

Commercial production of recombinant monoclonal antibodies in alfalfa.

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Medicago Inc. is pioneering the development of new-generation of biopharmaceutical products designed to fight major human diseases. Medicago has developed a new proprietary platform for the production of this new generation of products, combining natural characteristics of alfalfa with advanced genetic engineering techniques. More specifically, Medicago has succeeded in coupling the high flexibility and capacity of conventional plant-based technologies with the benefits of safety and control offered by producing in confined hi-tech greenhouses. Recent scientific advances towards the commercial production of monoclonal antibodies (mAbs) will be presented to demonstrate the potential of alfalfa as a bio-factory for recombinant protein production.

MABs represent an opportunity for plant-based production which offers many advantages such as capital cost savings, ability to scale up or down, and freedom from human pathogens. Medicago has been actively working to adapt its proprietary technology platform to the large scale production of mAbs. These developments used an alfalfa-derived mAbs, C5-1, a diagnostic anti-human IgG developed for phenotyping and cross matching red blood cells from donors and receivers in blood bank. Optimized C5-1 Mabs expression cassettes were designed and assayed through our transient expression system allowing rapid and efficient selection of suitable regulatory elements for best C5-1 protein expression. Then, stable alfalfa transformation was performed followed by an array of purification and characterization experiments aiming to confirmed alfalfa-produced C5-1 mAbs conformity and homogeneity. Two major processes were examined. First, we investigated recombinant C5-1 N-glycosylation, a post-translational modification often required for therapeutic bio-activity and responsible for immunogenic reactions. Second, research efforts were also directed towards the development of improved purification protocols amenable to large scale production of recombinant mAbs using C5-1 as a model.

In light of the strict regulatory framework that is likely to be implemented for plant-made-pharmaceutical's production, Medicago has committed to produce its first products in confined hi-tech greenhouses. The large numbers of recombinant mAbs presently in development, the market demands and the specific requirements for production of these proteins are all favorable conditions for production in confined environment. To meet this demand, Medicago is currently building a 1300 m² greenhouse complex in the Quebec City area to house various activities including scale up production, primary extraction and recovery of alfalfa made pharmaceuticals. In addition, this facility will allow further optimization of alfalfa growth in confined environment in relation to light requirements, bioburden, and homogeneity of raw biomass.