

- Higher eukaryotes like mammalian cells or insect or plant cells provide much lower yields and are harder to manage. Mammalian cells such as ovarian cells of CHO are commonly used to produce complex glycoproteins.
- Plant and transgenic animals produce therapeutic proteins in a tissue (in the case of plants) or in a fluid (most often milk for transgenic animals) in large quantities that are highly practical sources of future biological products.

Given that living entities are involved in the expression of proteins, it is easy to see how a change in bioprocessing conditions can readily alter the structure of proteins. Harder to manage are the variance in the glycan patterns, the antibody-dependent cell-mediated cytotoxicity, and other similar variations that might not necessarily be clinically meaningful, yet to prove it otherwise may be impossible, resulting in a biosimilar product developer modifying the bioprocessing to assure that the structure of protein expressed is as close as possible to the originator molecule.

### Bibliography

- Anderson, C. L. (2012 June) Applications of imaged capillary isoelectric focussing technique in development of biopharmaceutical glycoprotein-based products. *Electrophoresis* 33 (11): 1538–1544.
- Bártová, E., Krejčí, J., Harnicarová, A., Galiová, G., and Kozubek, S. (2008) Histone modifications and nuclear architecture: A review. *J Histochem Cytochem* 56 (8): 711–721.
- Beck, A., Sanglier-Cianférani, S., and Van Dorsselaer, A. (2012 June 5) Biosimilar, biobetter, and next generation antibody characterization by mass spectrometry. *Anal Chem* 84 (11): 4637–4646.
- Beck, A., Wurch, T., and Reichert, J. M. (2011 March–April 3) Sixth annual european antibody congress 2010: November 29–December 1, 2010, Geneva, Switzerland. *MAbs* 3 (2): 111–132.
- Boubeva, R., Reichert, C., Handrick, R., Müller, C., Hannemann, J., and Borcharda, G. (2012) New expression method and characterization of recombinant human granulocyte colonystimulating factor in a stable protein formulation. *Chimia (Aarau)* 66 (5): 281–285.
- Brennan, D. F. and Barford, D. (2009) Eliminylation: A post-translational modification catalyzed by phosphothreonine lyases. *Trends Biochem Sci* 34 (3): 108–114.
- Cantor, C. R. and Schimmel, P. R., *Biophysical Chemistry Part 1: The Conformation of Biological Macromolecules*. New York: W. H. Freeman and Co.; 1980.
- Cao, J., Sun, W., Gong, F., and Liu, W. (2014 May) Charge profiling and stability testing of biosimilar by capillary isoelectric focusing. *Electrophoresis* 35 (10): 1461–1468.
- Chen, S. L., Wu, S. L., Huang, L. J., Huang, J. B., and Chen, S. H. (2013 June) A global comparability approach for biosimilar monoclonal antibodies using LC-tandem MS based proteomics. *J Pharm Biomed Anal* 80: 126–135.
- Creighton, T. E., *Protein Structures and Molecular Properties*. Second ed., New York: W. H. Freeman and Co.; 1993.
- Creighton, T. E., *The Biophysical Chemistry of Nucleic Acids and Proteins*. London: Helvetian Press; 2010.