

## Biomass crop-produced recombinant human interleukin-2 and its activity against splenic cd4<sup>+</sup> t-cells

**Mariam Sticklen, Jason D. Matakas, Thang Nguyen, William F. Carson IV, Steven Kunkel, Dahai Gao, Venkatesh Balan and Federica Brandizzi**

Michigan State University, USA

Human interleukin-2 (IL-2) is a biopharmaceutical of great importance as it is the standard FDA-approved immunotherapeutic treatment for end-stage metastatic melanoma and renal cell cancer. The current production platform used for rhIL-2 is *E. coli*. The rhIL-2 was developed by Novartis Pharmaceuticals and released commercially under the name Proleukin (Aldesleukin). Proleukin is regularly used in clinical settings not only to treat patients with metastatic melanoma and renal cell cancers, but also used in research laboratories for the *in vitro* proliferation and maintenance of T-cells. The average cost of IL-2 alone for each course of treatment has been reported to be about \$11,400 USD (MTRAC, 1996).

Our Michigan State University and University of Michigan Teams explored the feasibility of producing biologically active recombinant human IL-2 in the green tissues of transgenic *Nicotiana benthamiana* (tobacco) and *Zea mays* (corn). Using the whole-plant expression system, rather than relying on the current *E. coli* platform, is anticipated to be more economic.

The human IL-2 gene was codon optimized to maximize its expression in the tobacco host system. A construct fusing red fluorescent protein to the IL-2 protein was developed and confocal microscopy was utilized to verify targeted accumulation, and thus proper folding in this system. Five additional constructs were developed for stable expression rhIL-2 with targeting to different sub-cellular compartments. Western blotting of the stably transformed lines demonstrated maximum accumulation of the appropriately sized protein in the endoplasmic reticulum and chloroplasts. The rhIL-2 was purified, and its biological activity was compared with that of commercially available *E. coli* produced rhIL-2 on murine splenic CD4<sup>+</sup> T-cells from C57BL/6 mice. Our research demonstrated the efficacy of using plant green tissues as a Bioproduction system for the production of biologically active recombinant human IL-2. We estimate the cost of production of plant-produced IL-2 to be a fraction of that of *E. coli*-produced version.

### Biography

Mariam Sticklen has been a faculty member for the last 29 years. She has served as consultant to the U.S. National Academy of Sciences on its NRC for over 10 years. She is the recipient of the MSU 2009 Outstanding Faculty Woman award, the 2008 University of Southern Mississippi and Hattiesburg Clinic Scholar Anti-HIV Speaker Award; and the 2000 Ralph Smuckler Award for Advancing Research, Studies and Programs at International level. Prof. Sticklen has published two books and over 160 articles. Presently, she serves as the Editor-In-Chief of one journal and as Editorial Board member of three other journals.

[stickle1@msu.edu](mailto:stickle1@msu.edu)