Development of Recombinant Human Interferon-β-1a Analogs using Serum Free Suspension Culture of CHO Cell

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Abstract

Recombinant human interferon-β-1a(rIFN-β) is a single glycosylated protein (at N80, 1N) with anti-viral activity. However, present drugs have a relatively short serum half-life of rIFN-β, thus patients suffer from frequent injections.[1] To improve its half-life, eight glycosylation analogs were prepared, which have additional N-linked glycosylation consensus sequences (N-X-T/S) within the IFN-β molecule and/or at C-terminal. Each rIFN-β analog was examined for the presence of additional N-linked glycosylation and the maintenance of anti-viral activity in CHO cells. The molecular weights of five analogs were not changed. However, two analogs, R27T within rIFN-β (27 kDa, 2N) and GNITVNITV at C-terminal (29 kDa, 2N), showed a clear increase in molecular weights, compared to native rIFN-β (23 kDa, 1N). And another combined analog of R27T+GNITVNITV showed increased molecular weight (33 kDa, 3N). It was confirmed that the molecular weight increment of analogs was caused by the N-linked glycosylation with the treatment of N-glycanase. In the case of anti-viral activity, the analog GNITVNITV showed a reduction in activity compared to native IFN-β, whereas the analogs R27T and R27T+GNITVNITV were found to have distinctly increased activities. Pharmacokinetic study in rats also disclosed that the analogs R27T and R27T+GNITVNITV had 2 3 fold increased serum half-life, respectively. In conclusion, the addition of N-linked glycosylation in rIFN-β increased serum half-life, thereby its less frequent administration will be expected.

Reference

1. Jone J. Alam, Interferon-β treatment of human disease(1995), Current opinion in Biotechnology, 6, 688-691.