Benjamin D. Cosgrove

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Education

Massachusetts Institute of Technology, Biological Engineering Division
Bioengineering Ph.D. candidate (2003-)

University of Minnesota, Department of Biomedical Engineering
B.Bm.E., Biomedical Engineering, *Summa cum laude* (1999-2003)

Publications

Cosgrove BD, Cheng C, Pritchard JR, Stolz DB, Lauffenburger DA, Griffith LG. An inducible autocrine cascade regulates rat hepatocyte proliferation and apoptosis responses to tumor necrosis factor-α. *submitted.*

Cosgrove BD, Griffith LG, Lauffenburger DA. Fusing tissue engineering and systems biology toward fulfulling their promise. *Cellular and Molecular Bioengineering*, 2008. *in press.*

Graduate Research

Massachusetts Institute of Technology (2004-)
Advisors: Prof. Linda G. Griffith and Prof. Douglas A. Lauffenburger
Ph.D. Thesis Project

"Quantitative Analysis of Cytokine-Induced Hepatocyte Proliferation, Apoptosis, and Toxicity"

Many therapeutic agents, including viral gene therapy vectors and small molecule pharmaceutical compounds, are confounded by liver toxicity due to, in part, relationships with inflammatory stimuli in eliciting hepatocyte toxicity and/or death. Our work focuses on developing physiologically relevant *in vitro* approaches to quantitatively assess how hepatocytes regulate, through the activities of intracellular and extracellular signaling networks, cell fate decisions related to proliferation, survival, apoptosis, and differentiated function following cytokine stimulation in the presence of viral gene therapy agents or small molecule drugs. Initially, we examined the role of a specific inflammatory cytokine, tumor necrosis factor alpha (TNF), which regulates both hepatocyte proliferation and apoptosis *in vivo*. We have shown that TNF stimulates hepatocyte proliferation and (adenoviral vector-sensitized) apoptosis *in vitro* through an inducible and time-varying autocrine cascade containing the growth factor TGF-α and the cytokines IL-1α/β and IL-1ra. This TGF-α–IL-1α/β–IL-1ra autocrine cascade regulates TNF-induced hepatocyte proliferation and apoptosis responses in a self-antagonizing manner by contributing to multiple signaling pathways, including Akt, ERK, JNK, p38, and IKK–NF-κB, downstream of TNFR. Currently, we are developing *in vitro* models of idiosyncratic drug hepatotoxicity by examining the interactions between multiple pharmaceutical compounds and inflammatory cytokines. In this work, we aim to elucidate how certain idiosyncratic hepatotoxic drugs exhibit synergistic toxicity relationships with inflammatory cytokines by collecting systems-level intracellular signaling data and phenotypic cellular toxicity data. This data set has been used to develop data-driven signaling-outcome models through partial least squares regression (PLSR) approaches to identify and predict key signaling activities that regulate a diverse set of hepatocyte toxicity phenotypes and to inform future therapeutic strategies.

Research Webpages

http://lauffenburger.openwetware.org/Ben_Cosgrove.html http://www.epernicus.com/users/338

Fellowships, Scholarships & Awards

Whitaker Foundation Graduate Fellowship in Biomedical Engineering (2003-2006)
Dean's List, Institute of Technology, University of Minnesota (Fall 1999-Spring 2003)
National Merit Scholarship (1999-2003)
U2000 Scholarship, University of Minnesota (1999-2003)
Robert C. Byrd Scholarship, State of Minnesota (1999-2003)
Biomedical Engineering Department Scholarship, University of Minnesota (2002)
Richfield (MN) Teachers' Union Scholarship (1999)

Podium Presentations

MIT Cell Decision Processes Center Annual Meeting (June 2007)
"Quantitative Analysis of Drug- and Cytokine-Induced Hepatotoxicity"

Conference of Systems Biology of Mammalian Cells (July 2006)
"Autocrine Cascades in Hepatocyte Proliferation and Death Responses to TNFα"

MIT Cell Decision Processes Center Annual Meeting (June 2006)
"Multivariate Cue-Signal-Response Analysis of TNFα-Induced Hepatocyte Proliferation and Apoptosis"

Poster Presentations

Engineering Cell Biology (August 2007)
"Quantitative Analysis of Cytokine-Induced Hepatocyte Proliferation, Apoptosis, and Toxicity"

Conference of Systems Biology of Mammalian Cells (July 2006)
"Quantitative Analysis of Autocrine Cascades in Hepatocyte Proliferation and Death Responses to TNFα"

MIT Cell Decision Processes Center Annual Meeting (June 2006)
"Multivariate Cue-Signal-Response Analysis of TNFα-Induced Hepatocyte Proliferation and Apoptosis"

MIT Biotechnology Process Engineering Center (BPEC) Poster Session (October 2004)
"Cell Signaling in *In Vitro* and *In Vivo* Models of Liver Regeneration"

Undergraduate Research Experience

University of Minnesota (2000-2003)
Advisor: Prof. David J. Odde

"Modeling Actin Filament Branching using Monte-Carlo Simulations"
Developed a Monte-Carlo computer model to simulate the three-dimensional growth and branching of actin filaments to examine statistical correlations to experimental observations.

"Cell Irradiation Analysis in a Laser-Guided Direct Writing System"
Designed and developed an assay for studying the effects of irradiation due to laser-guided direct writing of healthy human multi-potent adult progenitor cells.

"Laser-Guided Direct Writing System Design and Experimental Analysis"
Designed and developed a laser-guided direct writing system for demonstrational use at the Science Museum of Minnesota. Collected and analyzed data from particle trajectories in a laser guided direct writing system for comparison to theoretical predictions.

References

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