Plants4Nemavax

PROJECT SUMMARY

Parasitic nematodes are amongst the most common pathogens in grazing ruminants worldwide. The continuous exposure to these worms has a significant impact on the health status and productivity of the animals. Control of these infections currently relies almost completely on periodic mass administration of anthelmintic drugs. However, with the increasing incidence of anthelmintic resistance around the world, there is an urgent need for alternative control measures. Vaccination is often put forward as the most rational and cost-effective alternative to control infections with parasitic worms. In recent years it has been shown that it is possible to protect cattle and sheep against worm infections by vaccinating them with antigens isolated directly from the worms. Unfortunately, for most parasite species, this approach is unsustainable for large-scale application as it relies on infected host animals to produce the vaccines. The production of recombinant vaccines in heterologous expression systems seems the most obvious solution. However, of all the recombinantly produced subunit vaccines that were evaluated in the past, none induced sufficient levels of protection to consider further commercial development. One of the bottlenecks explaining why many vaccination trials with nematode vaccines have been unsuccessful is the inability of the expression systems to reconstitute the antigens with their native post-translational glycan modifications. Recent research has shown that the natural glycans present on the antigens can be critical in the context of vaccination as removal of the glycans from the antigens impaired the protective immune responses elicited by the vaccines. The glycans on a given protein can shape immune responses by influencing which receptors and cells of the immune system are targeted. In addition, helminth-glycoproteins carry very diverse and sometimes unique glycan structures, which can be highly immunogenic and major targets of the host's antibody responses. Therefore, reconstructing these sugar structures on recombinant nematode proteins may be key for successful vaccine development. However, bacterial expression systems are not able to perform complex glycan modifications and the glycan decorations that occur in eukaryotic expression systems, like yeast and insect cells, show little resemblance to the glycans naturally found on nematode proteins. Towards a flexible and sustainable solution to this problem significant progress has been made in recent years on adapting the post-translational machinery of plants, such as *Nicotiana benthamiana*, allowing the synthesis of nematode- glycoproteins with a defined and tailored glycan composition. The aim of this project is to use this versatile plant-based production platform to express a set of well-defined nematode vaccine antigens and deliver proof-of-concept that efficacious vaccines can be produced if glycans are taken into account properly.