Interview: Dr. Niall Barron â?? Director, National Institute for Cellular Biotechnology (NICB), Ireland

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Niall Barron, director of the NICB, discusses the Instituteâ??s research, which has included significant research into Chinese Hamster Ovary (CHO) cell engineering and the identification of micro-RNA mechanisms that can triple protein yields in some limited cases.

Could you please introduce the NICB to our global readers and the Instituteâ??s key research foci?

I am the current director of the National Institute for Cellular Biotechnology (NICB). We are an educational institute with different research foci related to biotechnology and biopharmaceuticals. NICB employs postdoctoral scientists and trains PhD students and other postgraduates, but we also accommodate undergraduates, physicians, and even high-school level students at times.

Our research mandate is essentially to look at the biotechnology of cell systems from the perspective of a variety of applications. This can range from looking at the different mechanisms that affect a cellâ??s performance as a biopharmaceutical expression platform, to examining how cells themselves can perform as therapies, or even how different physiological events occur within cells â?? specifically within tumor cells in our case.

Could you expand a bit on the projects the NICB is pursuing in each of these areas?

The first and biggest focus I have mentioned is our research into how to manipulate or optimize cell-lines, for example Chinese Hamster Ovary (CHO) cells, which are used for the production of protein-based bio-therapeutics. To do so, we monitor the way those cells behave in culture to identify the mechanisms that we can use to manipulate their behavior in terms of speed and quantity, as well as quality and consistency of protein folding and glycosylation patterns. This research has the potential to be extremely impactful on society and industry, as at present the cost of production of biopharmaceutics is very high, making them nearly unattainable for patients and healthcare systems in many countries. If we can improve the yields and efficiency of cells by a significant margin, then the cost savings should be considerable.

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We also have some very interesting projects looking at cellular therapies. In fact, the NICB was recently featured in the news due to our role in enabling the first corneal limbal stem cell transplantation in Ireland earlier this summer. Essentially, this therapy was conducted by collecting healthy limbal cells from a donor, cultivating them in-vitro until they have grown to a sufficient extent and then transplanting them into the patient to replace their damaged or diseased corneas. We are very proud to be involved in this story as the NICB, in conjunction with the Royal Victoria Eye and Ear Hospital and the Irish Blood Transfusion Service, played a key role in developing the processes which made this therapy available to Irish patients.

Our third research focus is in the area of diabetes. Under this heading we have a number of projects to identify biomarkers that better predict the onset and progression of diabetes, the mechanisms underlying the onset and development of diabetes type II, and very excitingly Islet cell transplantation for type I patients. With this project around Islet cell transplantation we have the ultimate goal to develop a bio-artificial pancreas.

Finally, we are also working on basic cancer research. Our main project in this area is in seeking to better understand drug resistance in oncology, looking at the mechanisms behind tumors developing resistance to certain drugs and biologic-therapies. However, we also are working in collaboration with Irish physicians, hospitals, and the Irish Clinical Trials Organization to use the molecular analytical techniques at our disposal to better design treatments for individual patients based on their individual characteristics.

Regarding your own research area, CHO cell engineering, we understand the NICB seeks to â??combine state-of-the art technologies in molecular biology, proteomics and bioinformatics to develop improved cell-lines in terms of growth and productivity.â?• How would you assess your progress towards this end?

Globally, only about a dozen laboratories have as strong of a focus on CHO cell engineering as we do here at NICB, and we could probably be counted among the upper half of those twelve in terms of the excellence and impact of our research. Typically, a research project in this area begins with taking a particular cell line, often from one of our industry collaborators, that features a particular good or bad trait or phenotype, and then comparing that cell line from a genetic point of view with other cell lines. In this way, we are able to identify some of the genes that may drive this particular behavior, and then we use several technologies to manipulate the expression of these genes to learn more about how they are related to the phenotypes in question.

In addition, our group is particularly focused on understanding micro-RNAs. These are small regulatory RNA molecules that impact the expressions of other genes. They act as modulators or shock absorbers within cells, and play an important role in controlling the degree to which cells respond to changes in their environment. We have published several papers based on our research on how CHO cells can be impacted by these micro-RNAs.

To what degree have you been able to increase the CHO cell lineâ??s expression of individual proteins in your research?

We have been able to identify several mechanisms related to cell growth and division, as well as the factors that identify the cells that are producing more of the proteins in question. By silencing particular micro-RNAs that we have identified as inhibiting protein production, we have seen protein yields increase by up to a multiple of three in the best cases. However, we have observed that these interventions tend to be cell line specific as weâ??ve carried out these procedures on several cell lines with a wide range of results. Currently we are working to discover why suppressing certain

micro-RNAs increases yields more in some cells than others, how the different genes involved interact, etc.

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A main feature of several research organizations in Ireland, like NIBRT and the NICB, is that your agendas are well aligned with the needs of industry. How would you describe the NICBâ??s relationship with the biopharma industry, particularly in terms of funding?

We engage with industry in a variety of ways, first as a supplier of well-trained students with advanced degrees. It is our goal to ensure that there is a good supply of PhDs and post-docs available to the pharmaceutical industry in Ireland and abroad, and help them gain a strong degree of experience dealing with biopharmaceutical topics before leaving the NICB for industry.

Second, we act as a research partner for the industry who has the time and resources to pursue topics of interest that may not be high enough priority for the companies to pursue on their own time; we provide the extra hands needed to improve and optimize certain processes and products. We also collaborate within some larger collaborative research projects led by the Synthesis and Solid State Pharmaceutical Center (SSPC), which is a major academic-private sector collaborative research group receiving major funding from both Science Foundation Ireland and a variety of major pharmaceutical companies.

How does the NICBâ??s Briclone product fit into this picture?

Briclone is a product that has been around for several years; this is a conditioned media weâ??ve developed for cloning hybridoma cells. We developed the process for making it for our own research, but have sold it at a commercially sustainable price for several years to other research institutions. Today itâ??s not a major source of income, but the profits do provide a nice safety net to support some of our studentâ??s research projects. Weâ??re actually currently exploring some ways to increase our sales going forward, as well as perhaps selling some other products along similar lines.

What sets the NICB apart as a world-class biotech research institution?

NICB is a very competitive institution publishing excellent and impactful research regularly, and moreover we are directly engaged with industry to work towards seeing our findings implemented. One of our key strengths is confidentiality and respect for IP â?? we work with several pharmaceutical companies simultaneously on sensitive products, and they would not agree to work with us in this manner if we hadnâ??t demonstrated that we have sufficient protocols, procedures and training in place to ensure confidentiality.

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