'Daedalus' Platform Introduces Major Advances in Recombinant Protein Production from Human Cell Lines

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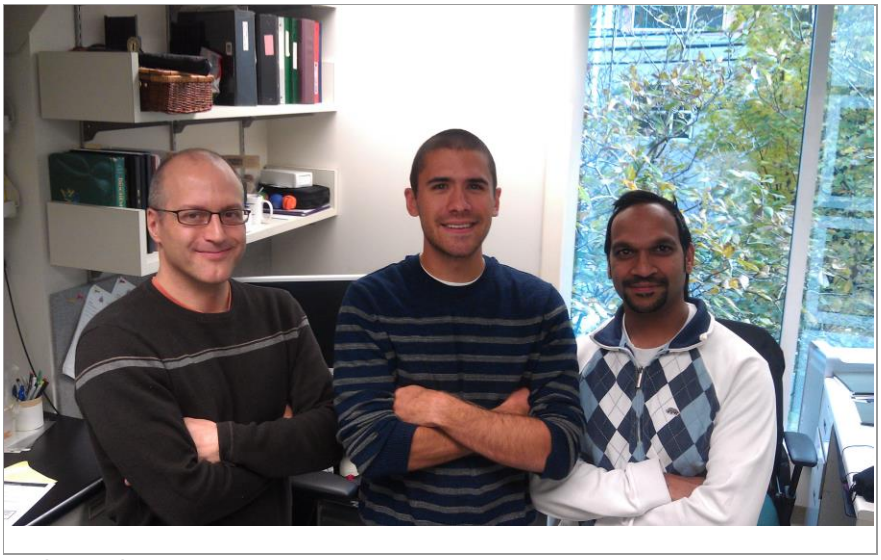
To ensure proper protein folding and post-translational modifications that are important for biological activity, recombinant human proteins should be expressed in human cell lines. However, this approach frequently suffers from low yields, costly transfection reagents and/or time-consuming techniques (e.g., the selection of optimal expression clones). These concerns are particularly relevant when high protein yields are required, as is the case for protein structure determination or for therapeutic applications. Graduate students Ashok Bandaranayake and Colin Correnti, their advisor and member of the Basic Sciences Division, Dr. Roland Strong, and colleagues developed a protein expression system that overcomes many of the above limitations. Appropriately named after a skilled craftsman in Greek mythology, Daedalus, this platform features an innovative lentiviral vector containing a minimized, ubiquitous chromatin opening element (UCOE0.7). This vector vastly enhances and sustains stable protein expression in commercially available human cell lines whose secretory pathways and adaptation to serum-free media facilitate purification.

Using Daedalus, the authors proceeded from lentiviral transduction to protein structure determination in a mere 18 days for one of the target proteins. In total, Bandaranayake *et al.* improved the production of highly pure, properly folded protein for 12 out of 14 targets, with yields ranging from 10-100 mg/L. They also showed that the recombinant human cytokines produced by Daedalus exhibited identical immune activity in cellular assays as commercial reagents, indicating that this platform may be appropriate for the manufacture of protein therapeutics. Although lentiviral vectors are generally constrained in terms of the amount of exogenous DNA they can package, the authors suggest that the current 70kDa limit on protein size may be readily overcome. Indeed, the minor vector modifications they propose will likely soon render Daedalus capable of producing full-length antibodies.

Bandaranayake AD, Correnti C, Ryu BY, Brault M, Strong RK, Rawlings DJ. 2011. Daedalus: a robust, turnkey platform for rapid production of decigram quantities of active recombinant proteins in human cell lines using novel lentiviral vectors. *Nucleic Acids Research*, Epub ahead of print, doi: 10.1093/nar/gkr706.



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