Development of the production process of recombinant human factor IX in Chinese hamster ovary (CHO) cells

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The human coagulation factor IX (FIX), vitamin K-dependent serine protease, has been used for the replacement therapy either as a plasme-derived or a recombinant protein for hemophilia B, a bleeding disorder caused by a congenital deficiency. However, the expression of recombinant FIX (rhFIX) in CHO cells has been complicated due to the several post-translational modifications that is required for its biological activity, resulting in the presence of abnormally processed inactive forms[1]. In order to produce the active rhFIX, we developed a number of recombinant CHO-rhFIX cells expressing rhFIX using the proprietary expression vector and host cell modifications. After they were adapted in gene amplification system, we were able to establish the CHO-rFIX cell lines. The high producer cell lines have adapted in suspension culture using serum-free media. The production of rhFIX was maximized by controlling the cultivation conditions including the culture temperature and osmotic pressure in the biphasic culture. Interistingly, the portion of active rhFIX was dependent on the cell lines. The purified rhFIX showed the comparable physiochemical properties with specific activity over 200 IU/mg. In conclusion, we are investigating the scale -up process for the rhFIX in CHO cells in order to develope into clinical applications.

Reference

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