

A

**APPL1**  
NP\_036228.1  
adaptor protein, phosphotyrosine interaction, PH domain and leucine zipper containing 1

**InterPro Domains**

Pfam Domain	InterPro Domain	HMMEr e-value	PDB ID	SCOP ID	p-value	Z-Score	Start	End	Top Position	Hits Count
PH	IPR001849	5.6e-05	1FGY	1fgya	9.00649664486e-35	10.7648	278	375	1	45
BAR	IPR004148	1	1URU	1urua	7.26029238822e-06	5.39926	4	224	1	1
PID	IPR006020	2.7e-07	1P3R	1p3ra	7.52005200536e-18	17.0381	502	633	1	7

**Domain Functions (GO)**

Pfam Domain	GO ID	GO Description
BAR	GO:0005515	protein binding
BAR	GO:0005737	cytoplasm

**HMMEr Alignments**

**BAR**

```

*->lkKqGgffnRasqllkeKvGkaekTkvLDedFeelerrfdttkvlv
+K ++++++T + ++++++
4 IDKL-----PIEETLEDSPTQR-----SLLGVFEEDATAISNYM 37
kklvketkllqppnaarakqkvlklskrqgvkrkgypqPetLLaetm
1 + + + + + + + + + + + + + + + + + + + + + + + + + + + + +
38 NQLYQAMHERYDAQNELSAATH-----LTSKLL 65
qeige...elgdsaedPfGkaLekygeamkqlqlleqldervkqndfP
+e+ + + + + + + + + + + + + + + + + + + + + + + + + + + + +
66 KEYEKqrfPLGDDEV-MSSTLQOFSKVIDELSSCHAVLSTQLADAMMPF 114
ltnllekefkeiqkiklerRrLDyDakrtrlkaktkkskakkDekkl
+t+ e++++kei + + + D Da+ z+ + + + + + + + + + + + + + + + +
115 ITQFKERDLKEILTKEVFQIASNDHDAANRYSRLSKKREND----- 157
akAdqleeElrqAqkqfEelneekeelpnllelevelvng.....lq
+ + + + + + + + + + + + + + + + + + + + + + + + + + + + +
158 -----KVKYEVTEDEVYTRKROHMHYFCALNQLQYKKKIallepLL 201
afweaqldfhqsgaglleqldk-
+ + + + + + + + + + + + + + + + + + + + + + + + + + + + +
202 GYMQAIGSFFKMG---SENLRQLEE 224
    
```

**InterPro Domains**

Name	ID	Database	Start/End	External DB	DB Name	e-value
Pfickstein-like	IPR001849	ProteinScan	177-177	[25500]	PH_DOMAIN	0.0
Phosphotyrosine interaction region	IPR000202	ProteinScan	502-638	[261179]	PID	0.0
Pfickstein homology-type	IPR011993	Gene3D	261-389	5.1D5A.3.20.20	PH_type	6.59998522638E-4
Pfickstein homology-type	IPR011993	Gene3D	502-629	6.1D5A.3.20.20	PH_type	3.4999851489220E-8

**CDT Domains**

Name	ID	Database	Start/End	e-value
PTB	2849	CD	499-627	1.99353e-20
PTB	4738	SMART	500-636	2.60749e-11
CE2-6	2922	CD	499-632	6.10087e-09
PID	3920	PFAM	502-632	3.7523e-06
CE2c_ADA1B	2916	CD	499-627	7.69986e-06
PH_centramin	2829	CD	280-372	0.000447861
PH	817	PFAM	279-375	0.00157929
PH	4736	SMART	278-376	0.00228719
PH_oligophrenin	2828	CD	314-367	0.00020776
HP	2980	CD	502-624	0.00037834
CDC9205	5129	COG	128-222	0.013973
PH-like	2848	CD	301-373	0.0125826
Numb	2991	CD	502-633	0.0937186

**Summary**

The protein encoded by this gene has been shown to be involved in the regulation of cell proliferation, and in the cross-talk between the adiponectin signaling and insulin signaling pathways. The encoded protein binds many other proteins, including RAB5A, DCC, AKT1, PRKCA, adiponectin receptors, and proteins of the NuRD/McCP1 complex. This protein is found associated with endosomal membranes, but can be released by EGF and translocated to the nucleus.

**Associated Literature**

- 18024721 The findings suggest a role for APPL1 and APPL2 protein as dynamic scaffolds that modulate RAB5-associated signaling endosomal membranes by their ability to undergo domain-mediated oligomerization, membrane targeting and phosphotyrosine binding.
- 16623116 APPL1 interacts with adiponectin receptors in mammalian cells and its interaction is stimulated by adiponectin.
- 17845569 These data suggest that APPL1 plays an important role in insulin-stimulated GLUT4 translocation in muscle and adipose tissues and that its N-terminal portion may be critical for APPL1 function.
- 18302781 These findings in APPL1 define a specific cellular site, and disruption of this interaction may play a role in disease.
- 17287464 APPL1 acts as a common downstream effector of Adiponectin receptors R1 and R2, mediating adiponectin-evoked endothelial nitric oxide production and endothelin-dependent vasodilation.
- 17496283 Observational study of gene-disease association. (HUGO Navigator)
- 12816128 The crystal structures of human APPL1 N-terminal BAR-PH domain motif, is reported.
- 17302208 The ability of APPL1 to interact with multiple signaling molecules and phospholipids supports an important role for this adaptor in cell signaling.
- 15303333 Identification of a pathway directly linking the small GTPase RAB5, a key regulator of endocytosis, to signal transduction and mitogenesis via APPL1 and APPL2, two RAB5 effectors.
- 15070827 APPL1 is a potential interactor with FSHR.

**Complete HMMEr Results**

Pfam Domain	e-value	Start/End
PH	0.13	504-633
BAR	1	4-224
RBF	2.9	49-197
CND	47	602-651
Thymidylate synth	47	84-275
5_3_exonuc_N	49	581-662

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**APPL1**  
NP\_036228.1  
adaptor protein, phosphotyrosine interaction, PH domain and leucine zipper containing 1

**Validated in:**

**PH\_type**

**PID**

**HMMErThread Hits**

Pfam Domain	InterPro Domain	HMMEr e-value	PDB ID	SCOP ID	p-value	Z-Score	Start	End	Top Position	Hits Count
PH	IPR001849	5.6e-05	1FGY	1fgya	9.00649664486e-35	10.7648	278	375	1	45
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