

Cary F Opel

<http://cfopel.com>

Education

Massachusetts Institute of Technology

Ph.D. Chemical Engineering, Koch Institute for Integrative Cancer Research

Advisor: K. Dane Wittrup

Thesis: T Cell Mediated Combination Immunotherapy

2015

Stanford University

Professional Certificate, Product Creation and Innovative Manufacturing

2007

University of California, Berkeley

B.S. Bioengineering, Highest Honors

2004

Work Experience

Research Scientist II

July, 2017 – Present

Gilead Sciences, Oceanside CA

Implemented cross functional data analysis workflows utilizing Matlab, Spotfire, and PI.

Developed advanced DOE algorithms in support of analyzing PC generated data. Developed

and implemented a platform process to accelerate early stage development programs.

Research Scientist I

September, 2015 – July, 2017

Gilead Sciences, Oceanside CA

Developed and supported cell culture manufacturing processes for clinical trials and commercial production. Ran scale down experiments, generated documents, and performed data analysis in support of process characterization for commercial product launch. Managed and developed lab personal.

Graduate Student Researcher

January, 2010 – September, 2015

Wittrup Lab, Massachusetts Institute of Technology, Cambridge MA

Developed T cell based therapies in K. Dane Wittrup's Lab at MIT. Designed, expressed and purified various proteins including immunocytokines and antibodies. Developed stable cell lines expressing secreted and transmembrane proteins. Optimized various viral vector production and transduction protocols including lentivirus and retrovirus vectors. Designed and executed preclinical animal studies. Carried out adoptive cell transfer experiments in mice. Combinations of up to four different agents targeting complementary therapeutic modalities were tested in a murine model of melanoma. Cancer vaccine treatment, cytokine therapy, checkpoint blockade,

and tumor targeting antibody dosing allowed various immunological mechanisms to be activated in a syngenetic mouse model. The most aggressive combinations cured large, established, subcutaneous tumors without the need for adoptive cell transfer. Extensive characterization of the immune system response to the tumor created by the combination therapy revealed a complex interplay of various cell types to mount a durable rejection of the primary tumor, as well as subsequent rechallenge.

Engineer I

August, 2006 – August, 2009

Genentech, Oceanside CA

Cell culture engineer in a cross-functional early stage process development group. Designed experiments to optimize mammalian cell culture parameters for clinical protein production. Technology development projects included the use of dielectric spectroscopy to monitor viable biomass online and optimizing a protein-retaining perfusion system to develop high titer processes. Led the setup and build-out of a new cell culture lab, which included leading a project team to design, commission, and install a 52-vessel DeltaV based bioreactor control system.

Operations Rotational Development Program Analyst

July, 2004 – August, 2006

Genentech, South San Francisco CA

Leadership development program that consisted of four six-month rotations throughout Genentech's Product Operations department.

Process Development – Late Stage Cell Culture

Evaluated new equipment for use in future cell culture processes. Set up and maintained small-scale cell culture runs. Generated experimental designs and performed data analysis. Worked with vendors to ensure equipment was functioning and used properly.

Manufacturing – Vacaville

Worked in a cGMP manufacturing facility as a technician in both cell culture and recovery operations. Learned CIP and SIP development principles. Implemented a tool to track and improve adherence to schedule.

Supply Chain Business Process Improvement

Acted as project manager for a cross-functional initiative to enhance Genentech's clinical drug supply chain. Utilized Class A / Operational Excellence principles to design and implement a process to track and verify the final disposition of drugs supplied during clinical trials. Completed basic courses in project management and meeting facilitation.

Manufacturing Science and Technology

Established and standardized best practices for pH and dissolved oxygen equipment maintenance across multiple manufacturing groups. Modified cGMP SOPs and created training procedures to support new activities. Assisted with the qualification campaign for the drug Lucentis. Participated in tank cleaning validation activities. Applied Kepner-Tregoe Root Cause Analysis procedures during process troubleshooting.

Lab Assistant/Undergraduate Researcher

May, 2002 – May, 2004

King Lab, UC Berkeley, Berkeley CA

Performed research on osteoarthritis for Professor Karen King. Tasks included microscopy, tissue processing, sectioning with a microtome, basic histology and immunohistochemistry. Carried out data analysis, established protocols, and assisted in writing publications. Wrote research funding proposals leading to several undergraduate grants.

Lab Technician

May, 2001 – May, 2004

Berkeley Microprop, Berkeley CA

Performed micro-propagation of various plants in a sterile lab environment. Performed activities independently and trained new employees on sterile technique and plant culture processes.

Glassware/Media Prep Technician

May, 2001 – May, 2002

Arriva Pharmaceuticals, Alameda CA

Cleaned and organized lab glassware. Stocked lab supplies and prepared media. Repaired and maintained laboratory equipment. Installed equipment and set-up stockrooms in a new laboratory facility.

Research Skills

In-vivo Cancer Models: Isogenic, xenogenic, and inducible murine models of cancer; adoptive cell transfer; survival surgery; husbandry

Molecular Biology: Vector design and construction; cloning; DNA isolation and purification; PCR

Flow Cytometry: 9 color panel design and analysis; Flowjo; BD FACS Diva; Accuri; Fortessa; LSR

Mammalian Cell Culture: Transient protein expression; stable cell line development; cytotoxicity assays; T cell culture and expansion; Bioreactor Operations; cGMP processes; perfusion; optical density; dielectric spectroscopy

Protein Analysis and Purification: SDS-PAGE; Western Blot; ELISA; GE AKTA; affinity chromatograph; SEC

Viral Vectors: Lentiviral/retroviral expression and transduction

Computer: Excel; Word; Powerpoint; Matlab; R; SigmaPlot; Prism; Spotfire; PI

Publications

Artificial Anti-Tumor Opsonizing Proteins with Fibronectin Scaffolds Engineered for Specificity to Each of the Murine FcγR Types. Chen TF, Li KK, Zhu EF, **Opel CF**, Kauke MJ, Kim H, Atolia E, Wittrup KD. JMB. 2018.

Biopolymers codelivering engineered T cells and STING agonists can eliminate heterogeneous tumors. Smith TT, Moffett HF, Stephan SB, **Opel CF**, Dumigan AG, Jiang X, Pillarisetty VG, Pillai SPS, Wittrup KD, Stephan MT. The Journal of Clinical Investigation. 2017.

Temporally Programmed CD8α+ DC Activation Enhances Combination Cancer Immunotherapy. Tzeng A, Kauke MJ, Zhu EF, Moynihan KD, **Opel CF**, Yang NJ, Mehta N, Kelly RL, Szeto GL, Overwijk WW, Irvine DJ, Wittrup KD. Cell Reports. 2016.

Eradication of large established tumors in mice by combination immunotherapy that engages

innate and adaptive immune responses. Moynihan KD*, **Opel CF***, Szeto GL, Tzeng A, Zhu EF, Engreitz JM, Williams RT, Rakhra K, Zhang MH, Rothschilds AM, Kumari S, Kelly RL, Kwan BH, Abraham W, Hu K, Mehta NK, Kauke MJ, Suh H, Cochran JR, Lauffenburger DA, Wittrup KD, Irvine DJ. Nature Medicine. 2016. ***Co-First Authors**

Synergistic Innate and Adaptive Immune Response to Combination Immunotherapy with Anti-Tumor Antigen Antibodies and Extended Serum Half-Life IL-2. Zhu EF*, Gai SA*, **Opel CF***, Kwan BH, Surana R, Mihm MC, Kauke MJ, Moynihan KD, Angelini A, Williams RT, Stephan MT, Kim JS, Yaffe MB, Irvine DJ, Weiner LM, Dranoff G, Wittrup KD. Cancer Cell. 2015. ***Co-First Authors**

Antigen Specificity Can Be Irrelevant to Immunocytokine Efficacy and Biodistribution. Tzeng A, Kwan BH, **Opel CF**, Navaratna T, Wittrup KD. PNAS. 2015.

A graphene-based physiometer array for the analysis of single biological cells. Paulus GL, Nelson JT, Lee KY, Wang QH, Reuel NF, Grassbaugh BR, Kruss S, Landry MP, Kang JW, Vander Ende E, Zhang J, Mu B, Dasari RR, **Opel CF**, Wittrup KD, Strano MS. Scientific Reports, 2014.

Emergent properties of nanosensor arrays: applications for monitoring IgG affinity distributions, weakly affined hypermannosylation, and colony selection for biomanufacturing. Reuel NF, Grassbaugh B, Kruss S, Mundy JZ, **Opel CF**, Ogunniyi AO, Egodage K, Wahl R, Helk B, Zhang J, Kalcioğlu ZI, Tvrdy K, Bellisario DO, Mu B, Blake SS, Van Vliet KJ, Love JC, Wittrup KD, Strano MS. ACS Nano. 2013.

Quantitative modeling of viable cell density, cell size, intracellular conductivity, and membrane capacitance in batch and fed-batch CHO processes using dielectric spectroscopy. **Opel CF**, Li J, and Amanullah A. Biotechnology Progress. 2010.

Cyclical articular joint loading leads to cartilage thinning and osteopontin production in a novel in vivo rabbit model of repetitive finger flexion. King KB, **Opel CF**, Rempel DM. OsteoArthritis and Cartilage. 2005.

Presentations and Posters

More Accurate Process Understanding from Process Characterization Studies Using Monte Carlo Simulation, Regularized Regression, and Classification Models. **Opel CF**, Hui CJ, Yang PY, Tien DJ, Derfus GE, Krishnan R. Cell Culture Engineering XVI. Tampa Bay. May 2018.

Identifying Upstream Critical Process Parameters Using Predictive Modeling Methods to Analyze Process Characterization Data. Hui CJ, **Opel CF**. Poster. BioProcess International West. Santa Clara. March 2018.

Monte Carlo Stepwise Regression for More Accurate Selection of Critical Process Parameters during Process Characterization. **Opel CF**, Hui CJ, Yang PY, Tien DJ. Presentation. AIChE Annual Meeting. Minneapolis. November 2017.

Enhanced Combination Immunotherapy Using Anti-PD-1 Antibodies and in Conjunction with Tumor Targeting Therapies. **Opel CF**, Moynihan KD, Irvine DJ, Wittrup KD. Presentation.

PEGS. Boston. May 2015.

Combined Treatment Using Adoptive Cell Therapy, IL-2, and Tumor-Specific Antibodies. **Opel CF**, Moynihan KD, Irvine DJ, Wittrup KD. Presentation. ImVacS. Boston. August 2014.

Combined treatment using adoptive cell therapy, extended pharmacokinetic IL-2, and tumor-specific antibodies leads to cures of established B16F10 tumors and extended in vivo T cell survival. **Opel CF**, Wittrup KD. Poster. SITC Annual Meeting. National Harbor. November 2013.

Engineering Chimeric Antigen Receptors Targeting an Endogenous Murine Tumor Associated Antigen. **Opel CF**, Stephan MT, Wittrup KD. Presentation. AIChE Annual Meeting. Pittsburgh. October 2012.

Advanced Applications of DeltaV in Cell Culture Process Development. Najmi Z, **Opel CF**. Workshop. Emerson Global Users Exchange. Orlando. October 2009.

Monitoring and Control of Cell Culture Bioreactors Using on-Line Scanning Dielectric Spectroscopy. **Opel CF**, Amanullah A. Presentation. AIChE Annual Meeting. Philadelphia. November 2008.

Application of on-line scanning dielectric spectroscopy to monitor CHO cell cultures. **Opel CF**, Amanullah A. Poster. ACS National Meeting. Philadelphia. August 2008.

On-line viable cell density measurements using scanning dielectric spectroscopy. **Opel CF**, Li F, Amanullah A. Poster. Cell Culture Engineering XI. Queensland, Australia. April 2008.

In Vivo Cyclical Joint Loading Decreases Unmineralized Cartilage Mean Thickness in the Rabbit Metacarpophalangeal. **Opel CF**, Portnoy A, King KB. Poster. Annual ORS Meeting. Washington DC. February 2005.

Analysis of an Animal Model Studying the Mechanobiology of Joint Loading. **Opel CF**, Portnoy A, King KB. Presentation. UC Systemwide Annual Bioengineering Symposium. San Diego. June 2003.

Patents

U.S. Provisional Application No. 62/036,947

Title: SYNERGISTIC TUMOR TREATMENT WITH IL-2, A THERAPEUTIC ANTIBODY, AND AN IMMUNE CHECKPOINT BLOCKER. Filing Date: August 13, 2014.

U.S. Provisional Application No. 62/036,595

Title: SYNERGISTIC TUMOR TREATMENT WITH IL-2, A THERAPEUTIC ANTIBODY, AN IMMUNE CHECKPOINT BLOCKER, AND A CANCER VACCINE. Filing Date: August 12, 2014.

U.S. Provisional Application No. 62/036,588

Title: SYNERGISTIC TUMOR TREATMENT WITH IL-2, A THERAPEUTIC ANTIBODY, AND A CANCER VACCINE. Filing Date: August 12, 2014.

U.S. Provisional Application No. 62/036,577
Title: SYNERGISTIC TUMOR TREATMENT WITH IL-2, A THERAPEUTIC ANTIBODY, AND AN IMMUNE CHECKPOINT BLOCKER. Filing Date: August 12, 2014.

U.S. Patent Application No. 14/304,438
Title: SYNERGISTIC TUMOR TREATMENT WITH EXTENDED-PK IL-2 AND ADOPTIVE CELL THERAPY. Filing Date: June 13, 2014.

Graduate Fellowships

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| NSF Graduate Research Fellow | 2010-2013 |
| Edward Walsh Memorial Presidential Fellow for Chemical Engineering | 2009-2010 |

Undergraduate Research Scholarships

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| Nathan and Violet David Research Scholar | 2003-2004 |
| Guidant Research Scholar | 2002 |

Honor Societies and Student Organizations

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| Chemical Engineering Graduate Student Council | 2010-2011 |
| Bioengineering Honor Society | 2003-2004 |
| Phi Beta Kappa | 2003-2004 |
| Golden Key Honor Society | 2002-2004 |
| Tau Beta Pi | 2002-2004 |
| Pre-Med Honor Society | 2001-2004 |
| Cal Lightweight Crew | 2001-2002 |
| Kappa Sigma | 2000-2004 |

Awards

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| Edward W Merrill Outstanding Teaching Assistant Award | 2012 |
| Tau Beta Pi Scholar | 2003-2004 |
| Kappa Sigma Scholarship-Leadership Award | 2003 |
| Robert C Byrd Scholar | 2000-2004 |
| Cal Alumni Leadership Award | 2000-2003 |

Professional Memberships

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| SITC | 2013-2015 |
| AIChE | 2008-Present |
| ACS | 2008-Present |

Volunteer Work

Veterans Upward Bound Tutor
2011-2012

Tutored military veterans in college preparatory math skills through the Suffolk University Veterans Upward Bound Program.

Junior Achievement High School Volunteer

2005

Designed and taught a course on basic business management. Assisted the students in forming their own one-day business venture.

Berkeley High School Tutor

2003

Individually tutored students with learning disabilities. Acted as a teaching assistant for an introductory chemistry class.