John Bechill

2536 N Wayne Unit 1F
Chicago, IL, 60614
cell phone: (708)-275-9135
john.bechill@gmail.com
http://www.johnbechill.com

EDUCATION:

PhD., Molecular Biology **2001-2008**
Loyola University-Maywood, IL
Advisor: Dr. Baker PhD
Thesis: Analysis of Coronavirus Infection and the Unfolded Protein Response

Bachelors of Science, Major in Microbiology **1998-2001**
Michigan State University, Lyman Briggs College-Lansing, MI

WORK HISTORY:

Research Staff-University of Chicago-Chicago, IL **2014-Current**
Advisor: Dr. Michael Spiotto MD, PhD

- Combining traditional therapeutics (cisplatin, taxol, radiation) with novel therapeutics
- Characterizing activity of small molecules found during side chain variant analysis

Research Scientist-Northwestern University-Chicago, IL **2010-2013**
Advisors: Dr. Muller MD, PhD and Dr. Longnecker PhD

- Development of *in vitro* assays to examine NK/T cell cytokine effects on cancer cells

Research Scientist-Northwestern University-Chicago, IL **2008-2010**
Advisor: Dr. Corey MD

- Studied macrophage solute uptake, cytokine secretion, and migration/invasion

MOLECULAR BIOLOGY SKILLS:

- **Lead small molecule validation** in *in vitro* system of head and neck and cervical cancer. Tested side-chain variants of lead small molecule for their ability to induce cell death and cell cycle arrest. Verified binding of compound to target protein by surface plasmon resonance (Biacore) and computational modeled compound to p53 and human papillomavirus E6. Analyzed p53 associated cell death pathways activated by compounds by flow cytometry, western blot, qRT-PCR and microscopy. Validated the small molecules targeted the p53 pathway by knockdown of p53 and PUMA. Combined traditional therapeutics (cisplatin, ionizing radiation, and doxorubicin) with our small molecule to identify synergy and additive efficiency in cell death and clonogenic assays.

- **T/NK cell mediated cell signaling in cancer cells** was measured in an *in vitro* culture system. Developed a NK/epithelial cell co-culture system to examine reciprocal signaling. *In vitro* cultured cancer cells were stimulated with recombinant purified soluble cytokines or receptor binding mutants. I examined cell signal after stimulation using western blot and luciferase reporters for the NF-kB, interferon and caspase signaling pathways. I also used quantitative flow cytometry assays to measure the receptor levels on the cells. Measured cytokine release following stimulation by ELISA and lumenix.

- **Explored macrophage biology** using different macrophage lineages. Isolated and cultured bone marrow macrophages and isolated peripheral blood monocytes for assays. Stimulated monocyte/macrophages and quantified uptake of various solutes and particles. Used absolute quantitation flow cytometry technique to measure TNF family receptor numbers. Stimulated macrophages with activators and examined cytokine secretion. Developed a macrophage/epithelial cell co-culture system to examine macrophage control of viral infection. Viewed macrophage movement and quantified viral infection by plaque assay.

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- **Investigation of new tumors suppressors/oncogenes** in cervical and head and neck cancer panels. A transposon screen identified several potential previously uncharacterized tumor suppressor/oncogenes. I cataloged the hits and cross-referenced the hits against the Cancer BioPortal database and known literature to identify novel targets. I developed a system to introduce the tumor suppressors/oncogenes into HPV positive and negative head and neck cell lines. Following introduction, cell death and proliferation was monitored. Transduced cells were treated with conventional therapeutics including DNA damaging agents and radiation to determine the change in oncogenic potential.

- **Expressed proteins** from cloned regions of viral proteins, cytokines, truncated cell surface receptors, and soluble cellular signaling proteins. Amino acid sequences of proteins were analyzed for hydrophobicity and post-translation modifications which could potentially disrupt purification. Produced recombinant proteins in E.Coli, CHO, and 293T expression systems. These recombinant proteins were purified using size exclusion chromatography and affinity tag chromatography.

- **Validated reactivity of antibodies targeting cell surface proteins by** screening panels of monoclonal antibodies to cell adhesion proteins and immune receptors. Tested antibodies for reactivity against target antigen using multiple assays (flow cytometry, western blot, immunoprecipitation, and fluorescence microscopy). Validated correct antibody target interactions using knockdown and knockout cell lines. Identified cell types expressing high levels of the target of interest. Expressed structurally similar family members to investigate cross-reactivity and specificity of antibody.

COMPUTER SKILLS:

- **Statistical and data management software include R, Excel, and Python.** R and excel were used for generation of charts and production of statistics (means, standard deviation, linear regression/logistic regression, correlation coefficients, t test, ANOVA analysis, and ED50s). R programs written for high-through-put data analysis, where raw data was serially imported and analyzed for rapid reporting. Python programs for image analysis and importing spreadsheets for graphing.

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PROJECT SUMMARIES:

2014-Recent, University of Chicago
Research Staff, Radiation Oncology, Mentor: Dr. Michael Spiotto
Project title: "p53 mediated carcinogenesis and inhibitor design"
Even with modern cancer medicine, oral pharyngeal cancer continues to be extremely difficult to treat. The current standard treatment is ionizing radiation and cisplatin therapy. Among the radio-resistant subtypes are oral pharyngeal carcinomas caused by HPV and p53 mutations. These carcinomas express HPV's E6 which inhibit p53, and mutations inactivating p53 DNA binding and transactivating capabilities, making therapies such as radiation and cisplatin less effective. Currently, I am characterizing small molecules targeting p53. Small molecules were isolated in a screen and lead compounds further characterized in HPV negative and positive cells and shown to induce cell cycle arrest, apoptosis and p53 target gene activation.

2010-2013, Northwestern University
Postdoctoral Fellow, Microbiology and Immunology, Mentor: Dr. Muller and Dr. Longnecker
Project title: "LIGHT signaling through HVEM and LTβR"
Herpes Simplex Virus infection causes a persistent life-long neuronal infection which causes sporadic out-breaks of cutaneous lesions of the mouth, genitals and skin. These lesions are caused by destruction of tissue by virus replication and inflammation. Several vaccine trials have been conducted towards a HSV but resulted in no efficiency. While adult infections rarely cause serious problems, pediatric infections have a 30% mortality rate and 60% morbidity rate and a serious concern. The reason for the poor outcome has not been fully elucidated but hypothesis include atypical spread of the virus or a hyperinflammatory response. Therefore, we developed projects to further understand HSV spread and associated inflammation for potential treatment.

2008-2010, Northwestern University
Postdoctoral Fellow, Immunology and Cancer Biology, Mentor: Dr. Corey
Project title: "Regulation of the Cdc42 interacting protein by Src kinases during macrophage micropinocytosis and invasion"
With the success of Dasatinib and low associated adverse effects, research into targeting src kinases for other purposes has gained interest. Src kinases have been associated with inflammation, glucose metabolism and proliferation/migration of cancer cells. Therefore, we researched these topics in pursuit of targeting src for future therapeutics.

2001-2008, Loyola University
Ph.D., Molecular Biology, Mentor: Dr. Baker Lab
Project title: "Activation and modulation of the unfolded protein response during mouse hepatitis virus infection"
Coronavirus belong to a class of emerging viral diseases. While previously known as an animal pathogen, coronaviruses were not associated with severe disease in humans. In 2003, a coronavirus was identified to be the etiological of SARS and since then several other coronaviruses have been implicated in severe human disease. Therefore, we developed projects to study coronavirus replication and identify potential targets for therapeutics such as protease inhibitors.

2000-2001, Michigan State University
Undergraduate research experience, Mentor: Dr. Kaminski
Project title: "Regulation of immune cell function by cannabinoid and aryl hydrocarbon receptors"

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AWARDS:

Arthur J. Schmitt Dissertation Fellowship	2005
Experimental Immunology Training Grant	2004-6
American Heart Association Fellowship	2008

PUBLICATIONS:

Bechill J, Zhong R, Zhang C, Solomaha E, Spiotto MT. 2016. A High-Throughput Cell-Based Screen Identified a 2-[(E)-2-Phenylvinyl]-8-Quinolinol Core Structure That Activates p53. PLos One. http://dx.doi.org/10.1371/journal.pone.0154125.

Zhong R, Bao R, Faber PW, Bindokas VP, **Bechill J**, Lingen MW, Spiotto MT. 2015. Notch1 Activation or Loss Promotes HPV-Induced Oral Tumorigenesis. Canc Res. 75(18):3958-69.

Bechill, J. and WJ. Muller. Herpesvirus entry mediator (HVEM) attenuates signals mediated by the lymphotoxin beta receptor (LTβR) in human cells stimulated by the shared ligand LIGHT. 2014. Molecular Immunology. 62: 96-103.

Pichot PS, Hartig, SM, Arvanitis C, Jensen SA, **Bechill J**, Marzouk S,Yu J,Frost JA,Corey SJ. 2010. Cdc42 Interacting Protein 4 promotes breast cancer cell invasion and formation of invadopodia through activation of N-WASp. Canc Res. 70:8347.

Y. Feng, SM. Hartig, **J. Bechill**, EG. Blanchard, E. Caudell, and SJ. Corey. 2010. The Cdc42 Interacting Protein 4 (CIP4) Gene Knockout Mouse Reveals Delayed and Decreased Endocytosis. J Biol Chem, 285: 4348–4354.

Bechill, J., Z. Chen, JW. Brewer, and SC. Baker. 2008. Coronavirus infection modulates the unfolded protein response and mediates sustained translational repression. J. Virol. 82: 4492-4501.

Bechill, J., Z. Chen, JW. Brewer, and SC. Baker. 2006. Mouse hepatitis virus infection activates the IRE1/XBP1 pathway of the unfolded protein response. Adv. Exp. Med. Biol. 581:139-44.

Harcourt, BH., D. Juckneliene, A. Kanjanahaluethai, **J. Bechill,** KM. Severson, C. Smith, P. Rota, and SC. Baker. 2004. Identification of severe acute respiratory syndrome coronavirus replicase products and characterization of papain-like protease activity. J. Virol. 78:13600-612.

ORAL PRESENTATIONS:

Americian Society for Virology: 25th Annual Meeting. Madison, WI, USA. 2006.

Xth International Nidovirus Symposium: Towards Control of SARS and Other Coronavirus Disease. Colorado Springs, CO, USA. 2005.

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ABSTRACTS:

Spiotto MT, Zhong R., **Bechill J**. Aurora Kinase Inhibition Sensitizes Primary Oral Tumors to Subtherapeutic Doses After Image Guided Radiation Therapy

Bechill J. and W. Muller. Mediator to Human Herpes Virus 2 glycoprotein D mediated entry and production of inflammatory cytokines. International Herpes Workshop. Calgary. 2012.

Brian P., Rossow M., **Bechill J.** , S. Corey. CIP4 and Src promote membrane rearrangements during endocytosis as demonstrated by advanced imaging techniques. Biophysical Society. San Francisco. 2010.

Bechill J., S. Jensen, S. Marzouk and S. Corey. Regulation of macropinocytosis by CIP4 in macrophages by Src kinase. American Society for Cell Biology. San Diego. 2009.

Bechill J., Z. Chen, JW Brewer, and SC. Baker. Mouse hepatitis virus activates and modulates the unfolded protein response. 2007. International Symposium on Positive Strand Viruses. Washington DC. 2007.

Bechill JE., Z. Chen, JW. Brewer and SC. Baker. Mouse hepatitis virus activates and regulates the XBP-1(S) branch of the unfolded protein response. Americian Society for Virology: 25th Annual Meeting. Madison, WI, USA. 2006.

Bechill J., Z. Chen, JW. Brewer, K. Mori, and SC. Baker. Mouse hepatitis virus activates the cellular unfolded protein response (UPR) and post-translationally regulates the IRE1-XBP-1 pathway. Xth International Nidovirus Symposium: Towards Control of SARS and Other Coronavirus Disease. Colorado Springs, CO, USA. 2005.