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Factors Affecting the Sialylation of Fc-Fusion Protein in Recombinant CHO Cell Culture

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Over the past decade, product titers from recombinant CHO cells have increased significantly. However, not only the product titer but also the product quality is important for therapeutic efficacy. When sodium butyrate (NaBu) was added to a culture of CHO cells producing Fc-fusion protein, it increased Fc-fusion protein titer, but it decreased sialylation of the Fc-fusion protein. Analysis of N-glycosylation-related genes revealed that altered expression patterns in st3gal3, neu 1, and neu3, which have roles in the sialic acid biosynthesis pathway, correlated with reduced sialic acid content of the Fc-fusion protein by NaBu. St3gal3, sialic transferase, was down-regulated and, nue1 and nue3, sialidases, were up-regulated by NaBu. Addition of LiCl decreased sialylation of Fc-fusion protein as well. However, unlike NaBu, LiCl did not affect the sialidase expression. Stressful culture conditions such as high ammonia concentration and hyperosmolality, which are encountered during the culture, also decreased the sialylation of Fc-fusion protein. In the case of ammonia, ammonia was found to increase the neu 1 and neu3 mRNA expression levels. Down-regulation of sialidases successfully increased the sialylation of Fc-fusion protein in the presence of ammonia. Interestingly, unlike ammonia treatment, hyperosmolality did not increase the sialidase mRNA expression level. Hyperosmolality appeared to increase the lysosomal exocytosis of sialidase 1 located in the lysosomes. Taken together, a number of factors can be seen to affect the sialyation of Fc-fusion protein in rCHO cell cultures, but through different mechanisms.