CURRICULUM VITAE

STEPHEN M. HATFIELD, Ph.D.

s.hatfield@neu.edu

IMPACT - SUMMARY OF MAJOR ACCOMPLISHMENTS

- Provided proof of principle that drug-mediated elimination of tumor-protecting hypoxic areas enables anti-tumor T cells to reject tumors.
- Publications in ***Science Translation Medicine*** and the ***Journal of Molecular Medicine*** were the first genetic and pharmacological in vivo evidence of a novel method to weaken immunosuppressive intratumoral hypoxia by oxygenation of tumors.
- The impact of these studies established the industry of repurposing anti-hypoxia and oxygenation agents for cancer immunotherapy to oxygenate tumors directly or to target hypoxic areas.
- These studies generated great excitement by experts and public interest as reflected in press releases, editorials, commentaries and subsequent evaluations in Nature Reviews Cancer, describing the work as *"groundbreaking"* and *"landmark"*. Commentaries appeared in top-tier journals and major media outlets including: Nature Reviews Cancer, Cancer Cell, Science cover (online), Associated Press "The Big Story", NY Times, Washington Post, BBC, NBC, NPR, and others.

EXPERIENCE

01/2020-present

NORTHEASTERN UNIVERSITY Boston, MA
ASSISTANT PROFESSOR, **Department of Pharmaceutical Sciences**

03/2017-12/2019

NORTHEASTERN UNIVERSITY Boston, MA
PRINCIPAL RESEARCH SCIENTIST, **New England Inflammation & Tissue Protection Institute**
Laboratory of Dr. Michail Sitkovsky

- Lead investigator on *in vivo/in vitro/ex vivo* tumor immunology assays of immune suppression in the tumor microenvironment (TME) with particular focus on T cells, NK cells, T regulatory cells, and MDSCs
- Led and supervised all projects and collaborations, performed and analyzed experiments, and authored manuscripts resulting in peer-reviewed publications in top-tier journals
- Selected, recruited and trained the most talented and competitive graduate and undergraduate students for research within the institute
- Leveraged unique expertise in the design and performance of assays of tumor immunology in combination with anti-hypoxia-adenosinergic treatments to develop creative reasoning to increase the probability of receiving grants and funding from industry
- Provided and analyzed key data resulting in sponsored research agreements with major biopharmaceutical companies
- Developed models to recapitulate the hypoxic and adenosine-rich TME in 2-D and 3-D cultures

01/2012-03/2017

NORTHEASTERN UNIVERSITY Boston, MA
ASSOCIATE RESEARCH SCIENTIST, **New England Inflammation & Tissue Protection Institute**

- Led projects and collaborations, performed and analyzed experiments, and authored manuscripts resulting in peer-reviewed publications in high impact journals
- Critical member of the team establishing that immune suppression can be prevented pharmacologically by selective antagonism of the A2A adenosine receptor (A2AR) using small molecule drugs
- Provided detailed proposals, experimental design, reasoning, and preliminary data to funding institutions
- Co-authored, served as Key Personnel, processed grant submissions and prepared all grant progress reports

• Developed and reviewed all IACUC animal protocols
• Supervised graduate and undergraduate student researchers

COURSE LECTURER
• TRACE - Instructor Effectiveness Rating of 4.9/5
• Developed and instructed both traditional lecture and online courses at the undergraduate and graduate level
Biotechnology/Bioinformatics Program
- Molecular Cell Biology for Biotechnology (Traditional and online course)
- Molecular Cell Biology for Bioinformatics (Online course)
Biology Department
- Introduction to Immunotherapies of Cancer
- Cell and Molecular Biology
- Genetics and Molecular Biology Laboratory
- Biochemistry Methods Laboratory
- Microbiology Laboratory (1-3)

09/06-01/2012

NORTHEASTERN UNIVERSITY Boston, MA
GRADUATE STUDENT/LAB MANAGER, **New England Inflammation & Tissue Protection Institute**

- Investigated anti-hypoxia-adenosinergic approaches to cancer immunotherapy including physiological and immunological checkpoint inhibitors
- Examined the role of respiratory hyperoxia in preventing the inhibition of endogenous or adoptively transferred T cells and NK cells
- Established and maintained long-term interactions with key collaborating scientists
- Managed lab inventory, safety protocols, radiation and hazardous waste, general lab maintenance, etc.
- Supervised undergraduate researchers

06/05-09/06

THE UNIVERSITY OF NEW HAMPSHIRE Durham, NH
ASSISTANT RESEARCH SCIENTIST/TECHNICIAN
Laboratory of Dr. Estelle Hrabak

- Investigated the sub-cellular localization of calcium-dependent protein kinases in *Arabidopsis Thaliani*
- Managed lab supply inventory, radiation and hazardous waste and general lab maintenance
- Supervised undergraduate researchers

PATENTS

- Issued USA Patent: **Method for generation of broadly neutralizing anti-pathogen antibodies**
  Inventors: Michail Sitkovsky, Robert Abbott, Stephen Hatfield

- Pending USA Patent: **Method for generation of oxygen-generating cryogels**
  Inventors: Sidi Bencherif, Thibault Colombani, Michail Sitkovsky, Adnan Memic, Stephen Hatfield

LABORATORY EXPERTISE

Immunology/Oncology *In vivo/in vitro/ex vivo* cancer immunology assays, adoptive T cell and NK cell therapy, cancer vaccines, experimental/spontaneous metastasis, orthotopic tumor models, intracranial/intradermal transplantable tumor models, isolation/culture/analysis of tumor infiltrating lymphocytes, CTL assays, suppressor assays

General Multi-parameter flow cytometry, histology, immunohistochemistry, fluorescent/confocal microscopy, ELISA, ELISPOT, multiplex cytokine assays, biochemical assays, cell sorting/purification, cell culture (2D/3D), mixed lymphocyte

culture, immunoblotting, molecular cloning, PCR/RT-PCR, animal models of inflammation and infectious diseases

CONFERENCES, TRAINING, AND AWARDS

1. ***Vaccine Forum 2019.*** Valencia, Spain. May 8-9, 2019. Invited Speaker.
2. ***Drug Discovery Chemistry.*** San Diego, Ca: April 8-12, 2016. Invited Speaker.
3. ***4th Annual Immuno-Oncology Summit.*** Boston, Ma: Aug 29-Sep. 2, 2016. Invited Speaker: "Anti-Hypoxia-A2-Adenosinergic Co-Adjuvants to Enable the Full Anti-Tumor Capacities of T- and Natural Killer Cells During Immunotherapies of Cancer"
4. ***The New England Immunology Conference.*** Woods Hole, Ma: October 17-18, 2015. Invited Speaker: "Respiratory hyperoxia reprograms the immunosuppressive metabolism in the hypoxic tumor microenvironment and enhances T and NK cell responses". **NEIC 2015 Young Investigator Award**
5. ***Purines.*** Bonn, Germany: July 23-27, 2014. Invited Speaker: "The anti-hypoxia adenosinergic approach to the immunotherapy of cancer"
6. ***Tumor Models for Cancer Immunotherapy.*** World Pharma Congress. Boston, Ma: May 21-23, 2014. Presentation: "A2A adenosine receptor gene-deletion or selective antagonism liberates anti-tumor CD8 T cells from tumor-induced suppression"
7. ***Immunology.*** American Association of Immunologists. May 3-7, 2014. Honolulu, Hawaii
8. ***BD Biosciences FACSAriaII / BD FACSAria III Operator Course.*** San Jose, California: Nov. 16-20, 2015.
9. ***Flocyte Regional Flow Cytometry Training Program.*** June 10-12, 2014. UMass Medical School, Worcester, MA

EDUCATION

NORTHEASTERN UNIVERSITY Boston, MA
Ph.D. in Biology
Graduated Jan, 2012

UNIVERSITY OF NEW HAMPSHIRE Durham, NH
B.S. in Molecular, Cellular, and Developmental Biology
Graduated May, 2005

RESEARCH MENTORING

PH.D./M.S MENTORING
Student

1. Katarina Veszeleiova
2. Joseph Steingold
3. Mayuri Shukla
4. Divya Parikh
5. Monica Kavarthapu
6. Murillo Silva
7. Shalini Sethumadhavan
8. Robert Abbott
9. Somya Jain
10. Priyal Desai
11. Radhika Barve

UNDERGRADUATE MENTORING
Student

1. Camille Bahr
2. Nuria Romero
3. Ashley Apro
4. Alexis Bloedel
5. Laura Rosenberg
6. Michael Mallouh
7. Olivia Sears
8. Thao Nguyen
9. Jaclyn Long
10. Ryan Cannici
11. Phaethon Philbrook
12. Rachel Debarge
13. Gemma Carter
14. Molly Thayer
15. Peter Georgiev

PUBLICATIONS

1. **Hatfield S**, Veszeleiova K, Steingold J, Sethuraman J, Sitkovsky M. **Mechanistic Justifications of Systemic Therapeutic Oxygenation of Tumors to Weaken the Hypoxia Inducible Factor 1α-Mediated Immunosuppression.** Adv Exp Med Biol. 2019;1136:113-121. doi: 10.1007/978-3-030-12734-3_8.

2. Sorrentino C, Hossain F, Rodriguez PC, Sierra RA, Pannuti A, **Hatfield S**, Osborne BA, Minter LM, Miele L, Morello S. **Adenosine A2A Receptor Stimulation Inhibits TCR-Induced Notch1 Activation in CD8+T-Cells.** Front Immunol. 2019 May 3;10:935. doi: 10.3389/fimmu.2019.00935. eCollection 2019.

3. Kjaergaard J*, **Hatfield SM***, Jones G, Ohta A and Sitkovsky M. **A2A adenosine receptor gene-deletion or synthetic A2A antagonist liberate tumor-reactive CD8+ T-cells from tumor-induced immunosuppression.** J Immunol. 2018 Jul 15;201(2):782-791. doi: 10.4049/jimmunol.1700850. Epub 2018 May 25.
   ***Authors contributed equally**

4. Silva M, Nguyen TH, Philbrook P, Chu M, Sears O, **Hatfield S**, Abbott RK, Kelsoe G, Sitkovsky MV. **Targeted Elimination of Immunodominant B Cells Drives the Germinal Center Reaction toward Subdominant Epitopes.** Cell Rep. 2017 Dec 26;21(13):3672-3680. doi: 10.1016/j.celrep.2017.12.014.

5. Yuan G, Jankins TC, Patrick CG Jr, Philbrook P, Sears O, **Hatfield S**, Sitkovsky M, Vasdev N, Liang SH, Ondrechen MJ, Pollastri MP, Jones GB. **Fluorinated Adenosine A2A Receptor Antagonists Inspired by Preladenant as Potential Cancer Immunotherapeutics.** Int J Med Chem. 2017;2017:4852537. doi: 10.1155/2017/4852537. Epub 2017 Oct 19.

6. Sethumadhavan S, Silva M, Philbrook P, Nguyen T, **Hatfield SM**, Ohta A, Sitkovsky MV. **Hypoxia and hypoxia- inducible factor (HIF) downregulate antigen-presenting MHC class I molecules limiting tumor cell recognition by T cells.** PLoS One. 2017 Nov 20;12(11):e0187314. doi: 10.1371/journal.pone.0187314. eCollection 2017.

7. Abbott RK, Silva M, Labuda J, Thayer M, Cain DW, Philbrook P, Sethumadhavan S, **Hatfield S**, Ohta A, Sitkovsky M. **The GS Protein-coupled A2a Adenosine Receptor Controls T Cell Help in the Germinal Center.** J Biol Chem. 2017. PMID: 27974461

8. Abbott RK, Thayer M, Labuda J, Silva M, Philbrook P, Cain DW, Kojima H, **Hatfield S**, Sethumadhavan S, Ohta A, Reinherz EL, Kelsoe G, Sitkovsky M. **Germinal Center Hypoxia Potentiates Immunoglobulin Class Switch Recombination.** J Immunol. 2016 Nov. PMID: 27798169

9. **Hatfield SM**, Sitkovsky M. **A2A Adenosine Receptor antagonists to weaken the hypoxia-HIF-1α driven immunosuppression and improve immunotherapies of cancer.** Curr Opin Pharmacol. 2016 Aug;29:90-6. doi: 10.1016/j.coph.2016.06.009. Epub 2016 Jul 17. PMID: 27429212

10. **Hatfield SM**, Sitkovsky M**. Oxygenation to improve cancer vaccines, adoptive cell transfer and blockade of immunological negative regulators.** Oncoimmunology. May 2015 DOI:10.1080/2162402X.2015.1052934

11. **Hatfield SM**, Kjaergaard J, Lukashev D, Schreiber TH, Belikoff B, Abbott R, Sethumadhavan S, Philbrook P, Ko K, Cannici R, Rodig S, Kutok JL, Karger B, Podack ER, Ohta A, Sitkovsky M. **Immunological mechanisms of the anti- tumor effects of supplemental oxygenation.** *Science Translational Medicine*, 2015 Mar 4;7(277):277ra30. doi: 10.1126/scitranslmed.aaa1260.

12. **Hatfield SM**, Kjaergaard J, Lukashev D, Belikoff B, Schreiber TH, Sethumadhavan S, Abbott R, Philbrook P, Thayer M, Shujia D, Rodig S, Kutok JL, Ren J, Ohta A, Podack ER, Karger B, Jackson EK, Sitkovsky M. **Systemic oxygenation weakens the hypoxia and hypoxia inducible factor 1α-dependent and extracellular adenosine- mediated tumor protection.** J Mol Med; 2014 Aug 15. PMID: 25120128

13. Sitkovsky MV, **Hatfield S**, Abbott R, Belikoff B, Lukashev D, Ohta A**. Hostile, hypoxia-A2-adenosinergic tumor biology as the next barrier to overcome for tumor immunologists.** Cancer Immunol Res. 2014 Jul;2(7):598-605. PMID: 24990240

14. Georgiev P, Belikoff BG, **Hatfield S**, Ohta A, Sitkovsky MV, Lukashev D. **Genetic deletion of the HIF-1α isoform I.1 in T cells enhances antibacterial immunity and improves survival in a murine peritonitis model.** Eur J Immunol 2013; 43:655-66. PMC 3757952

15. Thomas R, Lee J, Chevalier V, Sadler S, Selesniemi K, **Hatfield S**, Sitkovsky M, Ondrechen MJ, Jones GB. **Design and evaluation of xanthine-based adenosine receptor antagonists: potential hypoxia targeted immunotherapies.** Bioorg Med Chem 2013; 21:7453-64. PMID: 24126093

16. Belikoff B, **Hatfield S**, Georgiev P, Ohta A, Lukashev D, Buras JA, Remick DG, Sitkovsky M. **A2B Adenosine Receptor Blockade Enhances Macrophage-Mediated Bacterial Phagocytosis and Improves Polymicrobial Sepsis Survival in Mice.** J Immunol 2011;186:2444-53. PMC 3708265

17. Belikoff B, **Hatfield S**, Sitkovsky M, Remick DG. **Adenosine negative feedback on A2A adenosine receptors mediates hyporesponsiveness in chronically septic mice.** Shock 2011;35:382-7. PMC 3693562

18. **Hatfield S**, Belikoff B, Lukashev D, Sitkovsky M, Ohta A. **The antihypoxia-adenosinergic pathogenesis as a result of collateral damage by overactive immune cells.** J Leukoc Biol 2009;86:545-8. PMID: 1956