

Title (en)  
MIXED FEED RECOMBINANT YEAST FERMENTATION

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Application  
**EP 89911170 A 19890925**

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• US 24944688 A 19880926  
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Abstract (en)  
[origin: WO9003431A1] The invention provides a method of increasing the production of a recombinant gene product from a culture of a recombinant methylotrophic yeast host, wherein said product is made by expression from a recombinant gene sequence operably associated with a methanol-responsive expression control element. In the method of the invention, the methylotrophic yeast host is first cultured on a medium with a high concentration of multi-carbon, carbon-source nutriment, such as glycerol, but with little or no methanol, in order to increase the density of the host cells with little or no expression of the recombinant gene product. When the host cells have achieved a suitable density in the culture medium, the culture is subjected to a phase during which the concentration of multi-carbon, carbon-source nutriment is maintained sufficiently low that the methanol-responsive control element controlling expression of the recombinant gene encoding the desired product is derepressed. Finally, the culture is subjected to a phase of high production of the recombinant gene product by increasing the concentration of methanol while maintaining the concentration of multi-carbon, carbon-source nutriment at a low level. The invention is illustrated with production, using *Pichia pastoris*, of bovine lysozyme c2, human lysozyme, human epidermal growth factors (1-52) and (1-48), and human superoxide dismutase.

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Citation (search report)  
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• [Y] EP 0226846 A1 19870701 - PHILLIPS PETROLEUM CO [US]  
• [Y] BIOLOGICAL ABSTRACTS DATABASE, Abstract no.26044335, Accession no 84044335; R.J.White et al : "Ruminant stomach lysozymes functional peculiarities amino-acid sequence and genomic cloning " & Federation Proceedings ,1983, vol 42, no 7, page 1253  
• [A] PASCAL DATABASE Abstract no 88 0425984, Accession no 88425086. J.M.Cregg et al : " Development of the methylotropic yeast, *Pichia Pastoris*, as a host system for the production of foreign proteins " & Dev. in industrial microbiology, 1988 vol 29,supp 3,pages 33-41  
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**WO 9003431 A1 19900405**; AU 4332589 A 19900418; DK 55191 A 19910524; DK 55191 D0 19910326; EP 0436625 A1 19910717; EP 0436625 A4 19910821; IL 91765 A0 19900610; JP H04501662 A 19920326

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