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Cancer immunotherapy and vaccines using glycosylation as a barcode to produce better and safer antibodies

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The number of anti-cancer antibody candidates is increasing as humanized, engineered and bispecific formats to develop drugs that will act more efficiently at a lower dose. Lessons learn from the past are not sufficient to address new challenges for producing such difficult-to-express proteins. Productivity remains the key driver for process intensification, but product quality is most than often drastically altered because cell factories poorly adapt to high density culture, sustain cell growth and high titer production. Also, from lead identification to full scale bioproduction, regulators are now requesting deeper knowledge about the process and products.

So far, cancer immunotherapy has essentially focused on ADCC and CDC activities which can be increased by modifying antibody glycosylation in core fucose and galactose content respectively. Most antibodies are expressed in CHO cells which generally add excessive fucose and low galactose during bioprocesses, resulting in reduced biopotency. Accordingly, various strategies have been used including inhibitors or fucose -/- cells, but these cell lines do not perform as the parental cell lines in high density bioreactors. Galactose addition is low because of a metabolic bottleneck which blocks the completion of glycans during bioproduction. Optimal glycoengineering is therefore needed to get the most efficient products.

Glycosylation reflects the coordinated action of more than a hundred of synthetic enzymes on both the product and host cell proteins. Using glycosylation as a bar code for product quality can thus facilitate the overall production workflow for new candidates. At SiaMed'Xpress, we have developed a dedicated glycomonitoring to maximize product glycoprofile during early stage development. We could maximize the desired antibody glycoprofile during product development based on innovative glycotests: in our presentation, we will show that during cell line and product development, the fucose content of the antibody product can be substantially reduced and galactose largely increased. Glycomonitoring therefore provides a creative approach to maximize process consistency, make decision with confidence and without delay. It is fully complementary to current strategies in the cancer field and further aims at accelerating development timelines.

Biography

Catherine Ronin carried out a full academic career as Professor at Aix-Marseille University (France) and founded SiaMed'Xpress in 2010. She has published more than 35 papers related to TSH biological and immunological polymorphism in reputed journals and has been serving as expert, Vice Chair and Chair in Marie Curie ITN and JDP programs at the European, Research Agency over 12 years.