## BACKGROUND

Rap1 (Ras-proximity 1) is a member of the Ras superfamily of monomeric GTPases, closely related to Ras. There are two isoforms, Rap1A and Rap1B that share 95% identity and are encoded by two different genes. Rap1 proteins share 50% identity with Ras proteins, including the regions involved in GDP/GTP binding (hence Rap1A has very similar biochemical properties to Ras), C-terminal CAAX domain leading to prenylation (geranylgeranylation in the case of Rap1A), and effector region identical to that of Ras proteins causing Ras and Rap1 to share some potential effectors. Rap1 is activated by diverse extracellular stimuli. In its GTP-bound active form, Rap1 interacts with various effector molecules to initiate downstream signaling pathways. The first identified Rap1 function is the antagonism to Ras-dependent activation of the Raf-1/extracellular signal–regulated kinase cascade. Another Raf family member B-Raf, in contrast to Raf-1, is directly activated by Rap1, leading to the activation of the extracellular signal–regulated kinase pathway. The different Rap1 action on these two Raf kinases is attributable to the difference in affinity of Rap1 to the cysteine-rich domain.[1]

Rap1 plays a dominant role in the control of cell-cell and cell-matrix interactions by regulating the function of integrins and other adhesion molecules in various cell types. Rap1 in integrin-mediated cell adhesion was also regulated by its negative regulator SPA-1. Two Rap1 effectors, RAPL and RIAM, have been shown to act as a link between activated Rap1 and integrin. RAPL was isolated as a Rap1 effector enriched in lymphoid tissues, containing a Ras/Rap1-associating (RA) domain and was shown to induce lymphocyte polarization and the redistribution of LFA-1, leading to enhanced adhesion. In support of a pivotal role for RAPL, *RAPL* gene knockout, in fact, caused an impairment in lymphocyte adhesion and migration. Recently, the serine/threonine kinase Mst1 was identified as a binding protein of RAPL, and its involvement in chemokine-induced cell polarization and LFA-1–mediated adhesion was demonstrated.[2]

The activation of Rap1 in response to various upstream signals is mediated by GEFs. The first identified Rap1 GEF, termed C3G, associates with the adaptor protein Crk and forms a complex with receptor and nonreceptor protein tyrosine kinases in response to extracellular stimuli. Epac1 (also called cAMP-GEFI) and Epac2 (also called cAMP-GEFII) are activated by direct binding of cAMP, being responsible for cAMP-dependent Rap1 activation. Another Epac subfamily member called Repac (also called GFR/MR-GEF) binds to the activated form of M-Ras, which down-regulates the activity of Repac. The third subfamily is constituted of two calcium- and diacylglycerol-regulated Rap1 GEFs termed CalDAG-GEFI and CalDAG-GEFIII, which contain calcium-binding EF-hand and diacylglycerol-binding C1 domains. Two related GEFs called RA-GEF-1 (also called PDZ-GEF1/nRapGEP/CNrasGEF) and RA-GEF-2 constitute another Rap1 GEF subfamily. These two GEFs have both GEF and RA domains, serving not only as an upstream regulator, but also as a downstream target, of Ras family small GTPases. In fact, RA-GEF-1 acts both downstream and upstream of Rap1, amplifying Rap1-dependent B-Raf activation in the Golgi apparatus. On the other hand, RA-GEF-2 mediates M-Ras–dependent Rap1 activation in the plasma membrane.[3] Rap1GAP, which acts as a GTPase activator for Rap1, was a specific negative regulator of Rap1.

Importantly, Rap1 activation is tightly regulated in tissue cells, and dysregulations of the Rap1 signal in specific tissues result in certain disorders, including myeloproliferative disorders and leukemia, platelet dysfunction with defective hemostasis, leukocyte adhesion-deficiency syndrome, lupus-like systemic autoimmune disease, and T cell anergy. Many of these disorders resemble human diseases, and the Rap1 signal with its regulators may provide rational molecular targets for controlling certain human diseases including malignancy.[4]

**References**:

1. Okada, T. et al: Mol. Cell. Biol. 19:6057-64, 1999
2. Bernardi, B. et al: Blood 107:2728–35, 2006
3. Bos, J.L. et al: Nature Rev. Mol. Cell Biol. 2:369-77, 2001
4. Bailey, C.L. et al: Cancer Res. 69:4962-8, 2009

## TECHNICAL INFORMATION

**Source:**
Rap1 antibody is a rabbit antibody raised against a short peptide from N-terminal sequence of human Rap1A.

**Specificity and Sensitivity:**
This antibody detects both endogenous Rap1A and B proteins without cross-reactivity with other family members.

**Storage Buffer**: Rabbit IgG in phosphate buffered saline (without Mg2+ and Ca2+), pH 7.4, 150mM NaCl, 0.02% sodium azide and 50% glycerol.

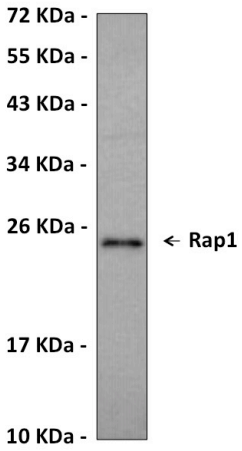
**Storage**:
Store at -20°C for at least one year. Store at 4°C for frequent use. Avoid repeated freeze-thaw cycles.

## APPLICATIONS

| Application: | *Dilution: |
|---|---|
| WB | 1:500-3000 |
| IP | n/d |
| IHC | n/d |
| ICC | n/d |
| FACS | n/d |

**Optimal dilutions must be determined by end user.*

## QUALITY CONTROL DATA




Western Blot analysis of RAP1A in extracts from MOLT4 using at a 1:1000 dilution