



### **Soybean seeds as bioreactor to produce recombinant proteins**

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The development of technologies for the introduction and expression of foreign genes in soybean has allowed studies of gene function and resulted in important advances toward plant genetic engineering carrying several input and output traits. The production of recombinant proteins in plants has several potential advantages over current systems such as mammalian and bacterial cell cultures, including the lower costs, scalability of agricultural production and the absence of human pathogens. A large number of plant host systems has been tested, including plant cell cultures, unicellular plants, aquatic plants grown in containment, and, most notably, food and non-food crops, which can be grown in greenhouses, underground growth facilities, or the open field. The use of genetically modified (GM) plants to synthesize proteins that are subsequently processed, regulated and sold as pharmaceuticals challenges two very different established regulatory frameworks, one concerning GM plants and the other covering the development of biotechnology-derived drugs. Within these regulatory systems, specific regulations and guidelines for plant-made pharmaceuticals – also referred to as plant-derived pharmaceuticals – are still evolving (Spok et al., 2008). The products nearing commercial viability will ultimately help to road test and fine-tune these regulations, and might help to reduce regulatory uncertainties. To understand what technical or economic forces have enticed a major hole in the pharmaceutical industry into the utilization of plant, one need to look at the relation cost/added value and time to develop a product (Rech, 2009, in press). Our research group has been actively involved in the evaluation of the potential utilization of soybean seeds as novel system to manufacture biopharmaceuticals (Rech et al., 2008). The human growth hormone, human coagulation factor IX, insulin, single-chain variable domain, cyanovirin and grifitisin (microbicides), plac, gage and lack (cancer antigens) and masp1 and masp2 (biofibers) genes under control of the seed specific regulatory sequences, including the phaseolin and conglycinin promoters were linked to different signal peptides in order to direct the recombinant proteins to the protein storage vacuoles present in the soybean seed. The transgenic events have been generated utilizing the biolistic technology (Rech & Aragao, 1997). The apical meristematic region of mature soybean embryonic axes were excised, and bombarded with the plasmid DNA's. Then, the bombarded embryonic axes were transferred to the culture medium containing MS basal salts, sucrose and cytokinin. After three to five weeks in culture, putative transgenic shoots were excised and transferred to the greenhouse to further development. Molecular and biochemical evaluation were conduct to determine integration and the recombinant proteins accumulation. We do believe that the results obtained, will form the foundation to evaluate the potential commercial utilization of soybean plants as bioreactor.

Spok A., Twyman R.M., Fischer R., Ma J.K.C. Ma, Sparrow P.A.C. Evolution of a regulatory framework for pharmaceuticals derived from genetically modified plants. *Trends in Biotechnology*, 26 (9) 506-517. 2008.

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Rech E.L. Biotechnology as a useful tool for biodiversity use and sustainability.

Rech E.L., Aragao F.J.L. A process for obtaining transgenic leguminous plants (Leguminosae) containing exogenous DNA PI9714887-3 – PCT – Patent issued.