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ENGINEERING OF A COTTON PLANT WITH NORMAL LEVELS OF PROTECTIVE TERPENOIDS BUT WITH SIGNIFICANT REDUCTION IN THE SEED-GOSSYPOL: OVERCOMING THE MAJOR WEAKNESS OF GLANDLESS COTTON

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Abstract

Global cottonseed production of 44 million metric tons (MMT), representing nearly 10 MMT of protein, can potentially provide the protein requirements for 500 million people per year at a rate of 50 g protein/day. However, gossypol, a cardio- and hepatotoxic terpenoids present in the glands, renders this abundant resource unfit for consumption by non-ruminants and use as food. A major portion of this abundant agricultural resource is utilized as feed for ruminant animals either as whole seeds or as meal following oil extraction; however, if consumed in sufficient amounts, cottonseed diminishes the reproductive performance of bulls. Therefore, elimination of gossypol from cottonseed has been a long-standing goal of geneticists. Attempts were made to meet this objective by developing so-called "glandless cotton" in the 1950s via conventional breeding techniques. However, the glandless varieties were commercially unviable because of the increased susceptibility of the plant to insect pests due to the systemic absence of glands that contain gossypol and other protective terpenoids. Thus, the promise of cottonseed in contributing to the food requirements of the burgeoning world population remained unfulfilled.

We examined whether RNA interference can be employed to disrupt a key step in the biosynthesis of gossypol in a seed-specific manner in cotton (*Gossypium hirsutum* L.). We demonstrate that targeted engineering of the gossypol biosynthetic pathway by interfering with the expression of the δ-cadinene synthase gene during seed development resulted in a significant reduction in cottonseed-gossypol levels and that this trait was heritable. Results from molecular and enzymatic analyses on the developing, transgenic embryos were consistent with the reduced gossypol phenotype in the mature seeds. Importantly, the levels of gossypol and related terpenoids that are derived from the same pathway were not diminished in the foliage and floral parts of these plants and thus remain available for plant defense against insects and diseases. These results illustrate that it is possible to modify a biosynthetic pathway selectively to overcome the limitations of plant breeding in achieving targeted removal of a toxic secondary metabolite. Thus, a single-step, targeted genetic modification applied to an agricultural byproduct provides a mechanism to open up a new source of nutrition for hundreds of millions of people.