

# Heterologous expression and purification of G-protein coupled receptors

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Knowledge of the three dimensional structures of G-protein coupled receptors is an absolute requirement for the better understanding and development of “side-effect free” drugs. Most pharmacological receptors are expressed in native tissues at very low levels and therefore, overexpression of the receptor gene in a suitable host the method of choice to obtain enough protein for subsequent crystallization trials.

We chose methylotrophic yeast *Pichia pastoris* as a host system for the overexpression of G-protein coupled receptors and one example, the Histamine H1 receptor will be presented. This yeast provides an expression system which is easy to manipulate, gives stable transformants and grows to high cell densities in simple media, allowing inexpensive large-volume fermentation. A number of constructs of the H1 receptor with different affinity tags for purification purposes were made and successfully overexpressed using the strong promoter of the alcohol oxidase I (AOXI) gene of *P. pastoris*. The receptors were subsequently solubilized and further studies are underway.