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研究报告

利用还原剂预处理提高药物蛋白稳定性

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摘　要: 开发蛋白药的一个主要问题是蛋白质的不稳定性。本研究利用对蛋白质进行还原剂预处理的策略，提高了具有潜在治疗活性的重组人胞外域 CD83 蛋白的稳定性。在生理条件下，蛋白治疗产品易于变性，形成聚集和沉淀，并最终被降解。由此证明还原剂预处理可以有效改善蛋白质的稳定性。

关键词: 降解，蛋白稳定性，人胞外域的 CD83 蛋白，还原剂预处理

Stability Improvement of a Therapeutic Protein by Reducing Agent Pretreatment

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Abstract: A major concern in developing protein-based biopharmaceuticals is protein instability. A strategy with the use of reducing agent pretreatment to improve protein stability was developed for recombinant hCD83ext (i.e. the extracellular domain of human CD83) with a potential therapeutic activity. Under physiological conditions, the therapeutic product tended to denature, form aggregates and precipitates, and eventually degrade. The reducing agent pretreatment was demonstrated to be effective in improving the protein stability.

Keywords: degradation, protein stability, hCD83ext, reducing agent pretreatment

REFERENCES

[1] Cleland JL, Powell MF, Shire SJ. The development of stable protein formulations-a close look at protein aggregation, deamidation and oxidation. *Crit Rev Ther Drug Carrier Syst*, 1993, **10**: 307–377.

[2] Krishnamurthy R, Manning MC. The stability factor: importance in formulation development. *Curr Pharm Biotechnol*, 2002, **3**: 361–371.

[3] Lechmann M, Kotzor N, Zinser E, *et al*. CD83 is a dimer: Comparative analysis of monomeric and dimeric isoforms. *Biochem Biophys Res Commun*, 2005, **329**: 132–139.

[4] Lechmann M, Kremmer E, Sticht H. Overexpression, purification, and biochemical characterization of the extracellular human CD83 domain and generation of monoclonal antibodies. *Protein Expr Purif*, 2002, **24**: 445–452.

[5] Manning MC, Patel K, Borchardt RT. Stability of protein pharmaceuticals. *Pharm Res*, 1989, **6**: 903–918.

[6] Pace CN, Grimsley GR, Thomson JA, *et al*. Conformational stability and activity of ribonuclease-T1 with zero, one, and 2 intact disulfide bonds. *J Biol Chem*, 1988, **263**: 11820–11825.

[7] Parkins DA, Lashmar UT. The formulation of biopharmaceutical products. *Pharmaceut Sci Tech.Today*, 2000, **3**: 129–137.

[8] Patro SY, Freund E. Protein formulation and fill-finish operations. *Biotechnol Ann Rev*, 2002, **8**: 55–84.

[9] Pearlman R, Wang YJ. Formulation, Charcterization, and Stability of Protein Drugs. New York: Plenum Press, 1996.

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[10] Schmidt FR. Recombinant expression systems in the pharmaceutical industry. *Appl Microbiol Biotechnol*, 2004, **65**: 363–372.
[11] Schultz. Cleavage at aspartic acid//W HCH, editor. Methods Enzymol. New York: Academic Press, 1967, 225–263.
[12] Sikorskaya SV, Ignatenko AV, Cherenkevich SN. Certain relationships of formation of the products of ozonization of tryptophan. *J Appl Chem USSR*, 1984, **57**: 1910–1914.
[13] Sreerama N, Woody RW. Circular dichroism of peptides and proteins//Berova N, Nakanishi K, Woody RW, editors. Circular dichroism: principles and applications. 2nd ed. New York: John wiley & Sons, Inc., 2000, 601–620.
[14] Walsh G. Biopharmaceutical benchmarks 2006. *Nat Biotechnol*, 2006, **24**: 769–776.
[15] Zinser E, Lechmann M, Golka A, *et al*. Prevention and treatment of experimental autoimmune encephalomyelitis by soluble CD83. *J Exp Med*, 2004, **200**: 345–351.