JENNIFER L GORI, PhD

SUMMARY OF QUALIFICATIONS

- Proven experience developing CRISPR editing, viral and non-viral gene and cell therapy platforms for therapeutic application with 15+ years of experience in stem cell biology, immunology, preclinical models, and translational research
- Passionate and successful in building and leading teams, and collaborations with scientists with diverse expertise
- Highly skilled at creative strategy development and problem solving with an eye on clinical translation

EXPERIENCE

OBSIDIAN THERAPEUTICS, CAMBRIDGE, MA (2018-), Associate Director in Cell Therapy, Head of Pharmacology

- Lead product strategy group to build our pipeline of regulated cell and gene therapy products
- Scout and secure academic collaborators and KOLs to accelerate proof of concept studies with new therapeutic modalities
- Advise program teams on identification of key decision points and go/no go decisions, on preclinical model study designs, and to define milestones and timelines critical for program advancement toward IND-enabling studies
- Direct, manage, and develop team of 6 scientists on immunotherapy and cell therapy preclinical studies toward supporting executing of IND-enabling studies for concurrent cell therapy programs

EDITAS MEDICINE, INC., CAMBRIDGE, MA (2014-2018), Senior Scientist (2017), Scientist III (2015), Scientist II (2014)

Program and project leadership

- Proposed, established, championed strategy and directed the preliminary cell biology and preclinical studies toward development of a gene-edited HSC product to treat Sickle Cell Disease (EDIT-301)
- Lead cross-functional team for CRISPR gene-edited hematopoietic stem cell (HSC) therapy program which included establishing a target product profile, work plans and timelines, coordinating cross-functional team meetings and activities, identifying key inflection points, gaps, milestones, and criteria for drug candidate selection for a CRISPR gene-edited HSC cell therapy program
- Strategized and developed long-range pipeline and product arc for *ex vivo* cell therapy programs
- Directed, managed, developed team of 5 scientists working on the HSC cell therapy program (PhD level and MS/BS level)

Drug discovery

- Identified lead guide (g)RNAs in $CD34^+$ HSCs and T cells that target disease-relevant genomic target sites
- Validated candidate gRNA molecules in human $CD34^+$ HSCs and T cells for genotype to phenotype correlation
- Evaluated persistence of gene editing and effect of editing on HSC function after transplantation

Exploratory research and platform enablement

- Identified market opportunities for gene-edited human $CD34^+$ HSC and T cell products
- Strengthened intellectual property position of company as inventor and writer of patent applications
- Directed research on gene disruption and targeted integration in human $CD34^+$ HSCs
- On-boarded research grade CRISPR/Cas9 tools and refined their application for use in human $CD34^+$ HSCs and T cells
- Developed method to monitor for clonal expansion of gene-edited human $CD34^+$ HSCs *in vivo*
- Established lab, mouse facility, protocols for gene editing and transplantation of human $CD34^+$ HSCs
- Established, managed sponsored research agreements and contracts with academic and industry and CROs

FRED HUTCH CANCER RESEARCH CENTER, SEATTLE, WA (2010-2014), Associate in Clinical Research

Mentor: Dr. Hans-Peter Kiem, Co-mentor: Dr. Shahin Rafii

Generation of long-term engrafting hematopoietic stem cells from induced pluripotent stem cells

- Developed novel strategy to produce the first reported long-term engrafting HSCs from iPSCs
- Managed and trained junior scientists (three technicians, one graduate student)
- Directed iPSC-derived HSC transplantation studies in immunodeficient mice and nonhuman primates

Translation of gene modified HSC products in animal models and in human patient

- Directed five novel gene-modified cell product transplantation in mice, dogs, and primates
- Contributed to data acquisition/analysis of samples from Glioblastoma patients after HSC gene therapy (NCT00669669)

Establishment of pluripotent stem cell laboratory

- Managed and contributed to several preclinical studies and extra-mural scientific collaborations
- Developed/validated protocols for iPSC differentiation into blood ($CD34^+$, lymphoid, myeloid cells), liver, and cardiac cells

ICAHN SCHOOL OF MEDICINE, MOUNT SINAI, NEW YORK, NY, (2009-2010), Postdoctoral Fellow

Development of gene-modified natural kill cell therapy for the treatment of HCV

- Developed research plan and conducted proof of concept studies for anti-HCV human iPSC-derived NK cell therapy

UNIVERSITY OF MINNESOTA, MINNEAPOLIS, MN (2005-2008), Graduate Student Research Assistant

Hematopoietic stem cell gene therapy

- Completed 3 aims of NIH R01 grant, resulting in 3 publications in peer-reviewed journals
- Constructed and prepared lentivirus vectors and evaluated transgene expression in lentivirus-transduced mouse and human HSCs
- Performed hematopoietic differentiation and transplantation of pluripotent stem cell derived $CD34^+$ cells

EDUCATION

UNIVERSITY OF MINNESOTA, Minneapolis, MN, **PhD Microbiology, Immunology, Cancer Biology, 2008**
Thesis: Methotrexate resistance gene transfer in stem cells, Advisor: Dr. R. Scott McIvor, Co-advisor: Dan Kaufman
Microbiology, Immunology & Cancer Biology Grant Award Recipient, Graduate School Fellowship, GPA: 3.9/4.0

SMITH COLLEGE – Northampton, MA**, B.A. Biochemistry,** Cum Laude, Dean's List, GPA: 3.6/4.0**,**

INVITED LECTURES

Exogenous Regulation of Protein Expression for Control of Gene and Cell Therapies. Genome Writer's Guild Conference, Minneapolis, MN (2018)

CRISPR-mediated genome editing for the treatment of β-Hemoglobinopathies. Scientific Symposium on Genome Editing: Therapeutic Editing of the Human Genome, ASGCT 20th Annual Meeting, Chicago, IL (2017).

Advancing CRISPR-Cas9 Technology Platform for Therapeutic Applications. Bioprocess International Conference and Exposition. Boston, MA (2015).

Vascular niche promotes hematopoietic multipotent progenitor formation from pluripotent stem cells. Nonhuman primate iPSC Workshop, National Heart, Blood, and Lung Institute, National Institutes of Health, Bethesda, MD (2015).

Vascular niche induction of hematopoietic stem and progenitor cells from monkey induced pluripotent stem cells. Ansary Stem Cell Institute, Weill Cornell Medical College, New York, NY (2013).

Robust differentiation and viral infection of pigtail macaque induced pluripotent stem cell-derived hepatic and hematopoietic cells. NIH Symposium: Improving animal models for regenerative medicine. National Institutes of Health Bethesda, MD (2012).

PUBLICATIONS

A. Manuscripts in Peer-Reviewed Journals

1. **Gori JL**, Butler JM, Kunar B, Poulos MG, Ginsberg M, Nolan DJ, Norgaard ZK, Adair JE, Rafii S, Kiem HP. Endothelial Cells Promote *Expansion of Long-Term Engrafting Marrow Hematopoietic Stem and Progenitor Cells in Primates.* Stem Cells Transl Med. 6(3):864-76 (2017).
2. **Gori JL,** Hsu PD, Maeder ML, Shen S, Welstead GG, Bumcrot D. *Delivery and specificity of CRISPR-Cas9 genome editing technologies for gene therapy.* Human Gene Therapy. 26(7):443-51 (2015).
3. **Gori JL**, Butler JM, Chan YY, Chandrasekaran D, Poulos MG, Ginsberg M, Nolan DJ, Elemento O, Wood BL, Adair JE, Rafii S, Kiem H-P. *Vascular niche promotes hematopoietic multipotent progenitor formation from pluripotent stem cells.* Journal of Clinical Investigation. 125(3):1243-54 (2015).
4. Adair JE, Johnston S, Mrugala M, Beard VC, Guyman L, Baldock A, Bridge C, Hawkins-Daruud A, **Gori JL**, Born D, Gonzalez-Cuyer L, Silbergeld D, Rockne R, Storer B, Rockhill J, Swanson K, Kiem H-P. *Gene therapy enhances chemotherapy tolerance and efficacy in glioblastoma patients.* Journal of Clinical Investigation. 124(9):4082-92 (2014).
5. **Gori JL,** Beard BC, Williams NP, Ironside C, Swanson D, McIvor RS, Kiem H-P. *In vivo protection of activated Tyr22-DHFR gene-modified canine T lymphocytes from methotrexate.* Journal of Gene Medicine. 15(6-7):233-41 (2013).
6. Sourrisseau M, Goldman O, He W, **Gori JL,** Kiem H-P, Gouon-Evans V, Evans MJ. *Pigtail macaque induced pluripotent stem cell-derived hepatocytes support hepatitis C virus infection.* Gastroenterology. S0016-5085(13):01077-9 (2013).
7. **Gori JL**, Chandrasekaran D, Kowalski JP, Adair JE, Beard BC, D'Souza SL, Kiem H-P. *Efficient generation, purification, and expansion of CD34$^+$ hematopoietic progenitor cells from nonhuman primate induced pluripotent stem cells.* Blood. 120(13):e35-44 (2012).
8. **Gori JL,** Beard BC, Ironside C, Karponi G, Kiem H-P. *In vivo selection of autologous MGMT gene-modified cells following reduced-intensity conditioning with BCNU and temozolomide in the dog model.* Cancer Gene Therapy. 19(8):523-9 (2012).
9. Zhong B, Watts KL, **Gori JL**, Wohlfardt ME, Enssle J, Adair JE, Kiem H-P. *Safeguarding nonhuman primate iPS cells with suicide genes.* Molecular Therapy. 19(9):1667-75 (2011).
10. **Gori JL,** McIvor RS, Kaufman DS. *Methotrexate supports in vivo selection of human embryonic stem cell-derived cells expressing dihydrofolate reductase.* Bioengineered Bugs. 1(6):434-436 (2010).
11. **Gori JL**, Tian X, Swanson D, Gunther R, Schultz L, McIvor RS, Kaufman DS. *In vivo selection of human embryonic stem cell-derived cells expressing methotrexate-resistant dihydrofolate reductase.* Gene Therapy. 17(2):238–249 (2010).
12. **Gori JL**, Podetz-Pedersen K, Swanson D, Karlen AD, Gunther R, Somia NV, McIvor RS. *Protection of mice from methotrexate toxicity by ex vivo transduction using lentivirus vectors expressing drug-resistant dihydrofolate reductase.* Journal of Pharmacology and Experimental Therapeutics. 322(3):989-997 (2007).
13. Converse A, Belur L, **Gori JL**, Liu G, Amaya F, Aguilar-Cordova E, Hackett PB, McIvor RS. *Counter selection and co-delivery of transposon and transposase functions for the study of Sleeping Beauty-mediated transposition in cultured mammalian cells.* Bioscience Reports. 24(6): 577-594 (2005).

B. Select Oral Abstract Presentations

1. Heath JM, Chalishazar A, Lee CS, Selleck W, Cotta-Ramusino C, Bumcrot B, **Gori JL.** CRISPR/Cas9 mediates highly efficient gene editing in long-term engrafting human hematopoietic stem/progenitor cells. American Society of Gene and Cell Therapy (ASGCT) 19th Annual Meeting, Washington DC (2016).
2. **Gori JL,** Butler JM, Chandrasekaran D, Nolan DJ, Ginsberg M, Elemento O, Adair JE, Rafii S, Kiem H-P. *Long-term engraftment and in vivo selection of hematopoietic stem/progenitor cells generated by vascular niche induction of induced*

pluripotent stem cells. Meritorious Abstract Travel Award, ASGCT 17th Annual Meeting, Washington DC (2014).

3. **Gori JL,** Butler JM, Ginsberg M, Nolan DJ, Adair JE, Rafii S, Kiem H-P. *Engraftment of gene-modified autologous hematopoietic stem/progenitor cells in the nonhuman primate after expansion on human vascular endothelium.* ASGCT 17th Annual Meeting, Washington DC (2014).
4. **Gori JL,** Butler JM, Chandrasekaran D, Beard BC, Nolan DJ, Ginsberg M, Adair JE, Rafii S, Kiem H-P. *In vivo selection and long-term engraftment of hematopoietic stem cells generated via vascular niche induction of nonhuman primate iPSCs.* American Society of Hematology (ASH) 55th Annual Meeting, New Orleans, LA (2013).
5. **Gori JL,** Beard BC, D'Souza SL, Kiem H-P. *Robust differentiation of hematopoietic progenitor cells from pigtail macaque induced pluripotent stem cells toward modeling human disease and stem cell therapies in vivo.* ASGCT, 15th Annual Meeting, Philadelphia, PA (2012).

C. Select Poster Presentations

1. Suri V and **Gori JL**. *Small molecule regulated cytokine expression enables potent and durable responses to engineered T cell therapy.* ASH 60th Annual Meeting, San Diego, CA.
2. Chalishazar A, Margulies CM, Nichanametla G, Labella J, Loveluck K, Viswanathan R, Heath JM, de Dreuzy E, Chang K, Jayaram H, Zuris J, Myer V, Albright C, Cotta-Ramusino C, **Gori JL**. *Expanding genome editing strategies in hematopoietic stem and progenitor cells for the treatment of hematologic disease*. ASH 59th Annual Meeting, Atlanta, GA.
3. Heath JM, Chalishazar A, Lee CS, Selleck W, Cotta-Ramusino C, Bumcrot B, **Gori JL**. *Precise and efficient CRISPR/Cas9 mediated gene editing in long-term engrafting human hematopoietic stem progenitor cells.* European Society of Gene and Cell Therapy (ESGCT) Annual Congress, Firenze, Italia (2016).
4. Heath JM, Chalishazar A, Lee CS, Selleck W, Cotta-Ramusino C, Bumcrot B, **Gori JL**. *Highly efficient CRISPR/Cas9 mediated gene editing in long-term engrafting human hematopoietic stem progenitor cells.* ESGCT Annual Congress, Firenze, Italia (2016).
5. **Gori JL**, Heath JM, Collins MA, Fang JW, Friedland AE, Welstead GG, Bumcrot D. *Efficient gene editing in hematopoietic stem progenitor cells with the CRISPR-Cas9 system.* ESGCT Annual Congress, Helsinki, Finland (2015).

D. Patent Applications *(inventor and author on all applications listed)*

1. WO/2016/182959 OPTIMIZED CRISPR/CAS9 SYSTEMS AND METHODS FOR GENE EDITING IN STEM CELLS
2. WO/2016/183236 CRISPR/CAS-RELATED METHODS AND COMPOSITIONS FOR TREATING HIV INFECTION AND AIDS
3. WO/2016/154596 CRISPR/CAS-RELATED METHODS, COMPOSITIONS AND COMPONENTS
4. WO/2016/154579 CRISPR/CAS-MEDIATED GENE CONVERSION
5. WO/2016/201047 CRISPR/CAS-RELATED METHODS AND COMPOSITIONS FOR IMPROVING TRANSPLANTATION
6. WO/2017/160890 CRISPR/CAS-RELATED METHODS AND COMPOSITIONS FOR TREATING BETA HEMOGLOBINOPATHIES
7. WO/2018/170184 SYSTEMS AND METHODS FOR THE TREATMENT OF HEMOGLOBINOPATHIES
8. WO/2018/209158 CRISPR/RNA-GUIDED NUCLEASE SYSTEMS AND METHODS

SCIENTIFIC SOCIETY AND COMMITTEE MEMBERSHIP

American Society of Hematology, Member since 2013

- Gene Therapy Committee Member and Abstract Coordinating Reviewer (2017)
- Gene Therapy Committee Member, Abstract Reviewer and Session Moderator (2015-2016)

American Society of Gene and Cell Therapy, Member since 2005

- Hematology/Immunology Committee Member and Abstract Reviewer (2015-Date) and Chair (2018-Date)
- New Investigator Committee Member (2014-Date)

European Society of Gene and Cell Therapy, Member since 2016
International Society of Stem Cell Research, Member since 2013
Society for the Immunotherapy of Cancer, Member since 2018

RESEARCH SKILLS

- ***Program Leadership -*** Coordination cross-functional team activities, timeline/milestone management, budget generation
- ***Scientific Communication*** - Data analysis and presentation [Microsoft Office, Graphpad Prism, Benchling], progress report, study report, grant and manuscript writing/editing, figure production [Adobe Design Suite]), patent application writing
- ***Drug Discovery*** - Establish criteria for lead discovery and progression from hit to lead validation for CRISPR-based cell therapies
- ***Molecular Biology*** - ddPCR, qPCR, sequencing, Southern blots, in vitro transcription, cloning
- ***Gene Editing*** - Gene editing of human T cells and $CD34^+$ HSCs with CRISPR Cas9/Cpf1 nucleases, gRNA design/engineering
- ***Gene Therapy*** - Virus vector production, viral (AAV, lentivirus) and non-viral (*Sleeping Beauty* transposon system, endonucleases) mediated gene transfer in mouse, primate, dog, human T cells and HSCs
- ***Stem Cell Biology*** - Pluripotent / HSC reprogramming and characterization; blood, cardiac, endothelial, and liver differentiation from PSCs, HSC isolation, culture, characterization, expansion, and differentiation (lymphoid, myeloid, erythroid)
- ***Transplantation Biology*** - Planning, execution, transplantation, and long-term follow-up of cell therapies in preclinical animal models (mouse, dog, nonhuman primate)
- ***Immunology*** - Primary cell isolation from tissues, 10-color flow cytometry and analysis, cell sorting , immunocytochemistry, scientific imaging / photography, and ex vivo immune assays (e.g., specific lysis, cytokine release, ELISA, western blot)
- ***Immuno-oncology*** – syngeneic/xenograft tumor model development/analysis, preclinical immunotherapy models
- ***In Vivo Pharmacology*** – PK/PD analysis of small molecules and cell therapy