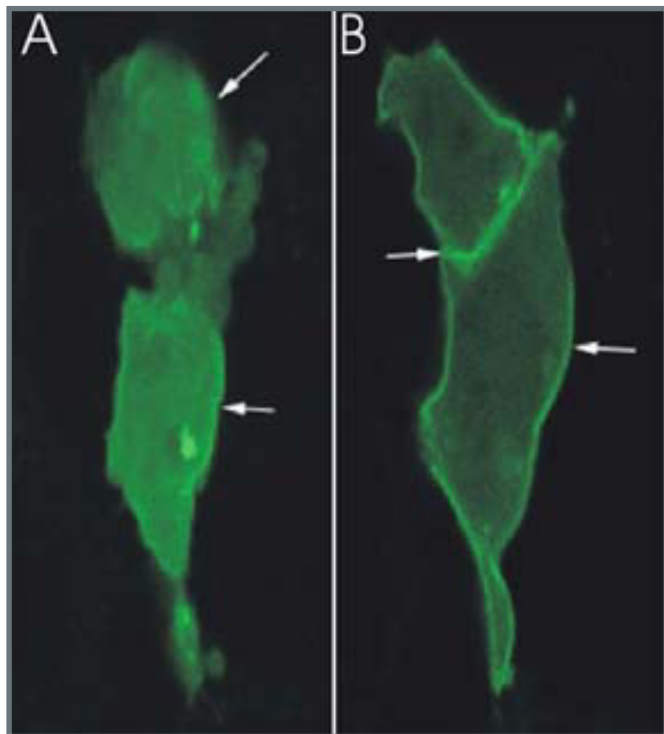


THERAPEUTIC / TARGET

Identification of new protein families possessing PH domains with novel phosphoinositide binding specificities



The PH domain of protein kinase B (a key substrate of PDK1) is shown in the cytosol of unstimulated cells (panel A). Upon stimulation of HEK293 cells with insulin, however, this PH domain translocates to the plasma membrane (panel B) and provides a readout for PI 3-kinase activity in individual, live cells.

- Specific phosphoinositide binding domains
- Pleckstrin homology domains
- Licences available for use of PH domains in assays

Researchers at the University of Dundee have identified three new mammalian protein families which show significance in a variety of cellular pathways. These provide drug targets for the treatment of cancer, strokes and diabetes.

Background

The phosphoinositide lipid, PtdIns (3,4,5) P₃ and its immediate breakdown product PtdIns (3,4) P₂, regulate a wide variety of cellular processes including cell proliferation and survival as well as responses to insulin. The pleckstrin homology (PH) domain is now well established as the region of a protein that is associated with lipid interaction. Proteins that contain a certain type of PH domain are able to interact and bind specifically to these important signalling second messengers. Numerous proteins have been identified to contain PH domains capable of interacting with these lipids including PKB, PDK1, BTK, the Rho/Rac GTP exchange factor VAV and the ADP-ribosylating factor GTP exchange factor GRP1. There fore, proteins

containing a similar PH domain may contribute to important signalling cascades associated with these lipid interacting proteins.

Opportunity

A patent application describing 3 new mammalian protein families which contain PH domains which possess novel phosphoinositide binding specificities has been filed. These proteins are termed TAPPI and TAPP2 (interact specifically with (PtdIns (3,4) P, FAPPI (binds specifically with PtdIns4P) and PEPP1, PEPP2 and PEPP3 (interacts specifically with PtdIns3P). Early data suggests that these proteins are likely to play an important role in a variety of cellular pathways and could be potential novel drug targets for the treatment of cancer, stroke and diabetes.

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We are currently seeking licensees to these novel targets. In addition licences to the use of PH domains in assay systems are available.

References

Dowler et al., 2000. Identification of pleckstrin-homology-domain... containing proteins with novel phosphoinositide-binding specificities. *Biochem. J.* 351, 19-31.

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