIKPFEDP
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NENIVRTVNVQPTSFIQELLRSSANGLPVL CMEYCEGGDLRRVLRVENC SGLREQDVRDVLRSR
NAVAYLHSLKI THRDIKPENLV LKQQGERFIYKADLG YAKALDKQSLNASLVGTVEYIAPDLIYCD
RYNCSVDYWSMGVIGYEIITGVRPFI PHAPI TRWMMHVQQKKSADIAITEDNRENYTYHTDIFPEN
HISDCLRKELESWFRLALEWNP KKRGYVPYTKAEP SLANGENGTKGVKQTEDNKPSTVLKIFSLLD
QILEKRILVLFSLYDCRWIDLEVT PETGMETLRDHVYRVGTGIPVDDIEFVLPLEQKQPAVGNDTRP
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QEQRLYGQVLDGIRNYGLMLNDNIARRKDE IGRMNKIVYAILGGVEYHKLT VCHARDALNVERRIP
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VECRYEQTRARLMEKILNEKSHMDMSQAVYECLKQRDVLRLRELGFLELQQQILDVRREIQEIEKVV
CKVIDVTEKYKRD LARLKL EHQDEVWKMLSDYGRSAAAGSCENGVVHLDN ILPLGVAHTDPPVINK
PNFLVGGPTTPQLQSTVSNESFDANQVCC LGYTDPNVEDLIAANETLIHTTTDLLSNSFSL LKLAD
GAE

Supplementary Text 2 : FASTA sequences of the genes from the IndInt strain involved in eiger mediated TNF pathway.