JENNIFER L GORI, PhD

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SUMMARY OF QUALIFICATIONS

- Passionate and successful in building and leading teams, internal and external collaborations with scientists with expertise
- Highly skilled at creative strategy development and problem solving with an eye on clinical translation
- Proven experience developing CRISPR editing, lentiviral gene transfer, and cell therapy platforms for therapeutic application
- >14 years of experience in hematopoietic stem cell (HSC) biology and transplantation immunology, viral vector mediated gene transfer, gene editing/therapy in HSCs and lymphocytes (T/NK cells), gene-modified HSC transplantation in preclinical animal models (mouse, canine, primate), and clinical translational research

EXPERIENCE

OBSIDIAN THERAPEUTICS, CAMBRIDGE, MA (2018-DATE)

ASSOCIATE DIRECTOR IN CELL THERAPY AND HEAD OF IN VIVO PHARMACOLOGY

- Strategize on potential targets for regulated cell and gene therapy drug development
- Advise program teams on program go/no go criteria and strategies for validation of regulated gene and cell therapy products
- Develop timelines for in vivo studies for all programs, identifying program milestones and key decision points
- Direct team of 5 in vivo pharmacology scientists on preclinical studies

EDITAS MEDICINE, INC., CAMBRIDGE, MA (2014-2018)

SENIOR SCIENTIST (2017-2018), SCIENTIST III (2015-2016), SCIENTIST II (2014-2015)

Project leadership

- Lead cross-functional team for CRISPR gene-edited cell therapy program
- Proposed, established, championed, directed cell biology/ preclinical studies for CRISPR gene-edited hematopoietic stem cell therapy program
- Directed discovery research, established work plans, timelines, coordinated project team meetings and activities, identified key inflection points, gaps, milestones, and criteria for drug candidate selection CRISPR gene-edited cell therapy program
- Strategized and developed long-range pipeline and product arc for *ex vivo* cell therapy programs

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 hematopoietic cell function after transplantation

Exploratory research and platform enablement

- Managed a team of five research scientists (PhD level and MS/BS level)
- Identified potential market opportunities for gene-edited human $CD34^+$ HSC and T cell products
- Strengthened intellectual property position of company as inventor and writer of several patent applications detailing novel work on gene editing methods in HSCs and T cells
- Directed research on gene disruption and targeted integration in human $CD34^+$ HSCs
- On-boarded research grade CRISPR/Cas9 tools and refined their application to efficiently edit human $CD34^+$ HSCs and T cells for gene disruption (NHEJ) and targeted integration/gene correction (HDR)
- Developed method to monitor for clonal expansion of gene-edited human $CD34^+$ HSCs *in vivo*
- Directed exploratory research activities for hematopoietic stem progenitor cell expansion
- 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 HUTCHINSON CANCER RESEARCH CENTER, SEATTLE, WA (2010-2014)

ASSOCIATE IN CLINICAL RESEARCH/FACULTY POSITION (2013-2014), RESEARCH ASSOCIATE (2011-2013), POSTDOCTORAL FELLOW (2010-2011)

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

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

- Devised 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 primates
- Scaled-up iPSC-HSC production and HSC expansion directed transplantation studies in primates

Safe, effective 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 and analysis for clinical trial on retroviral chemotherapy resistance gene therapy in HSCs for patients with Glioblastoma (ClinicalTrials.gov identifier: NCT00669669)
- Conducted transplantation studies with T cells expressing iCaspase-9 suicide gene to control GVHD

Establishment of pluripotent stem cell laboratory

- Managed and contributed to several preclinical studies and extra-mural scientific collaborations
- Developed and validated protocols for differentiation of iPSCs into blood, liver, and cardiac cells
- Differentiated iPSCs into T lymphocytes and macrophages and characterized their functionality *ex vivo* (e.g., cytokine production in response to stimulation/activation, susceptibility to HIV infection)

Development of in vivo primate disease models

- Established and characterized primate model of HCV infection
- Coordinated studies on gene-modified iPSC-cardiac cell implantation after myocardial infarction

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

POSTDOCTORAL RESEARCHER

Mentor: Dr. Matthew Evans, Co-mentors: Dr. Valerie Gouon-Evans, Dr. Sunita D'Souza

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

- Developed research plan for HCV targeted lentiviral vector modified natural killer (NK) cell therapy
- Characterized HCV infection in human iPSC-derived hepatic progenitors
- Engineered human iPSC-derived NK cells for specific killing of HCV infected cells

UNIVERSITY OF MINNESOTA, MINNEAPOLIS, MN (2005-2008)

GRADUATE STUDENT RESEARCH ASSISTANT

Advisor: Dr. Scott McIvor, Co-mentor: Dr. Dan Kaufman

Hematopoietic stem cell chemotherapy resistance lentiviral gene therapy

- Completed 3 aims of NIH R01 grant, resulting in 3 publications in peer-reviewed journals
- Constructed and prepared lentivirus vectors and evaluated gene expression in transduced cells
- Quantified transgene expression in transduced cells with enzyme activity assays and western blotting
- Performed hematopoietic differentiation and transplantation of HSCs and embryonic stem cell cells

EDUCATION

UNIVERSITY OF MINNESOTA – Minneapolis, MN

Ph.D. in Microbiology, Immunology, Cancer Biology, 2008, GPA: 3.9/4.0

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

SMITH COLLEGE – Northampton, MA

B.A. Biochemistry, GPA: 3.6/4.0

Cum Laude, Dean's List, First Group Scholars

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. Selected 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).
6. **Gori JL**, Beard BC, Gooch CM, Swanson D, McIvor RS, Kiem H-P. *Long-term expression of methotrexate resistant dihydrofolate reductase after lentiviral stem cell transduction and autologous transplantation in dogs.* ASGCT, 11th Annual Meeting, Boston, MA (2008).
7. **Gori JL**, Tian X, Morris JK, Swanson D, McIvor RS, Kaufman DS. *Differentiation and in vivo expansion of human embryonic stem cells expressing methotrexate-resistant dihydrofolate reductase.* ASGCT 11th Annual Meeting, Boston,

MA (2008).

8. **Gori JL**, Podetz-Pedersen K, Swanson D, Karlen AD, Somia NV, McIvor RS. *Chemoprotection of mouse marrow transplant recipients by ex vivo lentiviral transduction of murine tyr22 dihydrofolate reductase conferring resistance to methotrexate.* ASGCT 9th Annual Meeting, Baltimore, MD (2006).

C. Selected 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 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).
6. **Gori JL**, Welstead GG, Collins MA, Fang JW, Friedland AE, Bumcrot D. *Cas9-mediated genome editing in hematopoietic stem progenitor cells.* ASGCT 18th Annual Meeting, Washington, DC (2015).
7. **Gori JL,** Chandrasekaran D, Adair JE, Sauvageau G, Kiem H-P. *Engraftment of autologous gene-modified macaque CD34+ hematopoietic stem cells in the nonhuman primate after transduction and co-culture with the small molecule UM171.* ASGCT 17th Annual Meeting, Washington, DC (2014).
8. **Gori JL,** Butler JM, Beard BC, Chandrasekaran D, Adair JE, Ginsberg M, Nolan DJ, Rafii S, Kiem H-P. *Stable engraftment and effective MGMT-mediated in vivo selection of hematopoietic progenitor cells derived from nonhuman primate induced pluripotent stem cells.* International Society for Stem Cell Research 11th Annual Meeting, Boston, MA (2013).
9. **Gori JL,** Nelson VL, Kiem H-P, Beard BC. P140K-mediated In vivo selection strategies combining *AMD3100 with O6-BG and BCNU significantly enhances selection of gene-modified T lymphocytes*. ASGCT 15th Annual Meeting, Philadelphia, PA (2012).

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

1. WO2018209158A2 CRISPR/RNA-GUIDED NUCLEASE SYSTEMS AND METHODS
2. WO2018170184A1 SYSTEMS AND METHODS FOR THE TREATMENT OF HEMOGLOBINOPATHIES
3. WO2017160890A1 CRISPR/CAS-RELATED METHODS AND COMPOSITIONS FOR TREATING BETA HEMOGLOBINOPATHIES
4. WO2016201047A1 CRISPR/CAS-RELATED METHODS AND COMPOSITIONS FOR IMPROVING TRANSPLANTATION
5. WO2016183236A1CRISPR/CAS-RELATED METHODS AND COMPOSITIONS FOR TREATING HIV INFECTION AND AIDS
6. WO2016182959A1OPTIMIZED CRISPR/CAS9 SYSTEMS AND METHODS FOR GENE EDITING IN STEM CELLS
7. WO2016154596A1 CRISPR/CAS-RELATED METHODS, COMPOSITIONS AND COMPONENTS
8. WO2016154579A2 CRISPR/CAS-MEDIATED GENE CONVERSION

SCIENTIFIC SOCIETY AND COMMITTEE MEMBERSHIP

American Society of Hematology, Member since 2013

- Gene Therapy Abstract Coordinating Reviewer (2017)
- Gene Therapy 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 (2018-2019)
- New Investigator Committee Member (2014-Date)
- Meritorious Abstract Award Recipient (2014)

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

- ***Project and Program Management*** – Coordination cross-functional team activities, timeline and milestone management, budget generation/assembly
- ***Drug Discovery*** - Establish criteria for lead discovery of potential drug products and progression from hit to lead validation for CRISPR-based cell therapies
- ***Gene Editing*** - Gene editing (NHEJ and HDR) with Cas9 mRNA, CRISPR Cas9/Cpf1 proteins, gRNA design/engineering, gene editing of primary human T cells and human $CD34^+$ HSCs
- ***Stem Cell Biology*** - Pluripotent / hematopoietic stem cell reprogramming and characterization, blood, cardiac, endothelial, and liver differentiation from PSCs, hematopoietic stem cell 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
- ***Protein Analysis*** – CRISPR ribonucleoprotein complexation, HPLC
- ***Molecular Biology*** - ddPCR, qPCR, sequencing, Southern blots, in vitro transcription, cloning
- ***Virology / Gene Therapy*** - Virus vector production/purification, viral (AAV, lentivirus) and non-viral (*Sleeping Beauty* transposon system, endonucleases) mediated gene transfer in mouse, primate, dog, human patient T cells and HSCs
- ***Scientific Communication*** - Data analysis, presentation [Microsoft Office, Graphpad Prism, Benchling], progress report, study report, grant and manuscript writing/editing, figure production [Adobe Design Suite]), patent application writing

RESEARCH FUNDING

***CO-INVESTIGATOR*, NIH/NHLBI R01** HL 115128 (P.I.: Kiem, H.P., Co-P.I.: Rafii, S.) 08/01/13-06/30/18
Evaluation of pluripotent stem cell-derived blood cells in nonhuman primate model.
***POSTDOCTORAL RESEARCH FELLOW*, NIH/NIAID P01** AI097100-01 (P.I.: Kiem, H.P.) 08/07/12-07/31/17
Foamy viral gene therapy for X-linked severe combined immune deficiency
***CO-INVESTIGATOR*, ITHS/Primate Center Ignition Award** (PCIA) (P.I.: Kiem, H.P.) 08/01/13-04/30/14
University of Washington, NIH/ORIP/NCATS (P51 OD010425, UL1 TR000423)
Development of an in vivo model of Hepatitis C virus infection, replication and pathogenesis.
***POSTDOCTORAL RESEARCH FELLOW,* NIH/NHBLI R01** HL 098489 (P.I.: Kiem, H.P.) 01/21/10 -12/31/13
Development of safe and efficient gene therapy strategies for hemoglobinopathies.
***POSTDOCTORAL RESEARCH FELLOW,* NIH/NHLBI R01** HL092554 (P.I.: Kiem, H.P.) 10/1/2007-6/30/2012
LAGLIDADG homing endonuclease delivery and gene repair in canine hematopoietic stem cell.
POSTDOCTORAL RESEARCH FELLOW, ITHS (P.I.: Murry, C, Co-P.I.: Kiem, H.P.) 05/01/2011-04/30/2012 University of Washington, NIH/NCRR (P51 RR000166, UL1 RR025014)
Transplantation of M. nemestrina induced pluripotent stem cell (MniPSC) derived cardiomyocytes into nonhuman primates after myocardial infarction.