

烟草细胞中高效表达提高血清半衰期的药用蛋白

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摘要: 小分子治疗蛋白, 如干扰素 $\alpha 2b$ (IFN $\alpha 2$)和人生长激素(hGH), 由于其对血清蛋白酶的易感性及分子小, 可被肾迅速清除, 因而一般在血清中的半衰期都很短。化学衍生处理虽可以克服这些问题, 但却要以降低蛋白的生物活性为代价。本研究建立了一种新方法, 使干扰素 $\alpha 2b$ (IFN $\alpha 2$)和人类生长激素(hGH)在烟草细胞中高效表达为阿拉伯半乳糖聚糖糖蛋白嵌合体(AGP)。这样不仅提高了药用蛋白的产量, 而且提高了其血清半衰期。这种嵌合糖蛋白的分泌量比没有糖基化时高 500~1800 倍。重要的是, 与未糖基化的干扰素和人生长激素相比, 这种嵌合糖蛋白的体内血清半衰期提高 13 倍, 生物活性仍保持与未糖基化时相似。这种嵌合糖蛋白注射到小鼠体内未引起免疫性反应。

关键词: 植物细胞培养, 重组蛋白, 糖基化羟脯氨酸, 半衰期

High-yield Expression of Therapeutic Proteins with Extended Serum Half-life in Tobacco Cells

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Abstract: Small therapeutic proteins such as interferon $\alpha 2b$ (IFN $\alpha 2$) and human growth hormone (hGH) generally possess short serum half-lives due to their susceptibility to serum proteases and small size, hence rapid renal clearance. Chemical derivatization overcomes these problems but at the expense of decreased bioactivity. We developed a new method that yields biologically IFN $\alpha 2$ and hGH in high yields and with increased serum half-lives when expressed as arabinogalactan-protein (AGP) chimeras in cultured tobacco cells. The chimeric glycoproteins typically gave 500–1800 fold greater secreted yields than their non-glycosylated controls. Importantly, the chimeric glycoproteins showed an increased in vivo serum half-life of up to 13 fold while their biological activities remain similar to native IFN $\alpha 2$ and hGH. The AGP domain was not immunogenic when injected into mice.

Keywords: plant cell culture, recombinant protein, hydroxyproline-O-glycosylation, half-life

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The full-text article is available online at www.sciencedirect.com



Received: October 17, 2008; **Accepted:** November 25, 2008

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