P028 Phospholipid induced inhibition of the PI3Kγ phosphorylating activity

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Phosphoinositide interacting proteins are highly specific in terms of the phosphorylated position at the headgroup. This fact explains the unique relavance and the various involvements in membrane traffic. Our experiments clearly show that phospholipids in the inner leaflet of the membrane can be bound and phosphorylated by PI3Kγ even in the absence of other proteins. Furthermore, an inhibiting effect depending on the incubation time with lipids was found for the very first time. Using simultaneous *in vivo* experiments and experiments with artificial membrane models an additional regulation path for the PI3Kγ dependent signal transduction was identified. By infrared reflection absorption spectroscopy the following important structural requirements of the PI3Kγ adsorption and inhibition could be observed: Adsorbed at the air/buffer interface the protein shows α-helical as well as β-sheet secondary structure elements. It does not adsorb to zwitterionic and charged condensed monolayers, and is squeezed out from fluid monolayers on compression. Only in the case of 1-Stearoyl-2-Arachidonoyl-phosphatidic acid (negatively charged head group and fluid state) the kinase adsorbs, penetrates, and stays in the monolayer even at pressures well above the protein's equilibrium pressure. This indicates that the negative charge in the head group region and a special unsaturated fatty acid chain in the sn2-position of the glycerol backbone are crucial for the regulation of the PI3Kγ.