RECOMBINANT PROTEIN PRODUCTION

CIARÁN N. CRONIN, Associate Research Fellow, Head Parallel Protein Production Group, & Group Leader Gene-to-Structure, **Pfizer**

Dr Ciarán N. Cronin is Associate Research Fellow at Pfizer's La Jolla campus in San Diego, California, and heads the Parallel Protein Production Group (PPPG). The PPPG Group is part of Pfizer's Global Chemistry line and is responsible for protein expression construct screening and scale-up for all fit-for-purpose protein reagents required to support Pfizer's small molecule oncology drug discovery pipeline. The Group also has responsibilities for gene-to-structure efforts on a number of in-house structure-based drug design (SBDD) projects. Dr Cronin joined Pfizer in 2004 from Syrrx Inc., where he was Associate Director of Molecular Biology and Protein Chemistry. Prior to Syrrx, Dr Cronin was an Assistant Research Biochemist at the University of California San Francisco (1995-2001) and held Senior Scientist positions with Bioresearch Ireland (1992-1994), Biotrin Research, Ireland (1990-1992), and Qlone Ltd., Australia (1988-1989). Dr Cronin received both his Ph.D. and his primary honors degree in Biochemistry from Trinity College, Dublin, Ireland.

Prior to the 13th Annual Proteins & Antibodies Congress, we interviewed one of our highly distinguished speakers, Ciarán N. Cronin from Pfizer on the interesting work he is undertaking.

What is your role at Pfizer?

I have been with Pfizer for over 15 years and am currently an Associate Research Fellow in the Department of Structural Biology and Protein Sciences, within the Division of Cancer Medicinal Sciences, at the La Jolla Laboratories in San Diego, California. I oversee the Parallel Protein Production Group which is responsible for all protein expression microscreening and scale-up in Escherichia coli, baculovirus-infected insect cells (BEVS) and mammalian cells in support of the oncology small molecule drug discovery pipeline. My group also has responsibility for gene-to-structure efforts on a number of oncology drug discovery targets, and for fit-for-purpose protein reagent fulfillment for assay and HTS screening.

Briefly describe what work you have done in recombinant protein production/protein expression/difficult-to-express proteins and what your team is involved in.

I received my primary degree in biochemistry in 1979 and my PhD in protein biochemistry and enzymology in 1983, both from Trinity Collge Dublin, Ireland. I got involved in recombinant DNA technology during a post-doctoral position at UC Berkeley in 1986, and subsequently worked in the area of recombinant protein production in Escherichia coli in a couple of start-up companies in Australia and Ireland. In 1993 I first used the baculovirus expression vector system (BEVS) to produce active activin,and have used the BEVS system for over 25 years as the preferred recombinant protein production platform. The BEVS system is the work horse for protein production in support of structure-based oncology drug design at Pfizer and over the years has evolved into a highly efficient and successful platform, not just for SBDD, but also for generating fit-for-purpose protein reagents for assay and HTS. Part of that platform includes an in-house designed browser-accessible SQL database for tracking all facets of our protein production pipeline, from construct creation through micro-expression screening, scale-up and protein purification and analysis. Protein production in Escherichia coli and transient transfection of HEK293 cells are our two lesser platforms for recombinant protein production.

What are some of your recent exciting findings?

Recently we have become more involved in producing historically difficult protein targets and multiprotein complexes as drug discovery has moved towards prosecuting more challenging oncology drug targets. Towards this end we have been engineering BEVS transfer vectors for the production of multiple ORFs within a single virus. We have also produced active human aldehyde oxidase (AOX) in BEVS, a notoriously challenging enzyme to produce in recombinant form and a requisite enzyme activity to consider in the drug discovery process, and have deployed the enzyme in our AOX exposure screen for new chemical entities. In our protein production platform, we have completely eliminated cellbag technology from our BEVS scale-up process in preference for a lower cost, greater flexibility high-volume (5L) shake flask expression platform (see Cronin CN [2020] Protein Expression & Purification 165 in press, available online).

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