Vps34 is a phosphatidylinositol 3-kinase, not a phosphoinositide 3-kinase

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There seems to be some confusion regarding the naming of enzymes that phosphorylate certain lipids. In particular, we are referring to the lipid phosphatidylinositol and to phosphoinositides. Inositides are inositol-containing derivatives of phosphatidic acid (Fig. 1). The term phosphoinosside indicates that one or more of the hydroxyl groups of phosphatidylinositol is esterified with inorganic phosphate. Phosphatidylinositol is an inositide, but it is not a phosphoinositide, whereas phosphatidylinositol 3-phosphat (phosphatidylinositol that is phosphorylated on the three hydroxyl group of inositol) is a phosphoinositide (Fig. 1). In addition to phosphatidylinositol 3-phosphate, the lipids phosphatidylinositol 3,4-bisphosphate, phosphatidylinositol 3,5-bisphosphate and phosphatidylinositol 3,4,5-trisphosphate are all phosphoinositides.

There is a single enzyme that converts phosphatidylinositol to phosphatidylinositol 3-phosphate, and that is Vps34. Furthermore, Vps34 only phosphorylates phosphatidylinositol, and does not act on other substrates. Thus, Vps34 is not a phosphoinosside kinase, but rather is a phosphatidylinositol kinase that phosphorylates the three hydroxyl group, making it in particular a phosphatidylinositol 3-kinase. In contrast, Vps34 is not a phosphoinositide 3-kinase, because its substrate, phosphatidylinositol, is not a phosphoinosside. At this point it might be worth considering, albeit briefly, the origin of these terms. That is, the ending “-ide” refers to a chemical compound derived from or related to another such compound, or indicating one of a class of compounds. Thus, a phosphoinositide is related to phosphatidylinositol, and phosphatidylinositol 3-phosphate is one of a class of phosphoinositides. The suffix “-ol” is used in the names of chemical derivatives representing alcohol (inositol is a sugar alcohol; Fig. 1).

When you see the abbreviation “PI3K” it is not clear whether the author is referring to a phosphoinosside 3-kinase or a phosphatidylinositol 3-kinase. In contrast, “PtdIns3K” makes it quite clear that the enzyme is acting upon phosphatidylinositol. Perhaps we are being obsessive, but when it comes to Vps34 we think people should refer to it as a phosphatidylinositol 3-kinase because they are discussing the generation of phosphatidylinositol 3-phosphate or PtdIns(3)P, which is one of the lipids that we tend to be most concerned about with regard to macroautophagy. This is the reason that *Autophagy* uses the abbreviation “PtdIns3K” as the standard for the enzyme complex containing Vps34. Furthermore, you will not go wrong if you describe a phosphoinositide kinase such as Fab1 as a phosphatidylinositol 3-phosphate 5-kinase (PtdIns(3)}
P 5-kinase), for example, whereas you run the risk of incorrectly referring to an enzyme such as Vps34 as a phosphoinositide kinase.

There is one additional issue, and that concerns the distinction between the different classes of phosphatidylinositol kinases, and in particular the class I and class III enzymes. In this case, many people refer to the PI3KC3, which is a short and handy name, except when you consider that the official gene name in humans is “PIK3C3,” with the “3” and the “K” transposed, and both of these suffer from the problem of not making it clear whether we are really referring to a phosphatidylinositol 3-kinase or a phosphoinositide 3-kinase. Again, the class III enzyme that generates phosphatidylinositol 3-phosphate is not a phosphoinositide 3-kinase. In contrast, the enzyme that phosphorylates PtdIns(4,5) P2 to PtdIns(3,4,5)P3 can be correctly referred to as a phosphoinositide-3-kinase, but the substrate specificity is still not indicated. Therefore, Autophagy will use “PtdIns3KC3” to refer to the class III enzyme Vps34 when necessary, as this makes it clear that the substrate is phosphatidylinositol 3-phosphate.

We certainly hope this clears up any confusion.