

## ENGINEERING HIGH LEVELS OF SAFFRON APOCAROTENOIDS IN TOMATO

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Crocins and picrocrocin are high-value hydrophilic pigments produced in saffron and used commercially in the food and pharmaceutical industries. These apocarotenoids are derived from the oxidative cleavage of zeaxanthin by specific carotenoid cleavage dioxygenases. The pathway for crocins and picrocrocin biosynthesis was introduced into tomato using fruit specific and constitutive promoters and resulted in 14.48 mg/g of crocins and 2.92 mg/g of picrocrocin in the tomato DW, without compromising plant growth.

The strategy involved expression of CsCCD2L to produce crocetin dialdehyde and 2,6,6-trimethyl-4-hydroxy-1-carboxaldehyde-1-cyclohexene, and of glycosyltransferases UGT709G1 and CsUGT2 for picrocrocin and crocins production, respectively. Metabolic analyses of the engineered fruits revealed picrocrocin and crocetin-( $\beta$ -D-gentiobiosyl)-( $\beta$ -D-glucosyl)-ester, as the predominant crocin molecule, as well as safranal, at the expense of the usual tomato carotenoids. The results showed the highest crocins content ever obtained by metabolic engineering in heterologous systems. In addition, the engineered tomatoes showed higher antioxidant capacity and were able to protect against neurological disorders in a *Caenorhabditis elegans* model of Alzheimer's disease. Therefore, these new developed tomatoes could be exploited as a new platform to produce economically competitive saffron apocarotenoids with healthpromoting properties.