A small-molecule approach to identify chemical activators of brassinosteroid signaling

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Clathrin-mediated endocytosis (CME) is a major pathway for the uptake of membrane proteins, lipids, and extracellular molecules into plant cells and is of vital importance for the plant development as multiple cellular processes, including nutrient uptake, signal transduction, and plant- microbe interactions, require CME. Brassinosteroid (BR) hormones are perceived at the cell surface by the constitutively endocytosed receptor BRASSINOSTEROID INSENSITIVE1 (BRI1). Inhibition of CME of BRI1 prevented receptor desensitization and had a positive effect on brassinosteroid signaling suggesting that signaling responses can be modulate via CME. However, the genetic inhibition of CME is detrimental for plant growth. Chemical inhibitors of CME are an attractive alternative, but despite the available extensive structural and biochemical knowledge about CME in mammalian cells, the development of chemical tools to interfere with this process is still limited in all systems. Our study is focused on the identification and characterization of novel compounds that target CME and activate brassinosteroid signaling. The development of novel inhibitors will contribute to better molecular and functional dissection of CME in plants and to an increased understanding of how CME controls receptor-mediated signaling.