The mTOR pathway of translational control regulates cell growth via still not completely defined mechanisms. Similarly, the mechanisms underlying the regulation of mTOR kinase activity are not fully clear. Genetic and biochemical evidence has made a strong case for the small G-protein Rheb as an immediate upstream regulator of mTOR. However, it appears that mTOR is not a direct target of active Rheb-GTP and the identity of a potential Rheb effector linking Rheb to mTOR activity remains elusive. As a member of the Ras super family of small GTPases Rheb possesses a conserved, yet distinct, C-terminal region that is subject of various post-translational modifications. In analogy to other small GTPases Rheb does become prenylated at the most C-terminal cysteine. However, in contrast to most other members of the Ras-family, Rheb does not possess a second hydrophobicity motif, be it a polybasic stretch immediately adjacent to the CAAX prenylation motif, or additional cysteines residues that can experience the attachment of palmitate groups. Since this rather unusual pattern of modifications predicts a poor affinity for biological membranes and since the correct attachment of GTPases to subcellular membrane compartments is known to be crucial for the biological action, we have investigated the association of Rheb to cellular membranes and its impact on Rheb-dependent signalling. Our data suggest that the association of Rheb to membranes may be an important level of regulation within the Rheb/mTOR pathway.