Christopher Bourne
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Education

Graduate Student, Doctor of Philosophy, Immunology and Microbial Pathogenesis — **2017- Expected Graduation 2022-2023**
Scheinberg Lab (MSKCC)
Weill Cornell Medicine, New York, NY

Bachelor of Arts, Biology (Honors) — **Graduated: May 2017**
Minor in Spanish (Honors)
Bachelor of Arts, Spanish
Swarthmore College, Swarthmore, PA

Experience

Graduate Student — 07/2017 – present
Scheinberg Lab
Weill Cornell Medicine/ Sloan-Kettering Institute, New York, NY

Cancer immunotherapy is an emerging field which manipulates the immune system to fight cancer. My thesis work addresses two questions: How can CAR T cells be used for targeted delivery of chemotherapeutics? How do various chemotherapeutics affect cancer cell immunogenicity?

CAR T cell for drug delivery:
T cells are a form of adoptive immunotherapy where a patients' T cells are engineered *ex vivo* to eliminate cancer cells. While successful in certain blood cancers, CAR T cells have been unsuccessful against solid tumors. Chemotherapeutics have shown efficacy against solid tumors but patients relapse and experience drug-related toxicity. CAR T cells are good drug delivery vehicles because they localize in tumors. I am developing CAR T cells for drug delivery using enzyme-prodrug platforms, which our lab named Synthetic Enzyme-Armed KillER T cells (SEAKER).

Design CAR T cell platforms that secrete enzymes which can unmask prodrugs of toxic agents.
Develop proof-of-concept *in vitro* models to test enzyme accumulation and tumor lysis of SEAKER cell.
Establish *in vivo* tumor models to characterize SEAKER cell bio-distribution and efficacy in xenograft and syngeneic models.

Chemotherapeutics and cancer cell immunogenicity:
Drug treatments that target overactive cancer processes show efficacy in patients, but relapse is common. Chemotherapeutic treatments can lead to upregulation of seemingly unrelated immune response pathways in cancer cells. Furthermore, chemotherapeutics may generate neoantigens in cancer cells for targeting with immunotherapy. I am elucidating how drugs that target RET/ALK, epigenetic, and cell cycle pathways impact cancer cell antigen presentation and neoantigen generation. This will inform rational combinations of chemotherapeutics and immunotherapeutic.

Develop clinically relevant drug treatment models in vitro.
Evaluate antigen presentation pathways using Western blot, qRT-PCR and flow cytometry.
Perform cell growth and viability assays on drug-treated cells.
Lysis and cytokine assays to test the effect of drugs on cancer cell immunogenicity.

Student Researcher — 03/2015 – 05/2017
Swarthmore College, Swarthmore, PA

The fruit fly, *Drosophila melanogaster*, tracheal system is an excellent model for understanding tubulogenesis and branching morphogenesis. The tracheal terminal cell forms a lumen within itself without junctions. "Seamless" lumens without junctions are found extensively throughout human vasculature. Terminal cell tubulogenesis is dependent on vesicle trafficking. The objective of my project was to determine the role of early secretory pathway proteins in the

formation of the lumen and branching morphogenesis of the terminal cell. I performed an RNAi screen on *Drosophila melanogaster* larvae. Using confocal microscopy, I characterized phenotypes in early secretory pathway protein knock-down terminal cells. I also generated mosaic mutant clones in the tracheal system using sophisticated *Drosophila* breeding techniques for secretory pathway proteins.

Summer Intern 05/2014 - 08/2014
Purdue Pharma L.P., Cranbury, NJ

The goals of this project were to identify novel opioid compounds that could provide analgesia without the negative side effects typically associated with opioids such as addiction, respiratory depression, and constipation. I performed a high-throughput screen of compounds to identify ones that signaled through desired signal transduction pathways. I also worked alongside senior scientists to develop a plan for genotyping newly acquired mouse strains. At the completion of my summer, I presented my work to the Research and Development department.

Academic Poster, Presentations and Achievements

Graduate:
Oral Presentation at American Society for Gene and Cellular Therapy, Virtual, May 2020
Mechanisms of Adoptive T cell micropharmacies

Undergraduate:
Honors Thesis: Early Secretory Events Impact Seamless Tubulogenesis and Branching Morphogenesis in *Drosophila* Terminal Cells. Thesis advisor: Dr. Jodi Schottenfeld-Roames (May 2017)

Poster at American Society for Cell Biology, San Diego, CA, December 2015
Early Secretory Events Impact Seamless Tubulogenesis and Branching Morphogenesis in *Drosophila* Terminal Cells
Authors: Chris Bourne, Daniel Lai, Jodi Schottenfeld-Roames

Coursework

Graduate: Quantitative Methods in Biology, Tissue Immunity, Integration of Metabolism and Immunity, Fundamentals of Immunology
Undergraduate: Developmental Biology, Cellular Biology, Cells to Organs Seminar, Animal Behavior, Biomechanics Seminar, Calculus, Statistical Methods, Organic Chemistry 1.

Expertise and Techniques

Immunology, Gene Therapy, Tumor Immunology, Cancer Immunotherapy, CAR T cells, Chemotherapeutics, Drug Delivery, Drug Design, Biologics, Molecular Pharmacology, Data science, Computer Programming, Sequencing Analysis

Cell culture, primary lymphocyte culture, molecular cloning, multi-dimensional flow cytometry, retroviral transduction, Western blot, immunoprecipitation, qRT-PCR, Flow Cytometry, Mouse handling, Xenograft mouse cancer models, Syngeneic mouse cancer models, Bioluminescent tumor imaging, Confocal Microscopy

Computer Programming: Proficient in: R, GGplot2, R Studio, Python, PANDAS/Matplotlib, Jupyter Notebook, BASH, Bowtie2

Mentor and Leadership Roles

Diversity Consultant for the Social Justice and Anti-Racism Task Force (2020)

During the Summer of 2020, Black Lives Matter protests lead to a collective self-reflection on race. I organized a petition, alongside other graduate students who run Diversity, Equity, and Inclusion initiatives, to the Weill Cornell Graduate School to address the issues of systemic racism within our institution. Among the demands were unconscious

bias training, renewed support for DEI initiatives at the institution, and adjustments to faculty hiring to promote equity. As a result, I consulted the institution as a member of a task force which included graduate school administration, faculty, postdocs, and graduate students.

Graduate assistant for the virtual ACCESS summer undergraduate program for underrepresented students at Weill Cornell (Summer 2020).

Due to COVID-19, the ACCESS summer program (mentioned below), was completely virtual. I served as a Graduate Assistant for the ACCESS program. Before the summer program begun, I helped select applicants. Additionally, I helped plan a virtual curriculum for students that included research seminars from Weill Cornell trainees, and grant writing. I helped pair interns with appropriate mentors. During the program, I lead journal clubs, planned virtual bonding events for the students, executed a round-table discussion between ACCESS students and high school summer interns, read and revised NSF-GFRP proposals, and critiqued student oral presentations.

Selected as Teacher Assistant for the graduate Fundamentals of Immunology course (2018-2020).

I have served as a Teacher's assistant (TA) for the first year
Fundamental Immunology course. Being a teacher's assistant is not mandatory for graduate students at Weill Cornell. However, students who excel in their class may be asked to TA subsequent courses. For two years, I have served as TA, leading primary literature discussions, hosting exam review sessions, and orchestrating the logistics of the course. This

Graduate assistant for the ACCESS summer undergraduate program for underrepresented students at Weill Cornell (Summer 2019).

I participated in the ACCESS program for undergraduate students from diverse backgrounds at Weill Cornell. This program provides a summer research experience for undergraduates who are prospective PhD students. I served as a graduate assistant, organizing the 2019 summer program. My responsibilities to prepare for the program included reviewing applications to select our cohort and matching students with appropriate labs. My responsibilities during the summer program were organizing journal clubs for the students with Weill Cornell faculty, arranging mock interviews, participating in question and answer sessions and organizing social events for our cohort. At the conclusion of the program, the ACCESS program attends the Leadership Alliance conference, where I moderated a presentation session. Additionally, I mentored one of the ACCESS students in the lab over the summer.

Funding

1 F31 1F31CA254331-01 7/7/2020-7/6/2023
NCI $136,560.00
CAR T cells for tumor drug delivery

CAR T cells are a novel treatment modality for patients with certain B cell cancers, but CAR T cells have not seen comparable efficacy in solid tumors. Our lab developed SEAKER CAR T cells, which are CAR T cells capable of delivering chemotherapeutic agents to tumors. The current proposal addresses the mechanisms of SEAKER cell drug delivery to tumors using syngeneic mouse models for eventual clinical application to various solid tumors, such as ovarian cancer.
Role: Principle Investigator

Publications

Gardner, Thomas J., **Christopher M. Bourne**, Megan M. Dacek, Keifer Kurtz, Manish Malviya, Leila Peraro, Pedro C. Silberman, et al. 2020. "Targeted Cellular Micropharmacies: Cells Engineered for Localized Drug Delivery." *Cancers* 12 (8): 2175.

In this review, our lab summarized previous findings using cellular therapies to deliver orthogonal therapuetic payloads to tumors.

Claire Y Oh, Martin G Klatt, **Christopher Bourne**, Tao Dao, Megan M Dacek, Elliott J Brea, Sung Soo Mun, Aaron Y Chang, Tatyana Korontsvit and David A Scheinberg. 2019. ALK and RET inhibitors promote HLA class I antigen presentation and unmask new antigens within the tumor immunopeptidome. *Cancer Immunol Res.*
DOI: 10.1158/2326-6066.CIR-19-0056

T cell immunotherapies are often thwarted by the limited presentation of tumor-specific antigens abetted by the downregulation of human leukocyte antigen (HLA). We showed that drugs inhibiting ALK and RET produced dose-related increases in cell surface HLA in tumor cells bearing these mutated kinases in vitro and in vivo, as well as elevated transcript and protein expression of HLA and other antigen processing machinery. Subsequent analysis of HLA presented peptides after ALK and RET inhibitor treatment identified large changes in the immunopeptidome with the appearance of hundreds of new antigens, including T cell epitopes associated with impaired peptide processing (TEIPP) peptides. I helped uncover the mechanism through which ALK and RET inhibitors upregulated HLA expression during the review process.

Pre-print Manuscripts

Angel Charles*, **Christopher Bourne***, Zita E. Aretz, Sung S. Mun, Tanya Korontsvit, Tao Dao, Martin G. Klatt, and David A. Scheinberg. 2020. "Low-Dose CDK4/6 Inhibitors Induce Presentation of Pathway Specific MHC Ligands as Targets for Cancer Immunotherapy." *bioRxiv*.
https://doi.org/10.1101/2020.06.18.157800.
* These authors contributed equally

CDK4/6 inhibitors block cell cycle, and are used to treat breast cancer. We found that treatment of breast cancer cells with CDK4/6 inhibitors leads to presentation of cell-cycle derived peptides on MHC. These novel peptides are a result of increased ubiquitination of cell-cycle proteins. Drug-induced peptide-MHC complexes could be suitable targets for immunotherapy.