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Editorial overview: Biofortification of crops: achievements, future challenges, socio-economic, health and ethical aspects

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One of the biggest challenges humankind is facing in the 21st century is to sustainably feed the ever-growing population on the globe, estimated to exceed 11 billion by 2100 [1]. In 2015, chronic undernourishment decreased from over 1 billion to below 800 million for the first time in 25 years [2]. However, while caloric malnutrition (acute hunger) has decreased, micronutrient malnutrition, the so-called "hidden hunger" caused by a lack of vitamins and minerals, still affects 2 billion people and hence represents the most common form of malnutrition. Paradoxically, being overweight from food overconsumption affects another 1.9 billion people (although these may also suffer from hidden hunger) [3].

In April 2016, the United Nations (UN) declared the start of an "International Decade on Nutrition" to meet the nutrition-related targets of the Sustainable Development Goals (SDGs) adopted by its member nations last year [4]. As part of the SDGs, a major aim is to end all forms of malnutrition by 2030, overarching the objectives of ensuring both food and nutritional security. Ending hunger, achieving food security and improving nutritional quality of crop products will require a profound change of the food and agricultural system, as well as a major investment in nutrition education, both of which should foster diversity. Though this will empower farmers to grow – and consumers to choose – healthier crop products, there is not only a need to address the production and processing but also the marketing and advertisement of food products, which should collectively aim at healthy diets.

While not being limited to the developing world, micronutrient malnutrition has by far the most profound impact thereon. Micronutrient malnutrition has long-term effects on human health, learning ability and productivity and thus poses a major impediment to socioeconomic development and contributes to a vicious circle of underdevelopment [5]. Micronutrients are particularly low in the 5 major staple crops (rice, corn, wheat, cassava and potato), on which more than half of the world population relies for its daily caloric intake. Micronutrient content is further decreased due to post-harvest and processing losses [6,7].

Several strategies exist to fight micronutrient malnutrition, including supplementation (*e.g.* in the form of pills) and industrial fortification. Unfortunately, the latter have their limitations in practice. Supplements are not always taken on a regular basis, while food fortification requires quality

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control, imposing the need for specialized techniques and infrastructure, which usually are very restricted in developing countries. Fortified foods and supplements are often only available in cities and hence, cannot be benefited from by poor rural populations. Biofortification of staple crops is a complementary, cost-effective method to alleviate the global burden of micronutrient malnutrition [8]. Biofortification can be defined as the process by which the nutritional quality of food crops is improved through agricultural technologies, including conventional and molecular plant breeding, metabolic engineering through modern biotechnology such as genetic modification, fertilization techniques or, in the case of minerals, by biostimulants improving their bioavailability. Several efforts to biofortify staples have been undertaken, with vitamin A enhancement of rice and sweet potato as prime successful examples of metabolic engineering and breeding, respectively (Golden Rice, [9,10]; Orange Fleshed Sweet Potato, [11]. The growing recognition of biofortification as a means to fight micronutrient deficiencies was illustrated by the 2016 World Food Prize honoring Maria Andrade, Robert Mwanga, Jan Low, and Howarth Bouis for the development and implementation of biofortification by breeding critical micronutrients into staple crops, reducing ‘hidden hunger’ for millions (https://www.worldfoodprize.org). Despite a few attempts and the fact that there are no examples of multi-biofortification where the target levels of all enhanced micronutrients has been reached, the content of a series of single micronutrients has been successfully enhanced in several target crops, and their bio-availability has been proven.

This issue of *Current Opinion in Biotechnology* highlights metabolic engineering and breeding techniques towards biofortification of crop plants. Different reviews focus on carotenoid-derived vitamin A, vitamin B_1, B_6, B_9, C and E as well as two mineral micronutrients, iron and iodine.

Giuliano discusses the enhancement of carotenoids in crop products, with provitamin A being a major target. Worldwide an estimated 250 million preschool children are vitamin A deficient and between 250,000 to 500,000 vitamin A-deficient children become blind every year, half of them dying within 12 months of losing their sight. Since the development of first generation Golden Rice, enhancement of both provitamin A and non-provitamin A carotenoids has been obtained in a series of crops.

The efforts on B vitamin enhancement indicate the importance of balancing different vitamers, in particular for vitamin B_1 and B_6.

Thiamin (vitamin B_1) deficiency is common in populations whose diets are mostly based on high carbohydrate staples like white rice. Goyer summarizes the current knowledge about thiamin biosynthesis in plants and efforts that have been made to increase its content by genetic engineering. Together with the discovery of regulatory elements, the characterization of biosynthesis, transport and salvage genes has laid the foundation for the first successful thiamin engineering strategies. Yet many aspects of thiamin metabolism remain poorly understood, hindering further improvement in biofortification of this vitamin. Fudge et al. present a rationale for vitamin B_6 biofortification and the most recent advances in achieving this. Three of the world’s top five staple crops (rice, wheat and cassava) do not meet the recommended dietary intake for vitamin B_6, when consumed as a major proportion of the diet. In contrast to vitamin B_1, vitamin B_6 enhancement up to target levels has been achieved in cassava by genetic engineering. In addition, controlled enhancement of the appropriate B_6 vitamer in crops has the potential to confer stress resistance, as well as enhance bioavailability.