

The Dimorphic Yeast *Yarrowia lipolytica*: Its Application to Biotechnology

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Yeasts have been exploited to secrete a variety of biologically active proteins. However, the secretion levels ranged from tens of micrograms to over a gram per liter of culture broth depending on the kinds of proteins and host organisms. That is, the amount and the quality of the expressed heterologous proteins suffered from organism-specific limitations. Despite the similarities in protein secretion mechanisms among different organisms, certain parts of the secretory pathways seem to be quite species-specific. Therefore, extensive development is required to attain high secretion levels of important heterologous proteins in a specific organism.

Yarrowia lipolytica, a heterothallic yeast, is currently considered a good potential host for heterologous gene expression due to its ability to secrete large amounts of extracellular proteins and the easy cultivation to a high cell density. In addition, *Y. lipolytica* may be also useful for bioconversion of hydrophobic substrates because of its ability to degrade hydrophobic compounds, such as alkanes, fatty acids, and oils. Therefore, *Y. lipolytica* is a highly attractive yeast in the field of biotechnology.

Tissue inhibitors of metalloproteinases (TIMP-2), one of the four identified proteins in TIMP family, is able to bind to pro- and active form of MMP-2. Since TIMP-2 inhibits all the activated forms of MMPs, TIMP-2 acts as a key inhibitor molecule in angiogenesis and cancer metastasis. However, despite the potential of TIMP-2 as a therapeutic agent for angiogenesis-related diseases, there have been no reports concerning the overexpression of recombinant human TIMP-2.

Urokinase-type plasminogen activator (u-PA) is a serine protease which activates plasminogen to plasmin and causes fibrinolysis. Human u-PA is initially synthesized as a single-chain u-PA (scu-PA, pro-urokinase) that is a glycoprotein containing 12 disulfide bonds and the scu-PA is cleaved by plasmin to two-chain u-PA (high molecular weight or

low molecular weight tcu-PA) in which two chains are held together by one disulfide bond. Both scu-PA and tcu-PA can be used in thrombolytic therapy in patients with acute myocardial infarction.

The expression and secretion of the two human proteins, TIMP-2 and u-PA, in *Y. lipolytica* will be presented in this talk.

참고문헌

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