"Linking lipids to acetylation" novel roles of of PI(5)P and PIP4K in SIRT1 regulation and development

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Propositions

Belonging to the thesis

"LINKING LIPIDS TO ACETYLATION" NOVEL ROLES OF PI(5)P AND PIP4K IN SIRT1 REGULATION AND DEVELOPMENT

1. PI(5)P binds to the KRKKRK motif of SIRT1 and stimulates its deacetylase activity, thereby modulating downstream p53 acetylation and transcriptional activity (this thesis).
2. PIP4Kα expression and catalytic activity are essential for zebrafish embryonic development (this thesis).
3. Binding of PIP4Kβ to SIRT1 suggests a mechanism by which PI(5)P-stimulated SIRT1 activity could be regulated (this thesis).
4. Interaction between nuclear lipids and transcription factors/chromatin-modifying enzymes provides a signal transducing platform that can acutely respond to external cues and alter gene transcription programs (this thesis).
5. Conformational changes induced by endogenous SIRT1 modulators may "activate" SIRT1 through an as-yet undiscovered pathway (*Dittenhafer-Reed et al., The Journal of Biological Chemistry 287: 42419-27; 2012).*
6. The association of nuclear phosphoinositides with specific nuclear components indicates that nuclear phosphoinositide signaling, like its cytosolic counterpart, requires spatial regulation of phosphoinositide production (*Gonzales ML et al., Journal of Cellular Biochemistry 97: 252-60; 2006).*
7. The molecular diversity of PIP4K isoforms explains much of their catalytic properties and cellular behavior, but their physiological functions remain elusive (*Clarke JH et al., Biochemical Journal. 2013) [Epub ahead op print]*
8. The ability of PI(5)P levels to undergo rapid alterations in a temporarily and spatially regulated manner within the nucleus makes them an ideal modulator of nuclear processes like transcription (Gozani O *et al., Cell*; 114-1, 99-111; 2003).
9. If you're going through hell, keep going [Unknown].
10. When you bake, follow directions. When you cook, go by your own taste.
11. A smile is a curve that sets everything straight (Phyllis Diller, *The Phyllis Diller Special*, 1963).
12. A scientific experiment, no matter how outstanding the findings, is not complete until the results are published.