New vaccines and therapeutic antibodies from yeast

This year has seen another leap in the power of yeast to meet major pharmaceutical needs. One was the topic of the closing address by Prof Ian Frazer at the ASM's Annual Scientific Meeting at the Gold Coast. That address discussed the major worldwide problem of human papilloma virus (HPV) infection, especially in young women. More importantly, he described the cure – prevention by vaccination with the major capsid protein (L1) of HPV types 6, 11, 16 and 18.

The capsid protein forms virus-like particles (VLPs) when produced in cells of the yeast *Saccharomyces cerevisiae*. Such products effectively immunise recipients, protecting them from HPV infection and associated cancers of the cervix. In many respects, it is like the yeast-derived Hepatitis B virus (HBV) vaccine, which is also derived from a surface antigen that forms VLPs in yeast.

Both vaccines arrived on the market at a considerable cost. However, within a short time, the costs of the HBV vaccine were cut by 99% when the WHO negotiated for the vaccine to be made available in developing countries where HBV is of high incidence and causes frequent liver cancers. The powers of the HPV vaccine, produced as Gardasil by Merck to alleviate the incidence of HPV and cervical cancer, are great, especially with the introduction of programmes to vaccinate girls as they turn 16 years of age.

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Another advance in our repertoire of compounds to treat cancers or other over-proliferative cells are therapeutic antibodies. Therapeutic antibodies are currently derived from mammalian cells in culture; however, there is considerable scope for improvement using yeast. Yeast offers the advantages of its safety and of the safety of the media in which it is grown. Yeast culture media can be heat sterilised and is totally defined. Thus the incidence of mammalian viruses and prions is nil.

However, the biggest gains are in the product itself. The private US biotech company GlycoFi spent a decade developing 'mammalian-type glycosylation' in yeast. In comparison with mammalian cells, yeast glycosylation is of the high mannose type and less complex, reducing the value of mammalian glycoproteins produced in yeast. GlycoFi re-engineered the yeast *Pichia pastoris* to produce a number of strains capable of directing specific glycosylation patterns.

GlycoFi scientists showed that a therapeutic antibody, Rituxan, produced by CHO cells, comprised a mixture of glycoforms and that specific glycoforms had a significantly higher therapeutic activity than the commercial product [1]. By producing specific glycoforms in yeast strains they were able to generate yeast-derived therapeutic antibodies with a specific activity (ADCC) roughly 100 fold higher than the commercial product.

The potential of this technology to revolutionise the growing market of therapeutic antibodies was realised by Merck which acquired GlycoFi for US$400m, in the largest acquisition of a private company in the history of the biotechnology industry.

These developments and others will be highlighted at in a public open day that forms part of the 23rd International Conference on Yeast Genetics and Molecular Biology [www.yeast2007.org].

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