

## Novel genetically encoded coincidence sensors for phosphoinositide pools

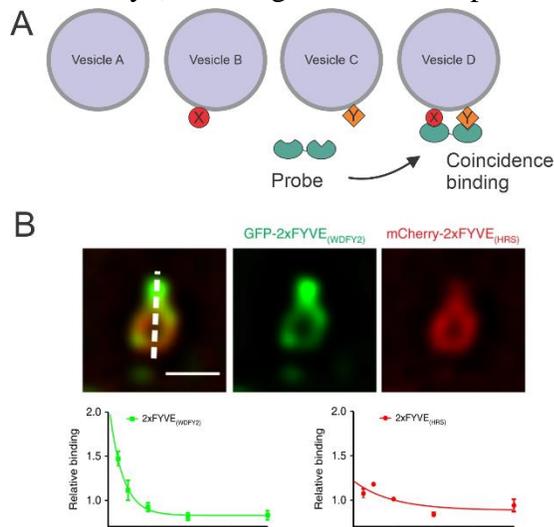
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Phosphoinositides lipids have emerged as key regulators of membrane identity in eukaryotic cells. Phosphatidylinositol-3-OH kinase can phosphorylate the 3', 4' and 5' residue of Phosphatidylinositol, yielding seven distinct phosphoinositide species. These lipids can recruit specific effector molecules and in conjunction with these proteins generate membranes with specific identities. By recruiting different sets of effector proteins, phosphoinositides can define the biochemical properties of their "host" membrane. Moreover, interconversion between different species occurs "on the fly", allowing the same compartment to change its identity while retaining its cargo.



In order to understand the various cellular functions of phosphoinositides, tools to detect and manipulate these pools are required. While several probes for different phosphoinositide species have been described, many of these probes do not detect all pools or have other shortcomings.

Here, we present novel biosensors to detect specific subcellular phosphoinositide pools based on coincidence sensing of multiple molecular cues.

We designed genetically encoded probes which contain lipid-binding protein domains binding to specific phosphoinositides and, in addition, sense other properties of the host membrane, e.g. the presence of other lipid species [1], the curvature of the membrane [2] or the presence of cytoskeleton elements. Using this dual detection, we can detect specific phosphoinositide pools which have been hard to detect and visualize them by high resolution live cell and superresolution microscopy

### References:

- [1] K.O. Schink, K.W. Tan, H Spangenberg, D. Martorana, M. Sneeggen, C. Campsteijn, C. Raiborg and H. Stenmark "The PI3P-binding protein Phafin2 escorts macropinosomes through the cortical actin cytoskeleton" *BioRxiv* 180760
- [2] M. Sneeggen, N.M. Pedersen, E.M. Haugsten, C. Campsteijn, H. Stenmark and K.O. Schink "WDFY2 controls cell migration and invasion by controlling Vamp3-dependent MT1-MMP secretion" *Nature Communications* 10(1):2850 (2019)