

# MATTHEW S. CROUGHAN

*George B. and Joy Rathmann Professor, Director of the Amgen Bioprocessing Center, and Focus Track Champion – Pharmaceutical Discovery and Development*

## AREAS OF EXPERTISE

Bioprocessing, biopharmaceutical development and manufacturing

## CONTACT INFORMATION

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Dr. Croughan earned a BS degree from University of California, Berkeley in chemical engineering with High Honors in 1983. He completed his PhD in chemical engineering at the Massachusetts Institute of Technology in 1988. He was subsequently hired by Genentech in South San Francisco as their expert in bioreactor design and scale up. At Genentech, he developed the first licensed, high-density, fed-batch cell culture process. This breakthrough platform technology was first used for Pulmozyme and is now used throughout the biopharmaceutical industry for nearly all antibody products. Dr. Croughan also led the development of a new licensed process for Activase, eliminating all animal-derived raw materials and tripling productivity. Lastly, he served on the design team for Genentech's Vacaville manufacturing facility. In 1993, Dr. Croughan served as the founding Director of Cell Processing and Expansion at Dendreon (formerly Activated Cell Therapy).

Prior to joining KGI, Dr. Croughan worked as an independent consultant providing expert guidance on biopharmaceutical process development and manufacturing to more than 50 firms. He also served part-time as the Industrial Liaison Officer for the Biotechnology Process Engineering Center at MIT. At KGI, he still consults one day per week and maintains very strong connections in industry.

He is a Fellow of the American Institute of Medical and Biological Engineers (top 2% of field).

## RESEARCH SYNOPSIS

While a graduate student at MIT studying under Institute Professor Daniel I.C. Wang, Dr. Croughan conducted research on hydrodynamic effects on animal cells in microcarrier bioreactors. His work resulted in a series of nine publications, one of which has been ranked one of the top 20 ever in the field. At Genentech, his research concentrated for many years on animal cell bioreactor design and scale up. At KGI, Dr. Croughan continues to conduct research in this field and has expanded the scope of his work to include stem cells and algae.

Dr. Croughan also conducts research on biopharmaceutical development, including technology management and strategy. His benchmarking work on 25 years of progress in CHO cell processes has shown that productivity has steadily doubled every 3.4 years; this trend is often referred to as "Croughan's Law." Dr. Croughan continues to consult and conduct research on fed-batch cell culture. His group has invented a novel method to eliminate lactic acid production in fed-batch cell culture.

## KEY RESEARCH CAPABILITIES

The Amgen Bioprocessing Center is capable of all aspects of industrial animal cell culture, including biopharmaceutical and stem cell process development, medium design, bioreactor design and scale up, operations management and scheduling, and regulatory requirements. The Center is equipped with a state-of-the-art, lab-scale pilot plant for animal cell culture with ten small scale bioreactors. The Center also has an Akta Pilot chromatography system, an Akta Cross Flow filtration system for purification and formulation of monoclonal antibodies and other biopharmaceuticals, and a 5-L microbial fermentor for production of biopharmaceutical products from *E. Coli* or *Pichia pastoris*.

## CURRENT RESEARCH PROJECTS

*A Novel Method to Control Lactic Acid Production and pH in Animal Cell Culture:* The Center has developed a novel method to completely eliminate lactic acid production in animal cell culture, one of the ongoing challenges in industrial animal cell culture. It involves culturing cells at very high (40 mM) lactate levels, which completely inhibits further lactic acid production, and adapting the cells to this otherwise toxic level of lactate. A patent on the technology has been filed.

*Scale-Up of Transient Cell Culture for Rapid Production of Antibodies in a Biodefense Emergency:* The Amgen Bioprocessing Center aims to produce 3 million doses of protective antibody in less than three months through transient cell culture at the 10,000 to 25,000-liter scale.

*Bioprocessing Education:* Biofuels, global warming, health care, and bioterrorism are some of the greatest challenges facing mankind. These can be successfully addressed only if a sufficient number of people are skilled in the area of bioprocessing. Successful culturing of living cells to manufacture products (bio-processing) will play an increasingly important role in our future. Even though there is an increasing demand for skilled bioprocessing professionals, there has been limited expansion in educational programs. Many of the current programs have laboratories that are decades behind leading industrial firms in their equipment and development and fail to attract large numbers of students into the field. KGI has developed an innovative bioprocessing curriculum, including many lab courses, and have grown the Bioprocessing focus track up to 15-20 graduates per year, one of the largest Master level bioprocessing programs. As part of this, The Amgen Bioprocessing Center has developed cell lines, medium, and bioreactor protocols that reflect current industry approaches but are not proprietary and can be used in an academic setting.

## FUTURE RESEARCH INTERESTS

*Creation of New Curricular Materials and Textbooks for Bioprocessing Education:* KGI hopes to expand the reach of our successful bioprocessing curriculum.

*Industrial Cell Culture:* Extension of Dr. Croughan's current research on biopharmaceutical process development and manufacturing, including the manufacture of novel biopharmaceuticals.

## SELECTED PATENTS

*A Novel Method to Reduce Lactate Acid Production and Control pH in Animal Cell Culture,* Patent Filing, 2009.

## SELECTED PUBLICATIONS

Arnold FH, Chalmers JJ, Saunders MS, Croughan MS, Blanch HW, Wilke CR. "A Rational Approach to the Scale-Up of Affinity-Chromatography". *Acc Symposium Series* 1985;271:113-122

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