**Matthew T. Witkowski, PhD**

matthew.witkowski@cuanschutz.edu

Department of Pediatrics

Hematology/Oncology/Bone Marrow Transplant Laboratories

University of Colorado Anschutz Medical Campus

12800 East 19th Avenue

Aurora, 80045

**PERSONAL STATEMENT**

My career is highlighted by an extensive commitment to understanding blood malignancies, particularly high-risk pediatric acute lymphoblastic leukemia (ALL). Utilizing a novel reversible RNAi approach, I uncovered a critical role for IKAROS/Ikaros in the maintenance and treatment resistance of both T-cell (Witkowski et al. *Leukemia* 2015) and B-cell ALL (Witkowski et al. *J Exp Med* 2017). Extending beyond ALL-intrinsic genetic drivers, my postdoctoral work provided novel insights into the role of microenvironment in ALL pathogenesis and treatment responsiveness (Witkowski et al. *Cancer Cell* 2020). Ultimately, my independent research group will investigate the precise function of leukemia-associated immune microenvironment in supporting B-ALL survival and establish new immune-based therapeutic approaches that improve the efficacy of conventional B-ALL therapies through modulation of B-ALL antigen abundance (Witkowski et al. *Nature Immunology* 2022).

**CURRENT POSITION**

**University of Colorado Anschutz Medical Campus Aurora, CO**

Department of Pediatrics 2022-Present

Assistant Professor

**EDUCATION**

**New York University School of Medicine New York, NY**

Aifantis laboratory, Department of Pathology 2015-2022

Postdoctoral Fellow

**Walter and Eliza Hall Institute of Medical Research Melbourne, Victoria, Australia**

PhD, Department of Medical Biology, University of Melbourne2011-2015

**University of Melbourne Melbourne, Victoria, Australia**Bachelor of Science (Honours) 2008-2011
Department of Genetics

**CURRENT FINANCIAL SUPPORT**

**Cancer League of Colorado Research Grant -** AWD#222549-MW

Duration: July 1st 2022 – June 30th, 2023

**NIH/NCI K22 Award -** 1K22CA258520-01

Duration: May 12th, 2022 – May 11th, 2025

**Laboratory Start-up**

Duration: February 1st, 2022 (non-expiring amount)

**GRANTS AND AWARDS**

**Cancer League of Colorado Research Grant** 2022-2023
AWD#222549-MW

**NIH/NCI K22 Award** 2022-2025

1K22CA258520-01

**ASH Restart Award Recipient** 2020

American Society of Hematology

**CDP (Fellow) Achievement Award** 2020

The Leukemia & Lymphoma Society

**Outstanding Postdoctoral Fellow Award** 2020

New York University School of Medicine

**Speaker Award Winner** 2020

Postdoctoral Research Day, New York University School of Medicine

**Eugene Cronkite Prize** 2019

First Prize Postdoctoral Speaker, International Society of Haematology Annual Meeting

**Children’s Oncology Group Foundation Award**  2019

Jeffrey Pride Pediatric Cancer Research Foundation

Children’s Oncology Group Foundation

**Career Development Program Fellowship** 2017-2019

Leukemia and Lymphoma Society

**Leukemia Foundation Australia PhD Scholarship** 2013-2015

Leukaemia Foundation Australia

**Speaker Award Winner** 2014Australian B Cell Dialogue Meeting 6 – Victoria, Australia

**Community Engagement Award** 2013Walter and Eliza Hall Institute of Medical Research

**Colman-Speed Medal** 2011

Top Honours Student, Walter and Eliza Hall Institute of Medical Research

**Valedictorian/Dean’s Honours List** 2011

Department of Medical Biology, University of Melbourne

**Undergraduate Research Opportunities Program Scholarship** 2009-2010

Biomedical Research Victoria

**RESEARCH EXPERIENCE**

**New York University School of Medicine** 2015-2022

Postdoctoral Fellow; Advisor: Iannis Aifantis, PhD

Dissecting the leukemic microenvironment of B-cell acute lymphoblastic leukemia (B-ALL):

* Utilized single-cell approaches to generate the first comprehensive map of the B-ALL immune microenvironment in primary human B-ALL throughout conventional chemotherapy (Witkowski et al. *Cancer Cell* 2020)
* Generated *ex vivo* (Ma et al. *Sci Adv* 2020) and *in vivo* pre-clinical platforms highlighting non-classical monocytes as a therapeutic target capable of improving existing targeted B-ALL therapeutic efficacy.

**Walter and Eliza Hall Institute of Medical Research** 2011-2015

Graduate Researcher; Advisor: Ross Dickins, PhD

Understanding the role of transcription factor, Ikaros, in acute lymphoblastic leukaemia using inducible RNAi:

* Generated multiple transgenic mouse models of both B- and T-cell progenitor ALL, allowing for inducible Ikaros knockdown *in vivo* through tet-regulated RNAi.
* Characterized Ikaros as a repressor of Notch pathway activation in murine and human T-cell ALL (Witkowski et al. *Leukemia* 2015).
* Identified prognostically-significant Ikaros target genes underpinning its tumor-suppressive functions in high-risk BCR-ABL+ B-ALL (Witkowski et al. *J Exp Med* 2017).

**Walter and Eliza Hall Institute of Medical Research** 2009-2010

Research Assistant; Advisors: Anne Verhagen, PhD, Douglas Hilton, PhD

**University of Melbourne, Department of Genetics** 2009

Undergraduate Research Assistant; Advisors: Christopher Cobbett, PhD

**TEACHING EXPERIENCE**

**Masters Program**  2022-2023

**Student: Jonathan** Hester-McCullough

Witkowski Laboratory, CU Anschutz

**Summer Undergraduate Student Supervisor** 2022

Student: Elijah Johnson

Witkowski Laboratory, CU Anschutz

**Postgraduate Student Supervisor** 2018-2019

Students: Sheetal Sreeram, Goyaert Roosen, Yuling Dai

Aifantis Laboratory, New York University School of Medicine

**Undergraduate Student Supervisor** 2014

Student: Oliver Le Grice

Dickins Laboratory, Walter and Eliza Hall Institute of Medical Research

**ONGOING PROFESSIONAL ASSOCIATIONS**

**Society for Immunotherapy of Cancer,** Active Member2022-Present

**American Society of Hematology,** Active Member 2020-2022

**Children’s Oncology Group** **Active Member** 2018-Present

Laboratory Science Discipline

**Significant Contributor**

Venetoclax Development

Walter and Eliza Hall Institute, Melbourne, Australia

**CONFERENCE PRESENTATIONS**

**Taru Hays Symposium,** CU Anschutz 2022

**Tumor Host Immunology Conference,** CU Anschutz 2022

**Session Chair,** ISEH 2020 Virtual Meeting 2020

**Invited Speaker,** NYU Department of Pathology, NYU Langone Health 2020

**Invited Speaker,** London Stem Cell Forum, London Stem Cell Network 2020

**Selected Abstract Speaker**, NYU Postdoctoral Research Day, NYU Langone Health 2020

**Invited Speaker,** Children’s Oncology Group, Biology Fall Retreat, Denver, CO 2019

**Selected Abstract Speaker,** International Society of Haematology Annual Meeting 2019

**Invited Speaker,** 10X Genomics New York User Group Meeting 2019

**Invited Speaker,** Department of Oncology, Johns Hopkins University, Baltimore, MD 2019

**Invited Speaker,** Australian Centre for Blood Diseases, Monash University, Australia 2018

**Short Oral Presentation,** New Directions in Leukaemia Research Meeting, Queensland, Australia. 2015

**Selected Abstract Speaker,** Australian B Cell Dialogue Meeting 6, Melbourne, Australia 2014

**REVIEW ARTICLES**

Iacobucci I, **Witkowski MT**, Mullighan CG. Single-cell analysis of acute lymphoblastic and lineage ambiguous leukemia - approaches and molecular insights. *Blood* doi: 10.1182/blood.2022016954. Online ahead of print (2022)

**Witkowski MT#**, Kousteni S, Aifantis I, Mapping and targeting of the leukemic microenvironment. J Exp Med 217(2), e20190589 *(*2020)

#Corresponding author

**Witkowski MT\*,#**, Lasry A\*, Carroll WL, Aifantis I. Immune-Based Therapies in Acute Leukemia. *Trends in Cancer* 5(10), 604-618 (2019)

#Corresponding author, \*co-first author

**PRIMARY RESEARCH PUBLICATIONS**

Lasry A, Nadorp B, Fornerod M, Nicolet D, Wu H, Walker CJ, Sun Z, **Witkowski MT**, Tikhonova AN, Guillamot-Ruano M, Cayanan G, Yeaton A, Robbins G, Obeng EA, Tsirigos A, Stone RM, Byrd JC, Pounds S, Carroll WL, Gruber TA, Eisfeld A & Aifantis I. An inflammatory state remodels the immune microenvironment and improves risk stratification in acute myeloid leukemia. *Nature Cancer* https://doi.org/10.1038/s43018-022-00480-0 (2022)

**Witkowski MT\*,#,** Lee S\*, Wang E\*, Lee AK, Talbot A, Ma C, Tsopoulidis N, Brumbaugh J, Zhao Y, Roberts KG, Hogg SJ, Nomikou S, Ghebrechristos YE, Thandapani P, Mullighan CG, Hochedlinger K, Chen W, Abdel-Wahab O, Eyquem J & Aifantis I#. NUDT21 limits CD19 levels through alternative mRNA polyadenylation in B cell acute lymphoblastic leukemia. *Nature Immunology* 23(10):1424-1432 (2022)

#Corresponding author, \*co-first author

Wang E, Mi X, Thompson MC, Montoya S, Notti RQ, Afaghani J, Durham BH, Penson A, **Witkowski MT**, Lu SX, Bourcier J, Hogg SJ, Erickson C, Cui D, Cho H, Singer M, Totiger TM, Chaudhry S, Geyer M, Alencar A, Linley AJ, Palomba ML, Coombs CC, Park JH, Zelenetz A, Roeker L, Rosendahl M, Tsai DE, Ebata K, Brandhuber B, Hyman DM, Aifantis I, Mato A, Taylor J, Abdel-Wahab O. Mechanisms of Resistance to Noncovalent Bruton's Tyrosine Kinase Inhibitors. *New England Journal of Medicine* 24;386(8):735-743 (2022)

Thandapani P, Kloetgen A, **Witkowski MT**, Glytsou C, Lee AK, Wang E, Wang J, LeBoeuf SE, Avrampou K, Papagiannakopoulos T, Tsirigos A, Aifantis I. Valine tRNA levels and availability regulate complex I assembly in leukaemia. *Nature*. 601(7893):428-433 (2022)

Wang E, Zhou H, Nadorp B, Cayanan G, Chen X, Yeaton AH, Nomikou S, **Witkowski MT**, Narang S, Kloetgen A, Thandapani P, Ravn-Boess N, Tsirigos A, Aifantis I. Surface antigen-guided CRISPR screens identify regulators of myeloid leukemia differentiation. *Cell Stem Cell* 28(4):718-731(2021)

Ma C, **Witkowski MT**, Harris J, Dolgalev I, Sreeram S, Qian W, Tong J, Chen X, Aifantis I, Chen W. Leukemia-on-a-chip: Dissecting the chemoresistance mechanisms in B cell acute lymphoblastic leukemia bone marrow niche. *Science Advances* 30;6(44) (2020)

**Witkowski MT\*,#,** Dolgalev I\*, Evensen NA, Ma C, Chambers T, Roberts CG, Sreeram S, Dai Y, Tikhonova AN, Lasry A, Qu C, Pei D, Cheng C, Robbins GA, Pierro J, Selvaraj S, Mezzano V, Daves M, Lupo PJ, Scheurer ME, Loomis CA, Mullighan CG, Chen W, Rabin KR, Tsirigos A, Carroll WL & Aifantis I. Extensive Remodeling of the Immune Microenvironment in B-cell Acute Lymphoblastic Leukemia**.** *Cancer Cell* 8;37(6), 867-882(2020)

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McKenzie MD, Ghisi M, Oxley EP, Ngo S, Cimmino L, Esnault C, Liu R, Salmon JM, Bell CC, Ahmed N, Erlichster M, **Witkowski MT**, Liu GJ, Chopin M, Dakic A, Simankowicz E, Pomilio G, Vu T, Krsmanovic P, Su S, Tian L, Baldwin TM, Zalcenstein DA, DiRago L, Wang S, Metcalf D, Johnstone RW, Croker BA, Lancaster GI, Murphy AJ, Naik SH, Nutt SL, Pospisil V, Schroeder T, Wall M, Dawson MA, Wei AH, de Thé H, Ritchie ME, Zuber J, Dickins RA. Interconversion between Tumorigenic and Differentiated States in Acute Myeloid Leukemia. *Cell Stem Cell* 25(2), 258-272 (2019)

Tikhonova AN, Dolgalev I, Hu H, Sivaraj KK, Hoxha E, Cuesta-Domínguez Á, Pinho S, Akhmetzyanova I, Gao J, **Witkowski M,** Guillamot M, Gutkin MC, Zhang Y, Marier C, Diefenbach C, Kousteni S, Heguy A, Zhong H, Fooksman DR, Butler JM, Economides A, Frenette PS, Adams RH, Satija R, Tsirigos A, Aifantis I. The bone marrow microenvironment at single-cell resolution. *Nature* 569(7755), 222-228 (2019)

McRae HM, Garnham AL, Hu Y, **Witkowski MT**, Corbett MA, Dixon MP, May RE, Sheikh BN, Chiang W, Kueh AJ, Nguyen TA, Man K, Gloury R, Aubrey BJ, Policheni A, Di Rago L, Alexander WS, Gray DHD, Strasser A, Hawkins ED, Wilcox S, Gécz J, Kallies A, McCormack MP, Smyth GK, Voss AK, Thomas T. PHF6 regulates hematopoietic stem and progenitor cells and its loss synergizes with expression of TLX3 to cause leukemia. 133(16), 1729-1741 (2019)

Cimmino L, Dolgalev I, Wang Y, Yoshimi A, Martin GH, Wang J, Ng V, Xia B, **Witkowski MT**, Mitchell-Flack M, Grillo I, Bakogianni S, Ndiaye-Lobry D, Martín MT, Guillamot M, Banh RS, Xu M, Figueroa ME, Dickins RA, Abdel-Wahab O, Park CY, Tsirigos A, Neel BG, Aifantis I. Restoration of TET2 Function Blocks Aberrant Self-Renewal and Leukemia Progression. *Cell* 6, 1079-1095 (2017)

**Witkowski MT,** Hu Y, Roberts KG, Boer JM, McKenzie MD, Liu GJ, Le Grice OD, Tremblay CS, Ghisi M, Willson TA, Horstmann MA, Aifantis I, Cimmino L, Frietze S, den Boer ML, Mullighan CG, Smyth GK, Dickins RA. Conserved IKAROS-regulated genes associated with B-progenitor acute lymphoblastic leukemia outcome. *J Exp Med* 214 (3), 773-791 (2017)

Lee EF, Grabow S, Chappaz S, Dewson G, Hockings C, Kluck RM, Debrincat MA, Gray DH, **Witkowski MT**, Evangelista M, Pettikiriarachchi A, Bouillet P, Lane RM, Czabotar PE, Colman PM, Smith BJ, Kile BT, Fairlie WD. Physiological restraint of Bak by Bcl-xL is essential for cell survival. *Genes Dev* 30 (10), 1240-50 (2016)

**Witkowski MT**, Cimmino L, Hu, Y, Trimarchi T, Tagoh H, McKenzie MD, Best SA, Tuohey L, Willson TA, Nutt SL, Busslinger M, Aifantis I, Smyth GK, Dickins RA. Activated Notch Signaling counteracts Ikaros tumor suppression in mouse and human T cell acute lymphoblastic leukemia*.* *Leukemia* 29, 1301-1311 (2015)

Liu GJ, Cimmino L, Jude JG, Hu Y, **Witkowski MT**, McKenzie MD, Kartal-Kaess M, Best SA, Tuohey L, Liao Y, Shi W, Mullighan CG, Farrar MA, Nutt SL, Smyth GK, Zuber J, Dickins RA. Pax5 loss imposes a reversible differentiation block in B-progenitor acute lymphoblastic leukemia. *Genes Dev*. 28 (12), 1337-50 (2014)

**REFERENCES**

Iannis Aifantis PhD

Chair, Department of Pathology

Hermann M. Biggs Professor of Pathology,

Department of Pathology

New York University School of Medicine

550 First Avenue, Smilow 1307

New York, NY 10016

United States

Ioannis.Aifantis@nyulangone.org

William Carroll MD

The Julie & Edward J. Minskoff Professor of Pediatrics and Pathology

Laura and Isaac Perlmutter Cancer Center

Stephen D. Hassenfeld Children's Center for Cancer and Blood Disorders

New York University School of Medicine

550 First Avenue, Smilow 1307

New York, NY 10016

United States

William.Carroll@nyulangone.org

Ross Dickins PhD

Associate Professor

Australian Centre for Blood Diseases

Monash University - Monash AMREP Building

Level 1 Walkway via The Alfred Centre
99 Commercial Road
Melbourne VIC 3004
Australia

Ross.Dickins@monash.edu