

**Wednesday September 26, 2018**

**4:15-4:45 p.m.**

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**The GA-biosynthesis pathway can be re-programmed in a model-driven manner  
using hormone activated Cas9-based repressors (HACRs)**

Maintaining food security requires the development of genetic tools to re-design morphological traits of crop plants for greater productivity in the face of climatic variability. Plant hormone circuitry is an obvious target for engineering as it regulates most developmental programs. The Nemhauser and Klavins labs have developed a set of synthetic and modular hormone activated Cas9-based repressors (HACRs) that respond to the phytohormones auxin, jasmonate and gibberellic acid (GA). Here, we will focus on how GA-HACRs can be used to reprogram development to improve yield-associated traits. We have programmed GA-HACRs to target GA biosynthesis and signaling components to modulate the total output of the GA hormone-signaling pathway. To most effectively predict and calibrate the impact of GA-HACRs, we implemented a mathematical model of GA production and signaling with and without GA-HACRs. We demonstrate that GA-HACRs are sensitive to the endogenous pattern of bioactive GA in tissues with well-documented GA maxima. We observed that targeting GA-HACRs to GA20 oxidase effectively reduces root length and delays flowering time, consistent with the predictions of the mathematical model. Tuning GA signaling by integrating GA-HACRs into the endogenous hormone pathway allows specific targeting of agriculturally relevant GA-responses such as dwarfing, flowering time, and male fertility. The modular and orthogonal nature of these synthetic transcription factors should allow ready application to a wide variety of plant species.