The mammalian target of rapamycin complex 1 (mTORC1) protein interactions

The mTORC1 protein is a key target for several cancer therapies. It is also involved in cell growth, aging, ribosome biogenesis, protein synthesis, actin-cytoskeletal organization, autophagy and metabolism. How the mTOR and associated protein, of which there are many, perform all these functions are unknown. The associated proteins include Rheb (R as homologue enriched in brain) a small GTP-binding protein, raptor (r egulatory a ssociated p rotein of mTOR), mLST8 and PRAS40. Knowledge of how the different proteins link together to function is key to developing new cancer drugs to target this protein pathway.

The challenge

Current cancer drugs against the mTOR pathway only works in some cases whilst others are not affected. The role of each of the proteins in the complex is unknown although some have been shown to be a scaffold for others to bind. The synergies between the proteins are also unclear. The Holy Grail discovery would be to determine the exact functions of the proteins individually and how they work together in concert since it is unlikely that the overall activity is a one to one relationship.

The solution

Pull down assays (breaking the cell apart and pulling down one protein to see what else comes with it) has shown that using this method certain proteins in the complex are associated. However in live cells, this may not be the case. Furthermore, real time experiments as well as visualisation of the environment of the individual proteins as well as any associations cannot be determined using the pull down method. Also any direct physical interactions are not clearly determined. Using advanced microscopy technique called fluorescence lifetime imaging microscopy

The benefits

Understanding the physical links between the complexes in the mTOR pathway could provide insight into how it works in differ cell lines and disease states such as cancer as well as the process of aging. Using this knowledge scientists and pharmaceutical companies could develop drugs and medicines to target this pathway better.