BEYOND CHO – NON-MAMMALIAN HOSTS COULD BE THE FUTURE EXPRESSION SYSTEMS OF CHOICE FOR RECOMBINANT BIOTHERAPEUTICS

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Over the last 30 years there have been tremendous advances in CHO cell culture process engineering. Novel process concepts, such as fed batch, perfusion and continuous cultures, evolved from a deep understand of CHO metabolic needs and extensive media/feed formulation development. This knowledge has led to large gains in protein productivity that can be captured with culture duration and/or scale. The biotechnology industry is consistently pressured to reduce cost of manufacturing and improve per batch productivity. Independent, but related to this burden, is the ability to support an ever growing patient population with high doses of therapeutic protein. As such, Biogen partnered with MIT to take a holistic view of the potential future of biomanufacturing to identify technologies that can make step changes in productivity and cost reduction. These efforts have cast doubt that CHO would be the optimal host in the future, whereas a non-mammalian host could be a key to realizing the most significant gains in productivity and reduction in cost of manufacturing.

Recombinant antibody production from non-mammalian hosts has been reported in the past, for example from the yeast *pichia* and filamentous fungi *Trichoderma*, and antibody material produced from pichia has been used in clinical trials. In the next phase of this initiative, we sought to take a more comprehensive approach to investigate alternative hosts in recombinant antibody production. Eight non-mammalian hosts were selected based on a number of properties, including proven secretion of recombinant protein products, ability to glycosylate proteins, established genome or molecular biology toolkit, amongst other characteristics. We designed an experimental plan that would enable more straightforward comparative analysis between hosts and included two main criteria to maintain a level playing field. First, only non-engineered, wild-type strains would be used as a starting point for all eight hosts of interest. Second, a single IgG1 model antibody was selected to be expressed by all hosts. In this presentation, the outcome of this comparative analysis will be discussed, including productivity values and details of the model antibody product quality. Based on this data the most productive strains will be made available for use without restrictions to allow others in the community to freely work with these hosts.