Function and structure analysis of human protein HECW1

G11:
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Neuronal precursor cell-expressed developmentally down-regulated 4

Nedd4

A family of E3 ubiquitin ligases that have a common domain architecture

Comprised of C-terminal HECT domain and N-terminal C2 domain and WW domains

H sapiens		
hNEDD4-1	XP_046129	
hNEDD4-2	NP_056092	
AIP4	NP_113671	
hWWP2	NP_008945	
hWWP1	NP_008944	
hSmurf2	NP_073576	
hSmurf1	NP_065162	
Bul1	NP_055867	
hNEDL2	XP_038999	

C2 Domain
WW Domain
HECT Domain

Physiological processes mediated by Nedd4 proteins
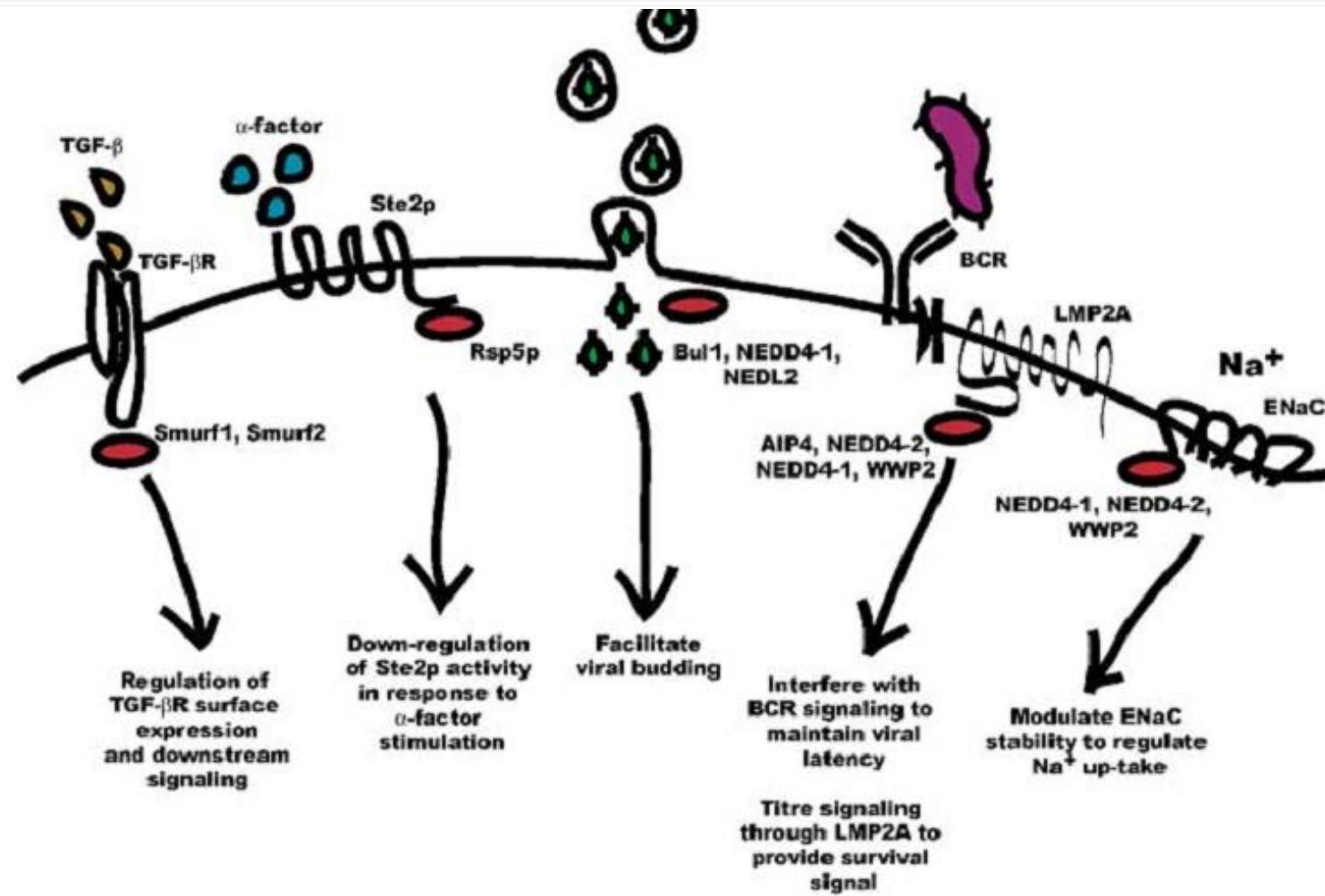
Research on HECW1

ELSEVIER

BBRC

RNF43 interacts with NEDL1 and regulates p53-mediated transcription

TNK2

TP53

RNF43

DVL1

HECW1

FBXL15

SSR4

SOD1

SCNN1A

NDFIP1

SCNN1B

Colorectal carcinogenesis

Mitosis

Kinetochore

Microtubules

Spindle pole

Monoattached chromosome

Defective checkpoint, cell fails to arrest

Sensor

Anaphase

Signal-transduction cascade

Effector

Metaphase — Anaphase

Segregation error

HECW2

Journal of Biomedicine and Biotechnology

IMPACT FACTOR 2.88
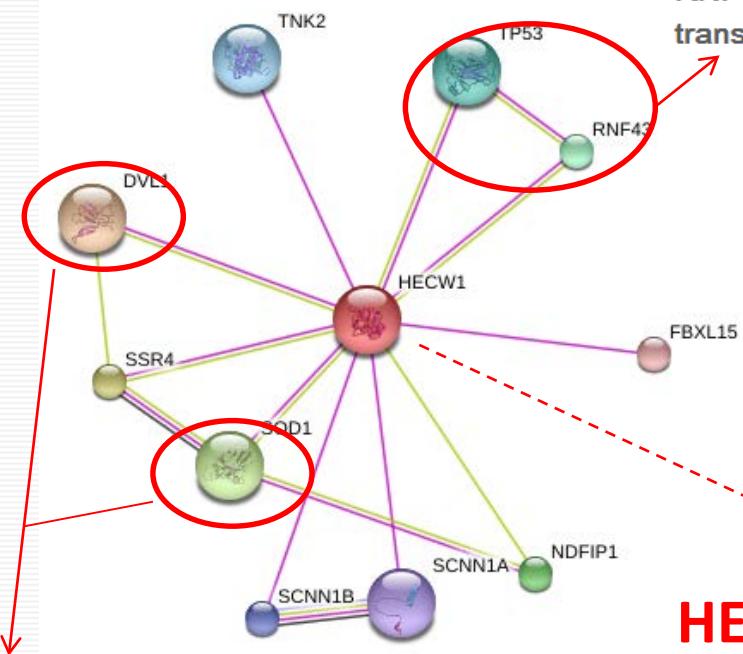
Muscle Atrophy and Motor Neuron Degeneration in Human NEDL1 Transgenic Mice

Amyotrophic lateral sclerosis

Recently published on J. Biol. Chem.

Bioinformatics analysis

Analysis of sequence

Q76N89 (HECW1_HUMAN)

Amino Acid composition
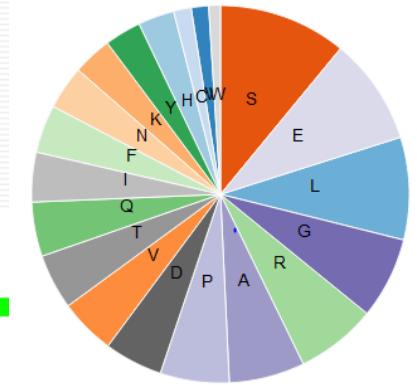

```
Molecule processing

☐  Chain              1 – 1606      1606  E3 ubiquitin-protein ligase HECW1

Regions

☐  Domain            192 – 302      111  C2
☐  Domain            829 – 862       34  WW
☐  Domain           1018 – 1051      34  WW 2
☐  Domain           1271 – 1606     336  HECT
☐  Coiled coil       870 – 901       32  (Potential)
☐  Compositional bias 456 – 519      64  Glu-rich
☐  Compositional bias 670 – 707      38  Cys-rich

Sites

☐  Active site       1574            1  Glycyl thioester intermediate (By similarity)
```

Substrate recognition

Cellular localization

Catalysis

Phylogenic analysis and tree construction
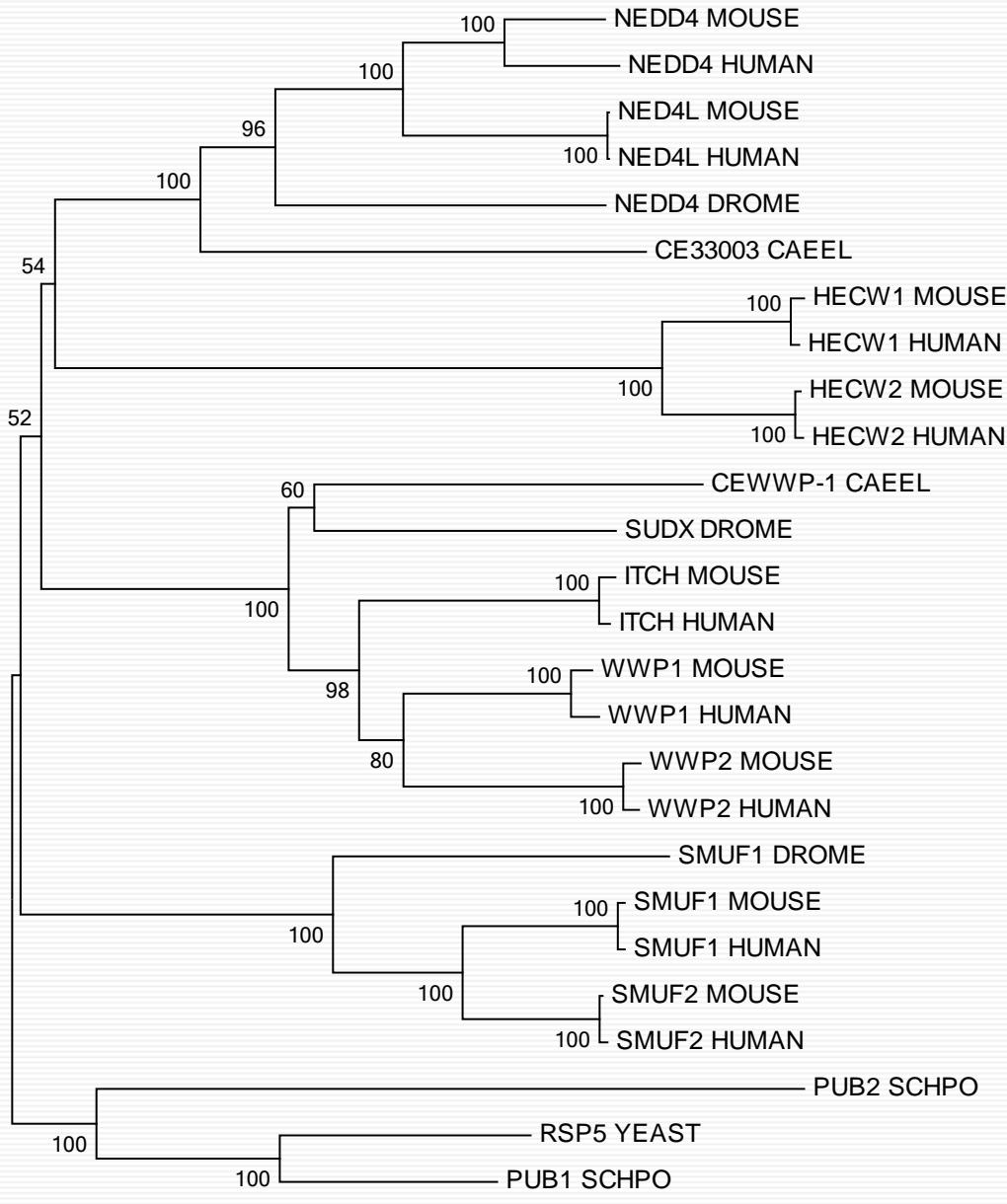
Analysis of conserved domain

C2 domain
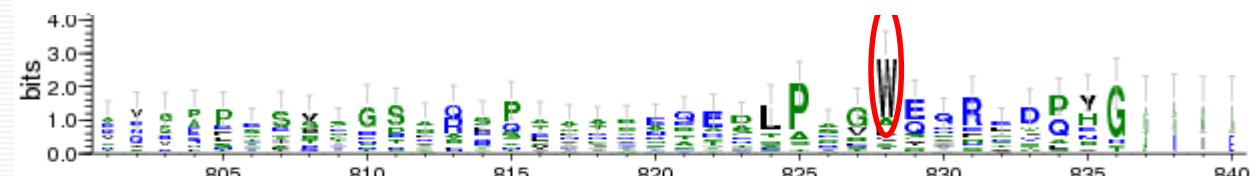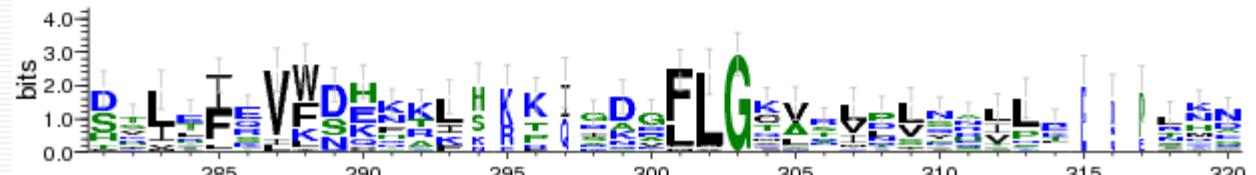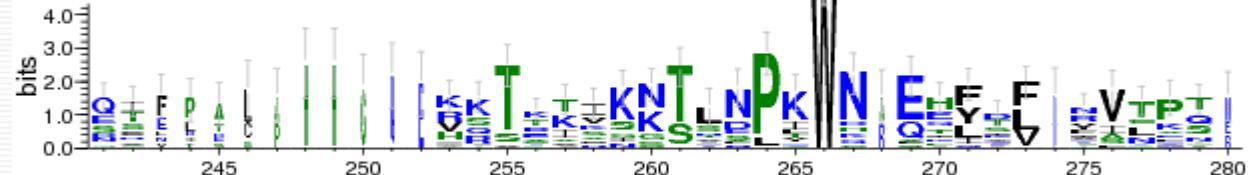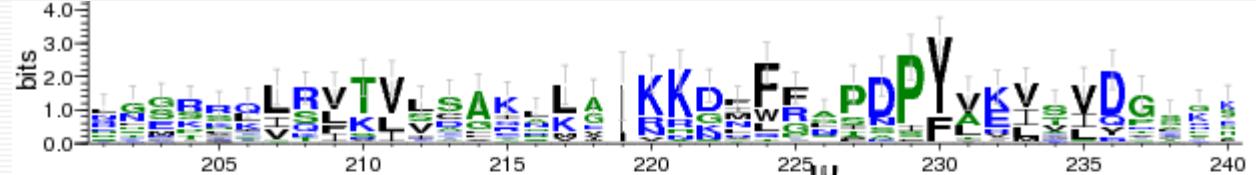
WW domain
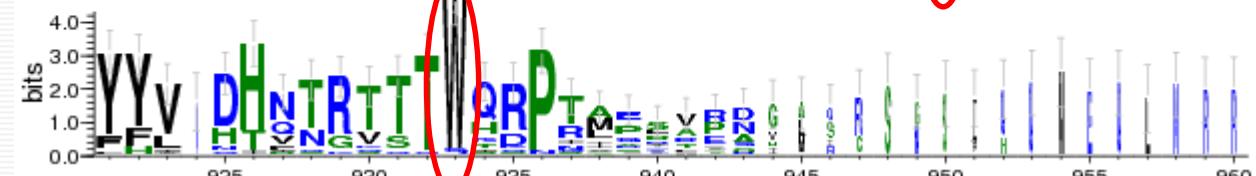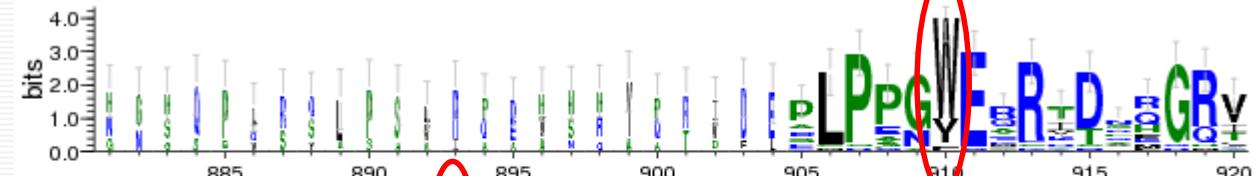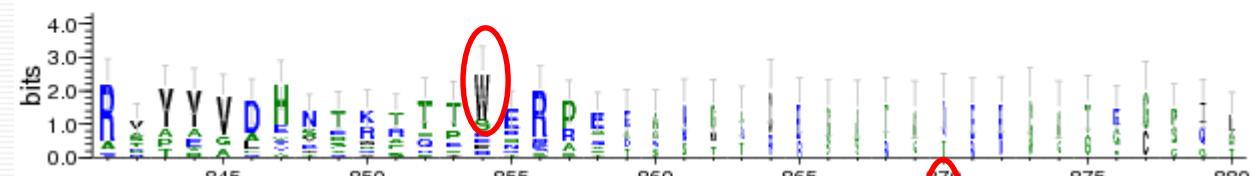
HECT domain
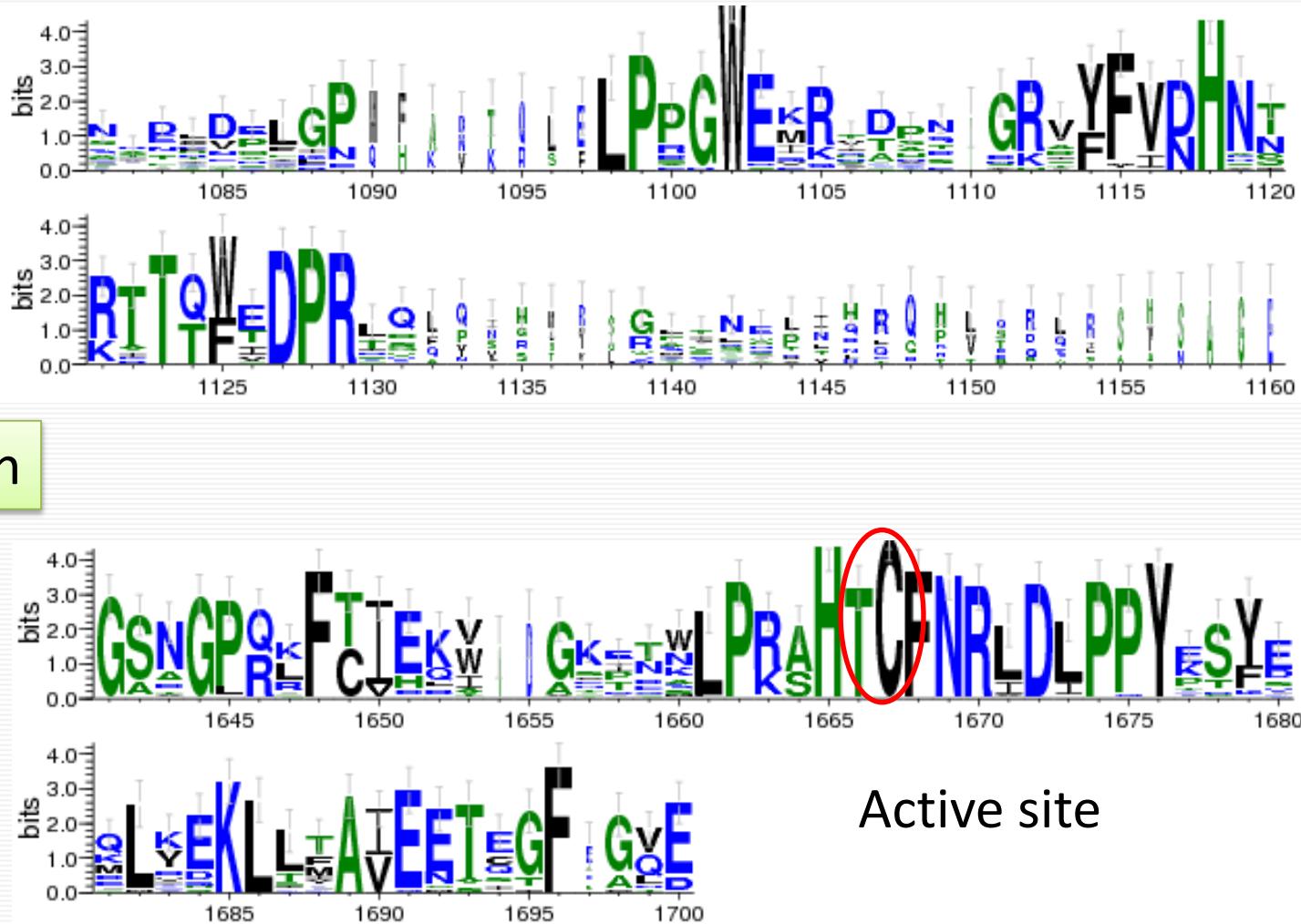
Active site

Analysis of structure


C2

WW WW

HECTc
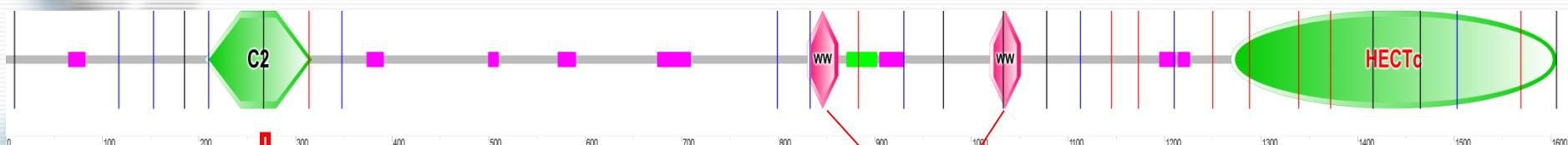
Model 3D Structure [+/-]

Model information:

Modelled residue range:	210 to 310
Based on template:	[4mjj]
Sequence Identity [%]:	27%
Model date:	2013-11-24
Revision date:	2013-11-19

Model 3D Structure [+/-]

Model information:

Modelled residue range:	830 to 861
Based on template:	[2kyk]
Sequence Identity [%]:	71%
Model date:	2013-11-24
Revision date:	2013-11-19

Model 3D Structure [+/-]
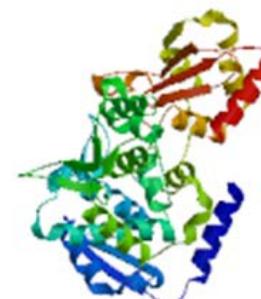
Model information:

Modelled residue range:	1227 to 1600
Based on template:	[1nd7]
Sequence Identity [%]:	49%
Model date:	2013-11-24
Revision date:	2013-11-19

C2 domain

Four-stranded β -sheets
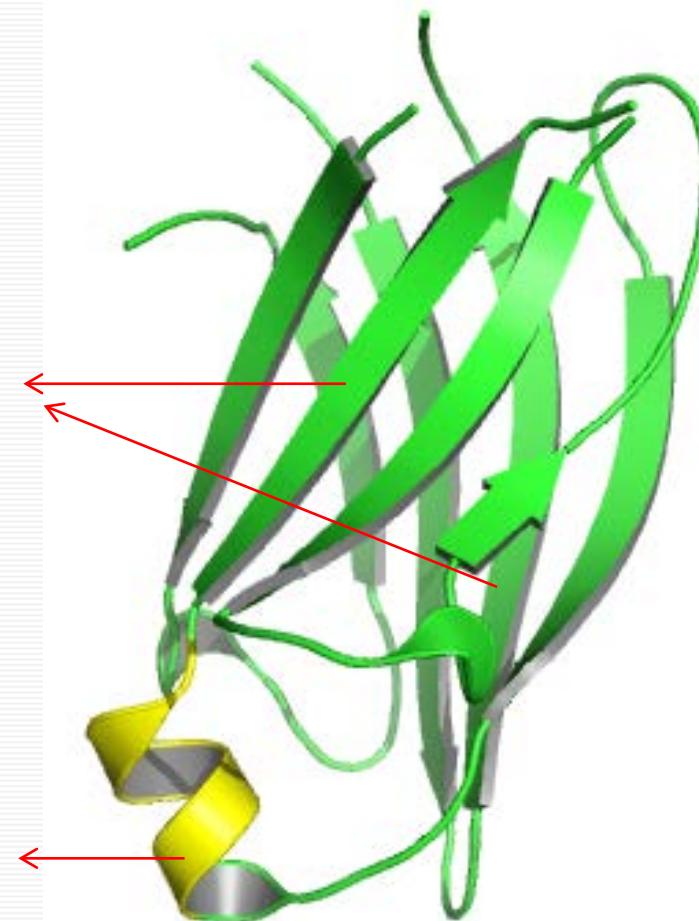
α-helix

Calcium and phospholipid binding region

3 stranded anti-parallel β-sheet fold

Hydrophobic ligand-binding groove

Bind predominately proline-rich motifs
PPxY PPLP PR pS/pTP

HECT domain
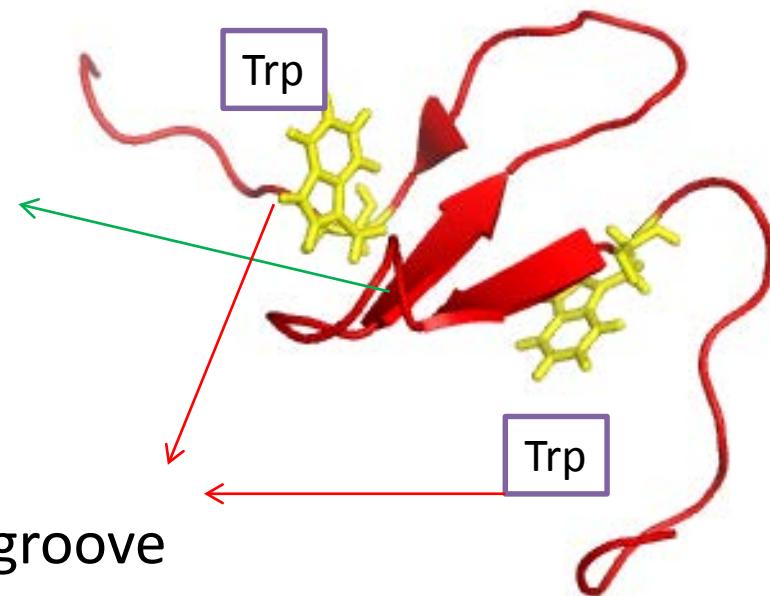
C-terminal lobe

Cys: Active site

40 Å → 16 Å

Distant from E3 catalytic cysteine to E2 cysteine–ubiquitin conjugate

Flexible hinge loop
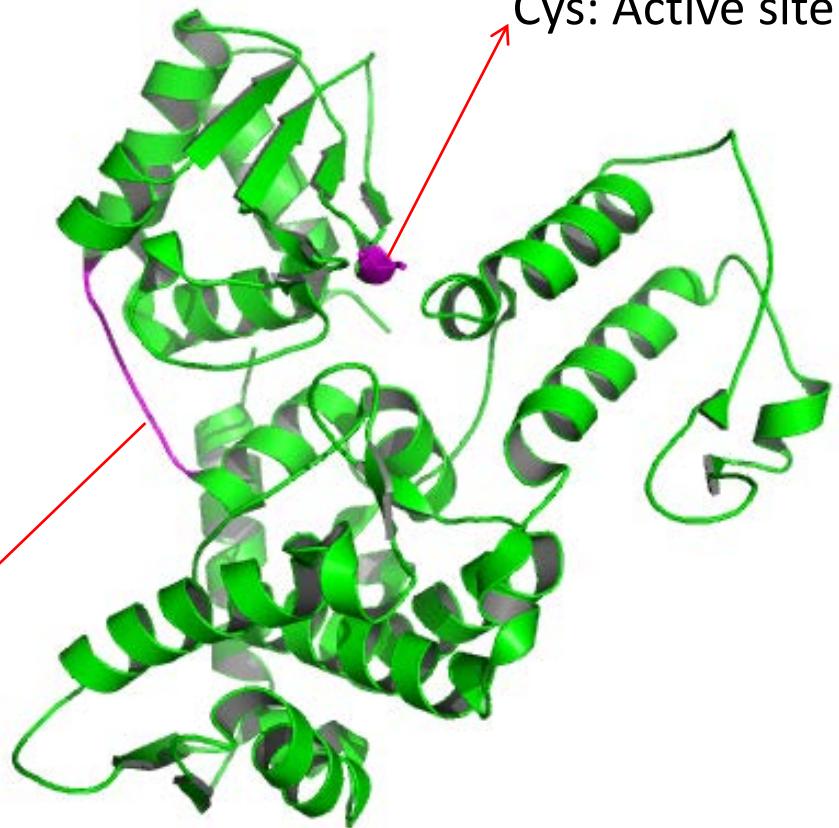
N-terminal lobe

Approximate gene expression patterns by EST profiles

Breakdown by Body Sites

	Hs.164453	
adipose tissue	0	0/12866
adrenal gland	0	0/32940
ascites	0	0/39834
bladder	0	0/29860
blood	0	0/122252
bone	13	1/71618
bone marrow	0	0/48737
brain	26	29/1092688
cervix	0	0/48486
connective tissue	6	1/149072
ear	0	0/16100
embryonic tissue	4	1/212896
esophagus	0	0/20154
eye	4	1/208840
heart	0	0/89524
intestine	0	0/231981
kidney	14	3/210778
larynx	0	0/23466
liver	0	0/205291
lung	2	1/334815
lymph	0	0/44302
lymph node	0	0/89748
mammary gland	0	0/151230
mouth	0	0/66150

muscle	0	0/106371
nerve	0	0/15535
ovary	0	0/101488
pancreas	0	0/213440
parathyroid	0	0/20594
pharynx	0	0/40725
pituitary gland	0	0/16526
placenta	0	0/283019
prostate	0	0/189536
salivary gland	0	0/20265
skin	4	1/210759
spleen	0	0/53397
stomach	0	0/95679
testis	18	8/435204
thymus	0	0/79697
thyroid	0	0/46583
tonsil	0	0/17021
trachea	19	1/51780
umbilical cord	0	0/13764
uterus	0	0/232093
vascular	0	0/51649

Breakdown by Health State

	Hs.164453	
adrenal tumor	0	0 / 12655
bladder carcinoma	0	0 / 17584
breast (mammary gland) tumor	0	0 / 93090
cervical tumor	0	0 / 34484
chondrosarcoma	12	1 / 82838
colorectal tumor	0	0 / 112517
esophageal tumor	0	0 / 17245
gastrointestinal tumor	0	0 / 118498
germ cell tumor	7	2 / 263230
glioma	0	0 / 107194
head and neck tumor	0	0 / 133826
kidney tumor	14	1 / 68872
leukemia	0	0 / 94479
liver tumor	0	0 / 96023
lung tumor	0	0 / 102765
lymphoma	0	0 / 72196
non-neoplasia	0	0 / 96623
normal	13	45 / 3328811
ovarian tumor	0	0 / 76185
pancreatic tumor	0	0 / 105004
primitive neuroectodermal tumor...	0	0 / 127001
prostate cancer	0	0 / 103844
retinoblastoma	0	0 / 46439
skin tumor	7	1 / 125373
soft tissue/muscle tissue tumor	7	1 / 125265
uterine tumor	0	0 / 90107

Breakdown by Developmental Stage

	Hs.164453	
embryoid body	0	0 / 69969
blastocyst	16	1 / 61448
fetus	10	6 / 556978
neonate	0	0 / 31070
infant	0	0 / 23511
juvenile	0	0 / 55574
adult	8	16 / 1921829

Subcellular location

SingalP

```
# Measure    Position   Value    Cutoff    signal peptide?
  max. C      123        0.463
  max. Y       32        0.389
  max. S       18        0.557
  mean S      1-31       0.345
       D      1-31       0.372    0.340    YES
Name=sp_Q76N89_HECW1_HUMAN          SP='YES' Cleavage site between pos. 31 and 32:
```

TargetP

```
Name                        Len       mTP     SP    other   Loc   RC
--------------------------------------------------------------------
sp_Q76N89_HECW1_HUMA 1606             0.720  0.041  0.311    M     3
--------------------------------------------------------------------
cutoff                               0.000  0.000  0.000
```

PSORT II

Results of the *k*-NN Prediction
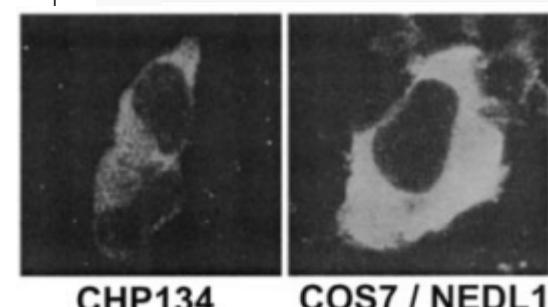
Score

k = 9/23

```
60.9 %: nuclear
21.7 %: mitochondrial
 8.7 %: cytoplasmic
 4.3 %: vesicles of secretory system
 4.3 %: endoplasmic reticulum
```

>> prediction for QUERY is nuc (k=23)

CHP134   COS7 / NEDL1

Predict NLS

Position
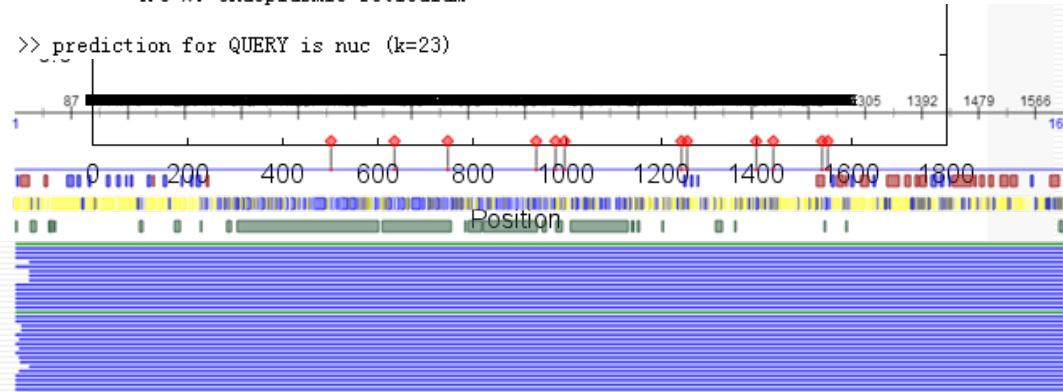
Thanks for Prof. Luo' s guidance on learning!
Thanks for all the classmates taking ABC!