



Laura Bassi Centres of Expertise - PlantBioP



Bayer CropScience



**Plant-Produced Glycan-Optimized Biopharmaceuticals  
(PlantBioP, 2010-1017, evaluation 2014)**

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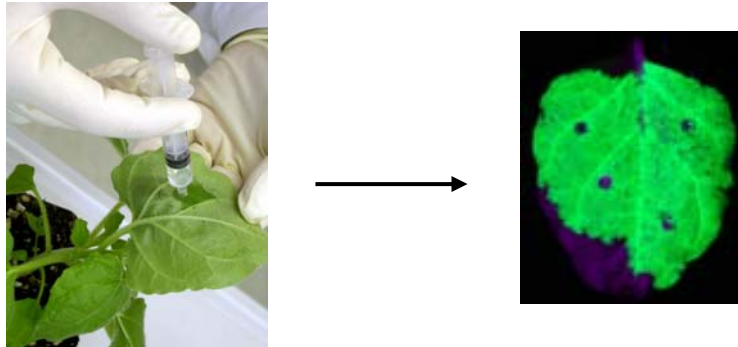
Recombinant proteins, like monoclonal antibodies, are a success story in drug development. About 150 recombinant protein therapeutics have been approved and command a market share of over 50 billion € with an estimated annual growth rate of 10-20%. Demand for these products by far exceeds the production capacity and their cost-intensive processes, which are mainly based on mammalian cells, are an enormous hurdle hindering world-wide application of the drugs.

New procedures for generating these biopharmaceutical products have been developed at the approved LB Centre. The major aims of the centre are (a) cost-efficient production of biopharmaceutical products, and (b) increased therapeutic potency via an optimized N-glycosylation pattern. These aims should be achieved by implementing plant-adapted expression systems.

The LV centre takes advantage of two recent important scientific achievements (i) the development of extremely efficient transient plant-viral-based expression systems which enable the generation of grams of recombinant proteins within days after the delivery of the respective DNA constructs into plants (magnicon<sup>®</sup>: Marillonnet et al., 2005); (ii) the generation of glycoengineered plant mutants that allow incorporation of a homogeneous, human-like glycosylation pattern into the recombinant proteins (Strasser et al., 2008, Strasser et al., 2009). An efficient generation of various therapeutically relevant proteins with different glycosylation profiles and the subsequent investigation of their biological activities will be the core competence of the LB centre.



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*Schematic presentation of the magnicon<sup>®</sup> system: (a) a bacterial suspension that carries the respective gene construct is introduced into plants via “Agroinfiltration” (in this case the gene of interest is GFP). (b) Expression of gfp (demonstrated by UV monitoring) is monitored 5 days after infiltration.*

Glycosylation, the addition of sugar residues, is an important protein modification. Serum proteins carry a heterobereous and complex N-glycosylation pattern. Although the biological impact of specific N-glycan profiles is largely unknown, many studies have demonstrated that certain N-glycan residues significantly enhance therapeutic potency. Consequently glycosylation is playing an increasingly important role in drug development. The expression systems in current use, which are mainly based on mammalian cells, allow only limited control over this important posttranslational modification and result in drugs with sub-optimal therapeutic activities. In contrast to mammals, plants glycosylate proteins naturally with a largely homogeneous pattern which, as successfully demonstrated in our laboratory, allows specific manipulation of these structures in a certain direction (Strasser et al., 2008, Strasser et al., 2009).

A series of plant glycosylation mutants will be generated in the LB centre that allow therapeutic proteins to be produced with a defined N-glycosylation pattern facilitating detailed investigation of the impact on the biological activity of specific N-glycan residues. A main focus will be the introduction of the mammalian sialylation pathway into plants. Protein sialylation, the most complex type of human glycosylation plays a key role in the biological activities of many proteins. We are confident that our research will result in the development of a production platform that allows the generation of highly active biopharmaceutical products obtained by an optimized N-glycosylation profile and that our data will contribute to the development of drugs with optimal therapeutic potency.



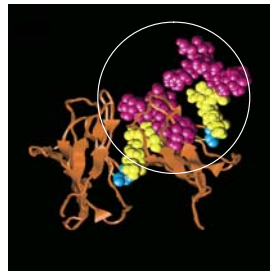
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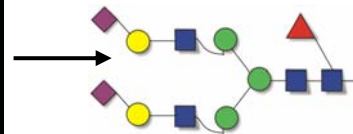
The project will be conducted in cooperation with the well recognized glyco biologist **Friedrich Altmann** (Chemistry Department, BOKU) and the globally active pharmaceutical company **BAYER** (Gent, Belgium).



*Model plant: Nicotiana benthamiana*



*Glycoprotein*

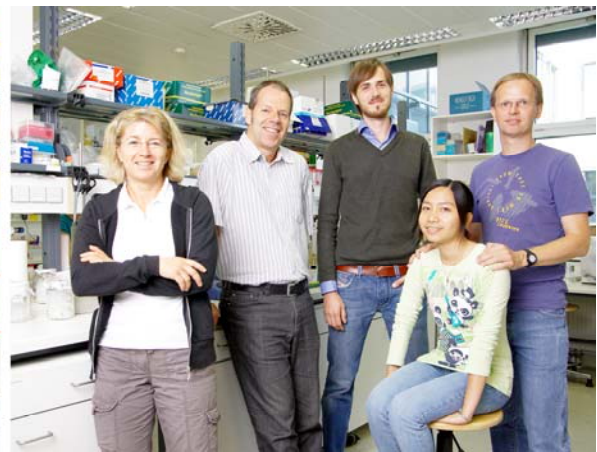


*Glycan structure  
(Sialic acid:purple)*

### Steinkellner group



### Altmann group



*Left foto: Andreas Loos (front), Herta Steinkellner, Jakub Jez, Alexandra Castilho, Pia Gattinger; right foto: Karin Polascek, Friedrich Altmann, Johannes Stadlmann, Yen Nguyen, Tommi Dalik)*