CAMBRIDGE HEALTHTECH INSTITUTE'S
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Inducible GPCR Cell Lines for Antibody Characterization

Eric Grazzini, Ph.D., Team Leader Rapid Protein Production, Senior Research Officer, Biologics, National Research Council of Canada, Canada

Cambridge Healthtech Institute's recently spoke with Eric Grazzini, Team Leader for the Rapid Protein Production group at National Research Council of Canada, about his upcoming presentation **"Inducible GPCR Cell Lines for Antibody Characterization"**, at the **Antibodies Against Membrane Protein Targets - Part 1** conference to be held **September 20-21, 2016**, as part of the **14th Annual Discovery on Target event in Boston.**

SPEAKER Q&A

Q: Can you describe the NRC CHO-BRI expression platform?

Experts at the National Research Council have engineered a proprietary cumate-inducible CHOBRI cell line for stable and transient gene expression. The cumate switch enables us to regulate the expression of target genes on demand. Using this system, we can generate stable CHO pools expressing high levels of target genes within 2-3 weeks post-transfection. The platform has also been widely used to generate stable clones.

Q: How does this platform behave in relation to comparable platforms?

This is the only platform on the market today where you can induce expression using the cumate gene switch - which makes it unique and offers the possibility of higher specific productivity. It's amenable to GMP manufacturing and is affordable.

Q: What are some applications of your expression platform?

Our expression platform has been successfully used to produce every protein you can think of: GPCRs, tyrosine kinase receptors catalytic domain, ion channels, FcRn, FcγR, mAbs, Fabs, bi-specific mAbs, enzymes, growth factors, receptors ectodomains, proteases…It's also being used to generate cell lines that express receptors for HTS applications, and can be used to generate proteins for crystallization studies.

Q: What is the major advantage for users, and what does it enable it them to do?

The speed of the pool and clone generation process, the low cost of the platform, and the product quality we are able to achieve are its major advantages. In addition, because the expression of target genes can be regulated, it's ideal for expression of difficult or toxic proteins.

Q: How is the platform used for drug discovery?

It's ideal for the transient production of small lots of several different variants, when a company is looking to screen a variety of potential candidates in a high throughput manner. Once a lead candidate has been locked in, it can also be used to generate a custom cell line based on the stable clone that best expresses that candidate.

Q: What is the greatest challenge in expressing GPCR or ion channels?

Overexpression of these signaling membrane proteins is often toxic to the cells. Being able to regulate their expression greatly facilitates the generation of stable cell lines. The ability to modulate GPCR expression levels also offers unique opportunities for studying their pharmacology when expressed at low, medium and high levels in cell plasma membranes.

Q: What are the next steps in the project – what else to you hope to achieve?

We are currently working to reduce the time it takes to generate stable cell lines, and we are aiming to improve upstream processes to increase volumetric productivity, particularly for mAbs.

Speaker Biography:

Eric Grazzini, Ph.D., *Team Leader Rapid Protein Production, Senior Research Officer, Biologics, National Research Council of Canada, Canada*

In 1996 I obtained my Ph.D in Biochemistry, Molecular Biology and Pharmacology studying the role of G protein-coupled receptors in steroids release from human and rat adrenal gland. After a post-doctoral fellowship at the Royal Victoria Hospital McGill University I served for 16 years within major pharma as a pharmacology project leader and manager. I have extensive experience in biologics and small molecules assay development and mechanistic analysis. I have particular expertise in the biology of GPCRs, ion channels, and transporters. In 2003 I received the AstraZeneca R&D Global Scientific and Technical Achievement Award for the deorphanisation of 6 orphan GPCRs that produced four new projects in two different therapeutic areas. I have authored or co-authored >25 publications appearing in Nature, Nature Neuroscience, Nature Cell Biology, and PNAS. In 2014 I joined the NRC as Senior Research Officer and have been appointed team leader of the Rapid Protein Production team. My mission at NRC is to manage staff and research and development projects related to preclinical recombinant protein production as well as collaboration with internal and external partners.