

# Cary F Opel

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<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**

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 CD8 $\alpha$ <sup>+</sup> 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

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

NSF Graduate Research Fellow

2010-2013

Edward Walsh Memorial Presidential Fellow for Chemical Engineering

2009-2010

## Undergraduate Research Scholarships

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

## Honor Societies and Student Organizations

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

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

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.