

Assessing the production of diagnostic proteins in plant cell cultures

Jose Gutierrez-Marcos from the University of Warwick was awarded Business Interaction Voucher funding from BioProNET to work with Mologic. Their project investigated ways to improve the production in plant cells of human chorionic gonadotropin (hCG)— a protein that could be used in cancer diagnostics.

The challenge – Plant cell cultures have several advantages over other protein expression systems; they are cost-effective, lack toxicity and are amenable to genetic modification. However, the lack of a cost-effective manufacturing process has hampered the use of plant cells to manufacture high-value proteins. In particular, cysteine knot proteins, including hCG, are difficult to produce as recombinant proteins in cultures.

The project – Low levels of protein production, purification and quality are major factors that limit protein production in plant cell cultures. We have assessed the impact that culture media has on the production, purification and quality of recombinant hCG, a protein that has potential use in cancer diagnostics.

Key findings – Expression of hCG in Nicotiana tobacco cell lines was highly dependent on media composition (that is, amounts of salts, vitamins and sugars).

By varying the concentrations of these media components, we identified optimal culture conditions for the expression of hCG. We also developed a system to simplify hCG purification that reduces protein aggregation and facilitates rapid protein enrichment. Finally, we determined the quality of the hCG product and found that around 85-90% of purified protein was correctly folded.

The collaboration – The project has provided Jose with a new insight into recombinant protein production using plant cell cultures and in their application in point-of-care diagnostic devices. It has also confirmed that plant cells can fold complex, difficult cysteine-knot proteins more efficiently than most other host cells can. As a result of this project, we have initiated a new collaboration with Mologic's "Centre for Advanced Rapid Diagnostics" to improve the expression of other recombinant proteins known to be challenging in other expression systems.

Outcomes and next steps

- A new collaboration has been initiated to improve the expression of seven additional proteins
- Data from the project will be used in a publication

"The purified hCG protein will be used to test Mologic's proprietary point-of-care and other diagnostic devices, as well as potentially being used as a kit reference standard"