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Molecular farming: hosting plants as green factories

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Agricultural biotechnology provided several novel tools to make fine tuning of genome structure and alternate the traits of interest in plants in a way that have never been possible before. One of the major beneficial outcomes of this technology is genetically modified (GM, transgenic) plants in which one or several genes have been inserted into plant genome from various sources by using different means such as *Agrobacterium tumefaciens*or particle bombardment.[1,2] Organel genome of certain plant species also become as target to generate transplastomic plants.[3,4] Although GM plants have come along with a number of controvertial issues,[1] the global planting area of GM plants constantly increased during last two decades and reached to 181.5billion ha all around the world.[5] Therefore, agricultural biotechnology is one of the most adaptive technologies used in plant production. However, the traditional use of transgenic plants has recently expanded beyond for food and feed production, and newer generations of GM plants hosted novel applications such as pharmaceutical manufacturing in agricultural scale.[6]

The traits of GM plants have mainly been classified into three groups:[7] First-generation GM crops involved in improvements of agronomic traits such as resistance to pests, herbicides or diseases. Second-generation of GM crops focused on biofortification of food or feed products such as golden rice or bioremediation.[8,9] Third-generation of GM plants were designed to produce special substances such as plant based pharmaceuticals or chemicals used for industrial purposes. Different terms are used to define the use of GM plants for the production of such therapeutics.[10,11] The term 'Pharming' is generally used to refer the use of plants for the production of pharmaceuticals although it often describes the use of animals for the production of drugs.[12] Therefore, the production of recombinant pharmaceutical proteins by using GM plants is spesifically defined as Plant Molecular Farming or Molecular Pharming per se and their products are defined as Plant-made Pharmaceuticals (or therapeutics) (PMP) or Plant Molecular Farming to avoid confusion with animal based techniques.[13,14] On the other hand, Biomanufacturing or Biopharmaceuticals also appear in the literature for the use of biological organisms to manufacture products of interest or pahrmaceuticals from biological organisms, respectively.[12] In addition, the term molecular farming is also used for the commercial nonpharmaceutical products of GM plants such as antibodies, enzymes, and growth factors that are used as research-grade or diagnostic reagents, cosmetic ingredients, biosensors, and biocatalysts to facilitate bioremediation.[15–17] Although most of them are currently produced on a small to medium scale, making it possible to rely on contained growing facilities rather than field cultivation,[16] the full potential of molecular farming will only be realized if large-scale production can be achieved.[18]

In the past, molecular farming was not an atractive expression system due to competitive traditional platforms. However, approval of the first plant-based biopharmaceutical in 2012 provided an emerging apportunity that transgenic plants can be used as an alternative production systems not only for medical practices of biopharmaceuticals but also for the commercial nonpharmaceutical products.[19–22] Therefore, recent advances in transgenic plant technology also revealed specific platforms and regulatory guidelines that unique products can be produced more successfully in plants than by bacteria or memmelian cells.[23,24] For instance, proteins extracted from transgenic plants grown in a field scale represent a promising strategy for affordable vaccine production that combines innovations in medical science and plant biology. One of the most lucrative new applications of biotechnology-derived enzymes is enzymatic biodiesel products since they are nonpolluting and carbon-neutral fuel.[25] In addition, the expression of polymer-degrading enzymes in plants would be cost effective compared to traditional platforms, and the enzymes could be purified and be used as crude extracts, or be preferably expressed in the biofuel crop directly.[11] The biorefinery concept of plant molecular farming will allow the design of low-waste processes in which all raw materials are converted into useful products.[23] The growth of the biofuel, paper manufacturing industry and food/feed additive industries may be involved more in plant molecular farming since the production of nonpharmaceutical antibodies in various formats has been demonstrated for applications in diagnostics, food processing, and quality validation in the past.[26–28]

Conclusion

In conclusion, along with those current prospects and future potential appoturnities mantioned above, molecular farming may not run away from the safety issues of genetically modified plants. An appropriate choice of host plant species e.g., self-fertilizing non-crop plants will be an important parameter in future aplications. Recent developments in omics technologies and precise genome editing tools such as CRISPR-cas9 may accelerate the adaption of plant based biological manufacturing to turn GM plants in green factories.

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Conflicts of interest

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