

PRODUCTION OF BIOACTIVE MOLECULES FOR HUMAN HEALTH IN PLANT CELLS: THREE CASE STUDIES

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Production of bioactive molecules for human health in plant cells: three case studies

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Plants have always been a source of metabolic compounds useful for human health. Today, the different genetic engineering techniques allow us to modify both whole plants and in vitro cultured tissues and organs for several purposes. These span from the elicitation of bioactive molecules that are already produced by these organisms to de novo biosynthesis of metabolites and recombinant proteins (Burnett et al., 2019). In particular, several studies have focused on the production of compounds with antioxidant, anti-inflammatory and hypoglycemic activity with the long term goals of exploiting their protective role in the prevention of neurodegenerative diseases and cancer, just to cite a few (Zhang et al.,

2015). Indeed, plant in vitro systems appear to be reliable and sustainable platforms for the production of such as molecules (Marchev and Georgiev, 2020).

Here we show three strategies we are currently pursuing for the production of compounds with antioxidant or immunomodulatory actions in planta.

They are based either on stable or transient genetic transformation of plant cells from (a) *Malus domestica*, (b) *Daucus carota* and (c) *Nicotiana tabacum*. In (a) calli derived from apple pulp have been transformed with the bHLH transcription factor Sn (TF) from *Zea mays*. This TF interacts with MYB and WD40 proteins to upregulate the biosynthesis of anthocyanins and/or proanthocyanidins in different plant species and growing conditions (Tonelli et al., 1991; Paolocci et al., 2005).

The second example concerns genetic engineering of carrot stem cells to produce astaxanthin. Astaxanthin is a carotenoid produced in few green algae as in *Haematococcus lacustris* (ex *pluvialis*), highly appreciated by pharmaceutical and nutritional industries for its high antioxidant capabilities. Here (b) we transformed carrot stem cells with the gene for β -carotene ketolase from *Chlamydomonas reinhardtii*: this enzyme converts β -carotene into astaxanthin in unicellular algae (Perozeni et al., 2020).

In the third case ©, we transiently transformed tobacco leaf protoplasts with a construct coding for the human enzyme IDO1. By promoting the degradation of tryptophan to produce kynurenines, molecules capable to modulate the immune system, this enzyme exerts a powerful immunoregulatory action. Therefore, we are currently testing the hypothesis of tobacco cells as a IDO1 biofactory.