O-22: DISCOVERY OF A PLANT LANOSTEROL SYNTHASE GENE AND MANIPULATION OF ITS CATALYTIC RESIDUES TO BIOSYNTHESIZE PARKEOL AND CYCLOARTENOL

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Plants biosynthesize sterols from cycloartenol using a pathway distinct from the animal and fungal route through lanosterol. Described herein are genome-mining experiments revealing that *Arabidopsis* encodes in addition to cycloartenol synthase, an accurate lanosterol synthase (LSS) - the first lanosterol synthase cloned from a plant. The coexistence of cycloartenol synthase and lanosterol synthase implies specific roles for both cyclopropyl and conventional sterols in plants. Phylogenetic reconstructions reveal that lanosterol synthases are broadly distributed in eudicots but evolved independently from those in animals and fungi. Novel catalytic motifs establish that plant lanosterol synthases comprise a third catalytically distinct class of lanosterol synthase. Mutagenesis studies established that Asn477 and V481 are catalytically important; the Asn477His Val481Ile double mutant forms no lanosterol but parkeol and cycloartenol (65:35). An unusual aspect of this work is the modifications result in a product that is thermodynamically disfavored relative to the product of the starting enzyme.

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