

## MOLECULE PAGE

# Rab 1

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Gene Symbols: [Rab1a](#), [Rab1b](#)

## 1. General Function

Rab1 is a small GTP binding protein that is expressed in virtually all mammalian cells, fish, worms and flies and is homologous to the yeast protein Ypt1. It is essential for ER to Golgi transport and has also been implicated in intra Golgi transport (19). There are two isoforms Rab1a (205 aa) and Rab1b (201aa) which are 92% identical at the amino acid level with most differences in the carboxyl terminus (16). These two isoforms are generally localized in the same cellular regions and have similar biochemical properties and functions. Rab1a may also play a role in transcytosis (8). In addition to localization by immunofluorescence in tissue culture cells, Rab1a has been localized by immunogold labeling to vesicles between the ER and Golgi region and over Golgi stacks in NRK cells (13).

The vesicular transport activity of Rab1 is dependent on its GTPase activity as a GDP bound mutant form, Rab1aS25N and the nucleotide free mutant (N124I) block transport from ER to Golgi and lead in some cases to disruption of the Golgi (10,15). Similar effects were seen with addition of Rab1b antibodies (11)

and overexpression of Rab1b mutants with disruption of the Golgi structure and release of Beta-COP. This latter finding indicates a role for Rab1b in COP I coat assembly. Note COP II coat formation is not affected.

Only a little is known of how Rab1 is regulated. Rab1, similar to other Rabs cycles between a membrane bound and cytosolic location with cytosolic Rab existing in the GDP-liganded state bound to Rab GDI as a 80 kDa complex (11). The GEF for Rab1 has not been identified. Whether all of the membrane bound Rab 1 is liganded with GTP has not been experimentally determined but seems likely. A Rab1 GAP has been identified and is the Tbc1D20 protein (6,14). Overexpression of Tbc1D20 blocked ER to Golgi transport of VSV-G protein and caused disruption of the Golgi. More is known of Rab1 effectors. The first identified effector was p115, a tethering factor that binds to the GTP-bound form of Rab1 (1). Rab1 recruits p115 to COP II vesicles and then p115 interacts with Golgi proteins. Subsequently Rab1 was shown to interact directly with the Golgi proteins GM130 (9) and giantin (3)

as well as MICAL-1 a scaffolding protein which links to the cytoskeleton (16).

Rab1 has been shown to be involved in a number of specific cellular functions that are related to its function in ER to Golgi transport. It has been shown to play an obligatory role in the trafficking of G protein coupled receptors to the cell surface (20). It has also recently been shown to be necessary for autophagosome formation (21). Finally, Rab 1 has been shown to be the target of the intracellular pathogen *Legionella pneumophila* which hijacks Rab1 to create a vacuole in which the bacteria replicates (7).

## 2. Rab1 in Pancreas

Surprisingly there has been little work evaluating the function of Rab1 in exocrine pancreatic cells. Rab1 was identified in rat pancreas microsomal subfractions by immunoblotting (13). Rab1 has also been observed in proteomic analysis of dog and rat pancreas RER (4,18) and in isolated rat zymogen granules where it was localized to the external face of the granule (5). It is not clear whether this presence in granules is due to a functional role, the fact that a fraction of Rab1 escapes recycling and moves down the secretory pathway or because it is present in contaminating ER or Golgi membranes. Because of the specialization of acinar cells for protein secretion it seems likely that Rab1 will play a similar role in ER to Golgi transport in acinar cells as observed in cultured cells. However, since these studies

used the transport of VSV-G, a membrane protein as a marker, it would be interesting to see if similar effects were seen on digestive enzyme transport.

## 3. Tools for Study of Rab1

### a. *cDNA*

cDNA clones for human Rab1a and HA tagged Rab1a in pcDNA 3.1 are available from the Missouri S & T cDNA Resource ([www.cdna.org/](http://www.cdna.org/)). Several studies have been published using constitutively active (Rab1 Q67L) or dominant negative (Rab1a S25N; Rab1b S22N; Rab1b N121I) mutant plasmids based on mutating residues known to be important in Ras (2,10,15). Note the residues mutated are slightly different for Rab1a and 1b.

### b. *Antibodies*

Rabbit polyclonal and mouse monoclonal antibodies have been raised against both full length expressed protein and peptide sequences (12), Santa Cruz sells rabbit and goat polyclonal antibodies against Rab1. One of these, a rabbit antibody against the carboxyl terminal (sc-311) should be specific for Rab1a. However we have not tested any of them.

### c. *Mouse lines*

None.

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