AIST RESEARCH HOT LINE

## Abstracts (August - November 2001)

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## Life Science & Technology

## Production of Therapeutic Glycoprotein in Yeast for Lysosomal Disease

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In order to produce the more economic therapeutics for replacement therapy of Fabry disease, we introduced human  $\alpha$ -galactosidase  $(\alpha$ -GalA) gene into S. cerevisiae mutant that disrupted the outer chains, and expressed. The recombinant  $\alpha$ -GalA had both neutral and also acidic oligosaccharides. Because mannose-6phosphate (Man-6-P) residue is needed to incorporate the  $\alpha$ -GalA into the lysosome, we trimmed down the oligosaccharides of the enzyme by a new bacterial  $\alpha$ -mannosidase. The  $\alpha$ -GalA treated with the  $\alpha$ -mannosidase had Man-6-P residues on non-reduced end of oligosaccharide chains. Incorporated α-GalA was targeted to the lysosome and degraded ceramide trihexoside in the fibroblast of the Fabry cells.



Strategy for the production of  $\alpha$ -GalA with Man-6-P residues from yeast