OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Dimitroff, Charles J.**

eRA COMMONS USER NAME: **cdimitroff**

POSITION TITLE: **Professor (with Tenure) of Translational Medicine**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date	FIELD OF STUDY
Columbia College, Columbia University, NY, NY	B.A.	1992	Pre-medical Sciences
State University of New York at Buffalo, Roswell Park Cancer Institute, Buffalo, NY	M.S.	1994	Tumor Glycobiology, Cancer Pharmacology
State University of New York at Buffalo, Roswell Park Cancer Institute, Buffalo, NY	Ph.D.	1999	Tumor Glycobiology, Cancer Pharmacology
Dept. of Dermatology, Brigham & Women's Hospital Harvard Medical School, Boston, MA	Post-doctoral Fellow	2003	Glycobiology of Hematopoietic Cells

A. Personal Statement

I have been studying the nature of lectin – carbohydrate interactions and their impact in inflammation and cancer for the last 26 years. I have an expertise in glycobiology studies relating to tumor biology and adaptive immunity. I am qualified to perform pre-clinical research investigating how glycome-related molecules contribute to the pathogenesis of inflammation and cancer. I conduct *in vitro* and *in vivo* experiments designed to characterize the identity and function of lectins and their carbohydrate-binding ligands on leukocytes and cancer cells. I have published on the role of lectins controlling T cell, B cell, NK cell, leukemic/hematopoietic stem cell and solid cancer cell trafficking (metastasis), adhesion, fate and/or differentiation. These efforts have resulted in several NIH R-award grants designed to study the role of selectin/galectin ligands in immunity and in malignant progression and metastasis. Glycomic exploratory analyses on native immune/cancer cell models have included the use of carbohydrate inhibitors, MALDI-TOF/TOF MS/MS, "home grown" selectin/galectin-human Fc chimeras and glycosyltransferase mutant cell lines/mice as tools to identity and characterize selectin/galectin ligands functioning in inflammation, tumorigenesis, metastasis and tumor-immune evasion.

My Research Program is subdivided into (2) components:

Cancer Research Program: We are currently exploring the glycobiology of melanoma progression. We have obtained exciting preliminary data that the glycomic signature of melanoma cells is vastly different from their normal melanocyte counterparts. The glycomics of melanocyte/melanoma cells are being investigated structurally and functionally to help ascertain whether a causal relationship helps drive metastatic melanoma.

Immune Research Program: Our current research focuses on defining glycomic signatures and related functions on B cell subsets during maturation, humoral immune response or B cell malignancy. Using lessons from our studies on cancer cell glycobiology, we are employing a battery of glycobiological tools to interrogate B cell surface glycans and candidate galectin-binding partners. We are making new observations on the types of glycans that encourage a unique galectin-binding activity that ultimately impacts the efficiency of a humoral immune response, effective vaccination or, even when dysregulated, potentially facilitate B cell malignancies.

The mission of my laboratory in the Translational Glycobiology Institute at Florida International University (TGIF) at Herbert Wertheim College of Medicine is to train MD and PhD students in the area of immune/cancer glycobiology and conduct innovative analyses on glycans in immunity/cancer. For decades, my laboratory is a model of racial diversity and gender equity amongst trainees. As Director of TGIF, I will lead all administrative, experimental and collaborative activities in this exciting new galectin-9 – human B cell biology R01 grant.

B. Positions and Honors

Positions and Employment

1999 – 2003 Research Fellow in Dermatology, Department of Dermatology
Brigham & Women's Hospital, Harvard Medical School, Boston, MA

2003 – 2005 Instructor in Dermatology, Department of Dermatology
Brigham & Women's Hospital, Harvard Medical School, Boston, MA

2005 – 2014 Assistant Professor of Dermatology, Department of Dermatology

Brigham & Women's Hospital, Harvard Medical School, Boston, MA
2014 – 2019 Associate Professor of Dermatology, Department of Dermatology
Brigham & Women's Hospital, Harvard Medical School, Boston, MA
2019 – Professor (with Tenure) of Translational Medicine
Herbert Wertheim College of Medicine, Florida International University (FIU)
2019 – Executive Associate Dean for Research, Herbert Wertheim College of Medicine, FIU
2019 – Director, Translational Glycobiology Institute at FIU (TGIF)

Other Experience, Memberships, Grant Review Committees

1994 – 2011 Member, The Metastasis Research Society
1994 – Member, The American Association for Cancer Research
1999 – 2005 Member, The American Association for the Advancement of Science
1999 – Member, The Society for Investigative Dermatology
1999 – Member, The American Society of Hematology
2001 – Member, Dana-Farber/Harvard Cancer Center
2006 – Member, The American Association of Immunologists
2006 – Faculty Member, Ph.D. Immunology Program, Div. of Med. Science, Harvard University
2008 – 2010 NIH Grant Reviewer, NCI POI Cellular and Tissue Biology Study Section
2009 – Investigator, NIH Consortium for Functional Glycomics
2009 NIH Grant Reviewer, NIAMS ZAR1 EHB-G (M1) 1 Study Section
2010 Merit Grant Reviewer, Department of Veteran Affairs (ONC-A)
2010 – Director, BWH Department of Dermatology Training Program
2011 NIH Grant Reviewer, NCCAM ZAT1 SM (23) Study Section
2011 – Member, BWH – BRI Research Oversight Committee
2011 – Member, BWH – BRI Internal Review Committee
2010 – Member, BWH-DFCI Melanoma Program
2010 – 2012 Grant Reviewer, American Cancer Society; Cell Structure and Metastasis Section
2012 NIH Grant Reviewer, NCCAM ZAT1 SM (25) Mech. Res. on Nat. Products Study Section
2012 NIH Grant Reviewer, Intercellular Interactions (ICI) Study Section
2012 – Research Operations Management Team, BWH Department of Dermatology
2013 NIH Grant Reviewer, NIH/NCCAM ZAT1 SM (29) Study Section
2013 – Research Faculty Liaison for Development, BWH Department of Dermatology
2013 – Chair, Scholarship Oversight Committee, BWH Department of Dermatology
2014 – Associate Director for Laboratory Research, BWH Department of Dermatology
2014 *Ad hoc* NIH Grant Reviewer, Intercellular Interactions (ICI) Study Section
2014 Grant Reviewer, Worldwide Cancer Research (Formally AICR)
2015 Grant Reviewer, Biomedicine & F.I.R.S.T. Program Israel Science Foundation
2015 *Ad hoc* NIH Grant Reviewer, Intercellular Interactions (ICI) Study Section
2015 – Member, Society for Glycobiology
2016 NIH Grant Reviewer, UO1 Glycoscience Study Section ZRG1 BST-J (50) R
2016 *Ad hoc* NIH Grant Reviewer, Tumor Microenvironment (TME) Study Section
2016 *Ad hoc* NIH Grant Reviewer, Intercellular Interactions (ICI) Study Section
2016 NIH Grant Reviewer, Cancer Biology ZRG1 OBT-Z (02) M Study Section
2017 NIH Grant Reviewer, Glycoscience Methods ZRG1 IMST-U (50) R Study Section
2017 *Ad hoc* NIH Grant Reviewer, Intercellular Interactions (ICI) Study Section
2017 Grant Reviewer, BWH Health & Technology Innovation Fund
2017 Internal Advisory Committee, NIH National Center for Functional Glycomics
2018 Co-Chair, NIH Grant Reviewer, Glycoscience UO1 ZRG1 IMST-B (51) R Study Section
2018 NIH Grant Reviewer, Glycoscience UO1 ZRG1 IMST-B (52) R Study Section
2018 Grant Reviewer, Bloodwise (UK)
2018 NIH Grant Reviewer, Intercellular Interactions (ICI) Study Section
2018 Grant Reviewer, BWH BRI Pilot and Innovation Grants Program
2018 BWH/BRI Grant Review, Smith Family Awards - Excellence in Biomed. Research
2018 Guest Editor for a Special *Glyco-immunology* issue in Frontiers in Immunology
2019 NIH Grant Reviewer, Methods for Analysis of Glycans UO1 ZRG1 IMST-U (51) Study Section
2019 NIH Grant Reviewer, Intercellular Interactions (ICI) Study Section
2019 – Member, NIH/NCI Alliance of Glycobiologists for Cancer Research

2020 NIH Grant Reviewer, Special Emphasis Panel, ZRG1 EMNR-S (55) R
2020 NIH Grant Reviewer, NIAID R34 Special Emphasis Panel, ZAI1 KGH-I (S1)
2020 NIH Grant Reviewer, NHLBI Program Project HLBP-Z (16) 1
2021 NIH Grant Reviewer, NIAID R34 Special Emphasis Panel ZAI1 KGH-I (M1) 1

Honors, Recognitions and Awards

1993 Recipient, American Association for Cancer Research Graduate Scholarship
1995 Sigma Xi Research Society
1995 Roswell Park Graduate School Poster Awardee
1996 Awardee, Histopathobiology of Neoplasia Smuckler Memorial AACR Educational Workshop
1998 Sigma Xi Research Society Scientific Poster Competition at SUNY @ Buffalo, 1st Place
2001 NIH/NCI, National Research Service Award
2002 Awardee, The Albert M. Kligman Fellowship by *The Society for Investigative Dermatology*
2003 Awardee, The Albert M. Kligman Fellowship by *The Society for Investigative Dermatology*
2004 Awardee, NIH Travel Stipend to *The Metastasis Research Society* Meeting in Genoa, Italy
2005 Recipient, American Cancer Society Research Scholar Award
2006 11th Prouts Neck Meeting on PCa, "*Emerging Strategies in PCa Therapy*."
2007 Harvard Medical School Leadership Development for Physicians & Scientists Program
2008 Nominated, Harvard Medical School Mentor Award, Harvard University
2009 Nominated, Harvard Medical School Mentor Award, Harvard University
2010 Nominated, Harvard Medical School Mentor Award, Harvard University
2011 Awardee, Junior Mentoring Award, Harvard Medical School, Harvard University
2012 Nominated, Dean's Community Service Faculty Award, Harvard Medical School, Harvard University
2013 Awardee, BWH Center for Faculty Development & Diversity Faculty Mentoring Leadership Program
2013 Nominated, BWH Center for Faculty Development & Diversity, Mentor Award
2013 Nominated, Harold Amos Faculty Diversity Award, Harvard Medical School, Harvard University
2013 Nominated, Dean's Community Service Award, Harvard Medical School, Harvard University
2014 Nominated, Harold Amos Faculty Diversity Award, Harvard Medical School, Harvard University
2014 Nominated, BWH Center for Faculty Development & Diversity, Mentor Award
2014 Awardee, BWH Center for Faculty Development & Diversity, Community Service Award
2014 Nominated, Dean's Community Service Award, Harvard Medical School, Harvard University
2015 Nominated, Harold Amos Faculty Diversity Award, Harvard Medical School, Harvard University
2015 Nominated, A. Clifford Barger Excellence in Mentoring Award, Harvard Medical School, Harvard U.
2016 Nominated, A. Clifford Barger Excellence in Mentoring Award, Harvard Medical School, Harvard U.
2017 Nominated, A. Clifford Barger Excellence in Mentoring Award, Harvard Medical School, Harvard U.
2017 Recipient, Innovation Recognition Award by Partners Healthcare, Inc.
2017 Nominated, Program Award of Culture for Excellence in Mentoring, Harvard Medical School
2018 Nominated, Program Award of Culture for Excellence in Mentoring, Harvard Medical School
2019 Nominated, Program Award of Culture for Excellence in Mentoring, Harvard Medical School

C. Contributions to Science

*MyNCBI:*http://www.ncbi.nlm.nih.gov/sites/myncbi/charles.dimitroff.1/bibliography/41133244/public/?sort=date&direction=ascending

"Impact of Glycosylation on Immunity and Cancer"

1.) Functional Characterization of Carbohydrate-Mediated Leukocyte/Cancer Cell Adhesion. My early contributions as a trainee were observations on how leukocyte/cancer cells adhered to vascular endothelium and homed/metastasized to tissues. I studied how human CCa cells and HSCs use galectin (Gal)-1 and E-selectin ligands (ESL) to mediate adhesion to ECM or vascular endothelium, respectively. I helped identify: 1.) LAMP-1 and CEA as Gal-1/E-selectin ligands on CCa cells as a mechanism for adhesion to ECM/blood vessels and 2.) CD44 as an ESL (known as HCELL) on HSCs and key mediator of vascular adhesion and bone-homing activity. These efforts solidified my interest on studies of the glycobiology of leukocytes and cancer cells. Below are (4) key papers illuminating these early efforts as a PhD/Post-doctoral trainee.

a. **Dimitroff CJ.**, et al. Cell surface N-acetylneuraminic acid α2,3-galactoside-dependent intercellular adhesion of human colon cancer cells, ***Biochem. Biophys. Res. Comm.***, 1996; 256:631-636.
b. Sackstein R, **Dimitroff CJ.** A hematopoietic cell L-selectin ligand that is distinct from PSGL-1 and displays N-glycan-dependent binding activity, ***BLOOD***, 2000; 96: 2765-2774.

c. **Dimitroff CJ.**, et al. A distinct glycoform of CD44 is an L-selectin ligand on human hematopoietic progenitor cells. ***Proc. Natl. Acad. Sci.***, 2000; 97(25), 13841-13846. PMC17663
d. **Dimitroff CJ.**, et al. CD44 is a major E-selectin ligand on human hematopoietic progenitor cells. ***J. Cell Biology***, 2001; 153:1277-86. PMC2192031

2.) Functional Characterization of Glycans on Bone-homing Cancer Cells. I published ground-breaking data on the role of E-selectin ligands (ESL) on prostate cancer (PCa) cell adhesion to vascular endothelium. Our data implicated PSGL-1, HCELL, CEA and ESL-1 as major ESLs and that α1,3 fucosyltransferases (FT) 3, 6 and 7 were critical regulators of PCa ESL activity. FT3, 6, and 7 were necessary for efficient PCa cell seeding in bone. These data support our hypothesis that ESLs are critical for PCa bone metastasis. Below are (4) landmark papers that helped establish the "ESL-dependent PCa Bone Metastasis" hypothesis:

a. **Dimitroff CJ.**, et al. Identification of Leukocyte E-selectin Ligands, P-selectin Glycoprotein Ligand-1 and E-selectin Ligand-1, on Human Metastatic Prostate Tumor Cells. ***Cancer Research***, 65(13):5750-5760, 2005. PMC1472661
b. Barthel SR, Gavino JD, Wiese GK, Jaynes JM, Siddiqui J and **Dimitroff CJ.** Analysis of glycosyltransferase expression in metastatic PCa cells capable of rolling activity on micro-vascular endothelial (E)-selectin. ***J. Glycobiology***, 18(10):806-17, 2008. PMC2574550
c. Barthel SR, Wiese GK, Cho J, Opperman MJ, Hays DL, Siddiqui J, Pienta KJ, Furie B and **Dimitroff CJ.** Alpha 1,3 fucosyltransferases are master regulators of prostate cancer cell trafficking. ***Proc. Natl. Acad. Sci.***, 106(46):19491-6, 2009. PMC2780742
d. Barthel SR, Hays DL, Yazawa EM, Opperman M, Walley KC, Nimrichter L, Burdick MM, Gillard BM, Moser MT, Pantel K, Foster BA, Pienta KJ and **Dimitroff CJ.** Definition of molecular determinants of prostate cancer cell bone extravasation. ***Cancer Research***, 73(2):942-52, 2013. PMC3548951

3.) Novel Glyco-Methods to Inhibit Dermal Inflammation or Boost Anti-tumor Immunity. To build a therapeutic angle into research, I studied how sugar analogs block key carbohydrate-building enzymes in effector T cells that generate E-selectin ligands (ESL) and facilitate T cell trafficking to skin. Our data showed that T cells actively synthesizing glycans were selectively susceptible to metabolic glycan antagonism (United States Patent: 20060281708). These anti-glycan effects on T cells inhibited galectin (Gal)-1-binding and obviated Gal-1-mediated immunomodulation. In models on skin inflammation and cancer, our findings revealed that: 1) Skin-homing T cells treated with non-toxic doses of sugar analogs were selectively modified and unable to bind E-/P-selectins and enter skin, and 2) Blocking Gal-1-binding glycans on anti-tumor T cells resulted in severely blunted tumor growth. These exciting studies led to several new projects designed to understand how glycans regulate T cell function and how Gal-1-binding glycans can be targeted to treat cancer. Here are (4) landmark papers demonstrating the importance of glycan antagonism in effector T cells.

a. **Dimitroff CJ.**, et al. Glycosylation-Dependent Inhibition of Cutaneous Lymphocyte-Associated Antigen: Implications in Modulating Lymphocyte Migration to Skin. ***BLOOD***, 101(2):602-610, 2003.
b. **Dimitroff CJ.**, et al. Prevention of Leukocyte Migration to Inflamed Skin with a Novel Fluorosugar Modifier of Cutaneous Lymphocyte-Associated Antigen. ***J. Clinical Investigation.*** 112, 1008-1018, 2003. PMC198531
c. Barthel SR, Antonopoulos A, Cedeno-Laurent F, Schaffer L, Hernandez G, Patil SA, North SJ, Dell A, Matta KL, Neelamegham S, Haslam SM and **Dimitroff CJ.** Peracetylated 4-fluoro-glucosamine reduces the content and repertoire of N- and O-glycans without direct incorporation. ***J. Biological Chemistry***, 286(24):21717-31, 2011. PMC3122228
d. Cedeno, F, Opperman MJ, Barthel SR, Hays D, Schatton T, Zhan Q, He X, Matta KL, Supko, J, Frank M, Murphy GF, **Dimitroff CJ.** Metabolic inhibition of Gal-1-binding carbohydrates accentuates anti-tumor immunity. ***J. Investigative Dermatology***, 132(2):410-20, 2012. PMC3258338

4.) Function of Galectins and Their Glycan Ligands on T and B cell Fate. My glycobiology program has established a foothold in studies on galectin-binding glycans as critical determinants for immune homeostasis, surveillance and anti-tumor killing. Early work focused on identifying Gal-1 ligands and their function on T cells. Our data show that Gal-1 triggers T cell immunoregulation and anti-inflammation activity - Gal-1-binding glycan inhibitors boosted anti-melanoma immunity. These exciting observations led to pioneering explorations the glycomic nature of human B cells. We found that Gal-9-binding to CD45 N-glycans regulated by GCNT2 impact B cell activation and related BCR signaling; and B cell differentiation features a progressive shortening of O-glycans governed by ST3Gal-1 expression and loss of GCNT1. Most recent work has revealed major influence of Gal-9 on B cell function, including Gal-9-depedent induction of SLAMF7. In all, our findings show that galectins and stage-specific glycans are key regulators of T and B cell-dependent immune responses. Here are (4) milestone papers on how galectin/glycans regulate adaptive immunity.

a. Cedeno F, Watanabe R, Teague JE, Kupper TS, Clark RA and **Dimitroff CJ.** Galectin-1 inhibits viability, proliferation & Th1 cytokine production of non-malignant T cells in patients with leukemic cutaneous T cell lymphoma. ***BLOOD***, 119(15):3534-8, 2012. PMC3325040
b. Giovannone N, Liang J, Aristotelis A, Geddes-Sweeney J, King SL, Pochebit SM, Neil Bhattacharyya N., Dell A, Widlund HR, Haslam SM and **Dimitroff CJ**. Galectin-9 suppresses B cell receptor signaling and is regulated by I-branching on N-glycans. ***Nature Commun***, 9:3287, 2018. PMC6098069
c. Giovannone N, Antonopoulos A, Liang J, Geddes Sweeney J, Kudelka MR, King, SL, Lee GS, Cummings RD, Dell A, Barthel SR, Widlund HR, Haslam SM and **Dimitroff CJ**. Human B cell differentiation is characterized by progressive remodeling of O-linked glycans. ***Frontiers in Immunology***, 9:2857, 2018. PMC6302748
d. Chakraborty A, Staudinger C, King SL, Clemente Erickson F, Lau LS, Bernasconi A, Luscinskas FW, Perlyn C, and **Dimitroff CJ**. Galectin-9 bridges human B cell – vascular endothelial cells while programming regulatory pathways. ***J. Autoimmunity***, 117:102575.2020. PMID: 33285511

5.) The Glycobiology of Malignant Melanoma. My cancer research program is currently focused on identifying glycomic features of malignant melanomas that are either unique to their malignant potential and exhibit a functional role in the progression from a normal melanocyte to malignancy to metastasis. Our work has revealed that I/i-antigens and related glycan-synthesizing enzyme GCNT2 regulate malignant and metastatic behavior of melanomas. Our data demonstrate that I/i-antigens can serve as novel biomarkers of melanoma malignancy or melanoma metastasis, respectively. This work has led to (2) US patents applications, *Using galectin-binding carbohydrates as predictors of melanoma progression and metastasis* and *Identification of glycomic biomarkers of melanoma progression*. These markers are currently under investigation to elucidate their functional role in the glyco-pathogenesis of melanoma progression. Here are (4) milestone papers showing which/how glycans/glycosyltransferases regulate melanoma malignancy.

a. Yazawa EM, Geddes Sweeney JE, Cedeno-Laurent F, Walley KC, Barthel SR, Opperman MJ, Liang J, Lin JY, Schatton T, Laga AC, Mihm MC, Qureshi AA, Widlund HR, Murphy GF and **Dimitroff CJ.** Melanoma cell galectin-1 ligands functionally correlate with malignant potential. ***J. Investigative Dermatology***, 2015, 135(7):1849-62. PMC4466041
b. **Dimitroff CJ.** Galectin-binding O-glycosylations as regulators of malignancy. ***Cancer Research***, 2015, 75(16):3195-202. PMC4537818
c. Geddes Sweeney J, Liang J, Aristotelis A, Giovannone N, Kang S, Mondala A, King SL, Head SR, Tani Y, Brackett D, Dell A, Murphy GF, Haslam SM, Widlund HR, **Dimitroff CJ**. Loss of GCNT2/I-branched glycans enhances melanoma growth & survival. ***Nature Commun***, 9:3368, 2018. PMC6105653
d. **Dimitroff CJ**. I-branched carbohydrates as emerging effectors of malignant progression. ***Proc. Natl. Acad. Sci.***, 116(28):13729-13737, 2019. PMC6628663

D. Research Support

Current

1.) NIH/NCI U01 CA225644 Role: Principal Investigator (Dimitroff, CJ) 2019 – 2024
Analysis of glycomic regulators in melanoma progression
The goal of this cooperative grant is to study the role of GCNT2/I-branching on melanoma progression.

2.) NIH/NIAID R21 AI146368 Role: Principal Investigator (Dimitroff, CJ) 2019 – 2021
Analysis of Vascular Galectin-9 as an Immunomodulator of B cell Activity *(Impact score = 17)*
The goal of this exploratory grant is to study how vascular endothelial cell galectin-9 regulates B cell function.

3.) NIH/NHLBI K12 HL141953 Role: Subcontract (Dimitroff, CJ) 2019 – 2024
Forging Translational Glycobiologists: Intermeshing Glycoscience Training and Clinical Education
The goal is to provide career development/training for the next generation of translational glycobiologists.

Completed

1.) Mizutani Foundation Role: Principal Investigator (Dimitroff, CJ) 2019 – 2020
Functional analysis of human endothelial cell galectin-9 on human B cells
The goal of this pilot grant was to unearth downstream effectors of vascular Gal-9 on human B cells.

2.) NIH/NIAID R21 AI125476 Role: Principal Investigator (Dimitroff, CJ) 2016 – 2018
Glycomic Characterization of Germinal Center B cells *(Impact score - 13)*
The goal of this grant is to identify novel glycomic features and regulators of human B cell differentiation.

3.) NIH/NCI R01 CA173610 Role: Principal Investigator (Dimitroff, CJ) 2013 – 2018
Functional Analysis of Galectin-1 Ligands in Melanoma Progression *(Impact score - 11)*
The goal of this grant is to identify the functional expression of galectin-1 ligands in malignant melanoma.