A0301

Expression and Functional Characterization of Recombinant Human Erythropoietin (rhEPO) Produced in the Milk of Transgenic Mice

권득남, 박종이, 이소영, 황규찬, 양민정, 김진희

경상대학교 낙농학과

The milk of transgenic animals may provide an attractive vehicle for large-scale production of hEPO. Since glycosylation is cell type specific, recombinant human EPO (rhEPO) produced in different host cells contain different patterns of oligosaccharides, which could affect the biological functions. However, there have been no reports on the characteristics of rhEPO derived from milk of transgenic animals. To address this objective, several transgenic mice by using pWAPhEPO and/or pBC1hEPO expression vector were produced. However, 2 lines of pWAPhEPO founder female mouse died during late gestational day (day 18) before offspring could be obtained. They showed a severe splenomegaly. Unlike those of pWAPhEPO, mammary gland epithelial cells from biopsies of lactating pBC1hEPO transgenic mice had marked immunoreactivity to EPO and any activity was not detected in other tissues. The expression level of rhEPO is about 0.7% of mammary gland cellular total soluble proteins and an amount of 300~500 mg/L rhEPO is secreted into milk. Furthermore, the pBC1hEPO transgenic mice transmitted this character to their progeny in mendelian manner. In order to determine the extent of glycosylation variation, N-linked oligosaccharide structures present in the milk-derived rhEPO were characterized. Most of milk-derived rhEPO is fully glycosylated. the biological activity of milk-derived rhEPO was comparable to that of purified CHO-derived rhEPO, and milk-derived rhEPO showed relatively stable after freezing and thawing. Taken together, the results illustrate the potential of transgenic animals in the large-scale production of biopharmaceuticals.

Key words) ***Recombinant Human Erythropoietin(rhEPO), Transgenic Mice, Mammary gland***