

Oral Presentation

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The moss bioreactor offers best of both worlds for biopharmaceutical production

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Transgenic plants are promising alternatives for the production of recombinant pharmaceutical proteins (plant molecular farming). Plants as higher eukaryotes perform posttranslational modifications similar to those of mammalian cell lines. Low-cost cultivation and safe pathogen-free production are further advantages. However, field cultivation of transgenic plants raises social, environmental and regulatory challenges that need to be addressed when considering how plant-made pharmaceuticals might be successfully commercialized. Especially GMP conditions are hard to achieve for the field production of pharmaceuticals. Moreover, plant-specific protein N-glycosylation was shown to be immunogenic, a fact that represents a drawback for many plant systems as biofactories for a broad spectrum of biopharmaceuticals. The moss *Physcomitrella patens* offers unique properties as a safe contained system for protein production [1]. It is grown in the dominant haploid gametophytic stage as tissue suspension cultures in photobioreactors. Photo-autotrophic growth enables cultivation in a simple and cheap mineral medium. The generation of stable transgenic lines is easy and a relatively short-term procedure. The moss is genetically well characterized and displays no special codon usage preferences allowing the high-level expression of human cDNAs without prior codon optimization. Strong promoters for foreign gene expression have been characterized from both, heterologous as well as endogenous genes. Efficient secretory signals and a transient transfection system allow the secretion of freshly synthesized proteins to the surrounding medium. The secretory system offers continuous harvesting of the product without the necessity to lyse the producing cells and eased down-

stream isolation and purification steps. The key advantage of *Physcomitrella* compared to other plant systems is its high degree of nuclear homologous recombination enabling targeted gene replacements. By this means, plant-specific glycosyltransferase genes, i.e. beta1,2-xylosyltransferase and alpha1,3-fucosyltransferase were specifically knocked out and human-type beta1,4-galactosyltransferase was introduced. The resultant moss strains provide proteins with non-immunogenic humanized glycan patterns.

Here we present an overview of the relevant aspects for establishing moss as a production system for recombinant biopharmaceuticals.

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References

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