

## Matthew T. Witkowski, PhD

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Department of Pediatrics

Hematology/Oncology/Bone Marrow Transplant Laboratories

University of Colorado Anschutz Medical Campus

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### 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**

Department of Pediatrics

Assistant Professor

**Aurora, CO**

2022-Present

### EDUCATION

**New York University School of Medicine**

Aifantis laboratory, Department of Pathology

Postdoctoral Fellow

**New York, NY**

2015-2022

**Walter and Eliza Hall Institute of Medical Research**

PhD, Department of Medical Biology, University of Melbourne

**Melbourne, Victoria, Australia**

2011-2015

**University of Melbourne**

Bachelor of Science (Honours)

Department of Genetics

**Melbourne, Victoria, Australia**

2008-2011

### CURRENT FINANCIAL SUPPORT

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

Duration: July 1<sup>st</sup> 2022 – June 30<sup>th</sup>, 2023

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

Duration: May 12<sup>th</sup>, 2022 – May 11<sup>th</sup>, 2025

**Laboratory Start-up**

Duration: February 1<sup>st</sup>, 2022 (non-expiring amount)

### GRANTS AND AWARDS

**Cancer League of Colorado Research Grant**

AWD#222549-MW

2022-2023

**NIH/NCI K22 Award**

1K22CA258520-01

2022-2025

**ASH Restart Award Recipient**

American Society of Hematology

2020

<b>CDP (Fellow) Achievement Award</b> The Leukemia & Lymphoma Society	2020
<b>Outstanding Postdoctoral Fellow Award</b> New York University School of Medicine	2020
<b>Speaker Award Winner</b> Postdoctoral Research Day, New York University School of Medicine	2020
<b>Eugene Cronkite Prize</b> First Prize Postdoctoral Speaker, International Society of Haematology Annual Meeting	2019
<b>Children's Oncology Group Foundation Award</b> Jeffrey Pride Pediatric Cancer Research Foundation Children's Oncology Group Foundation	2019
<b>Career Development Program Fellowship</b> Leukemia and Lymphoma Society	2017-2019
<b>Leukemia Foundation Australia PhD Scholarship</b> Leukaemia Foundation Australia	2013-2015
<b>Speaker Award Winner</b> Australian B Cell Dialogue Meeting 6 – Victoria, Australia	2014
<b>Community Engagement Award</b> Walter and Eliza Hall Institute of Medical Research	2013
<b>Colman-Speed Medal</b> Top Honours Student, Walter and Eliza Hall Institute of Medical Research	2011
<b>Valedictorian/Dean's Honours List</b> Department of Medical Biology, University of Melbourne	2011
<b>Undergraduate Research Opportunities Program Scholarship</b> Biomedical Research Victoria	2009-2010

## **RESEARCH EXPERIENCE**

<b>New York University School of Medicine</b> Postdoctoral Fellow; Advisor: Iannis Aifantis, PhD Dissecting the leukemic microenvironment of B-cell acute lymphoblastic leukemia (B-ALL): <ul style="list-style-type: none"><li>- 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. <i>Cancer Cell</i> 2020)</li><li>- Generated <i>ex vivo</i> (Ma et al. <i>Sci Adv</i> 2020) and <i>in vivo</i> pre-clinical platforms highlighting non-classical monocytes as a therapeutic target capable of improving existing targeted B-ALL therapeutic efficacy.</li></ul>	2015-2022
<b>Walter and Eliza Hall Institute of Medical Research</b> Graduate Researcher; Advisor: Ross Dickins, PhD Understanding the role of transcription factor, Ikaros, in acute lymphoblastic leukaemia using inducible RNAi: <ul style="list-style-type: none"><li>- Generated multiple transgenic mouse models of both B- and T-cell progenitor ALL, allowing for inducible Ikaros knockdown <i>in vivo</i> through tet-regulated RNAi.</li><li>- Characterized Ikaros as a repressor of Notch pathway activation in murine and human T-cell ALL (Witkowski et al. <i>Leukemia</i> 2015).</li><li>- Identified prognostically-significant Ikaros target genes underpinning its tumor-suppressive functions in high-risk BCR-ABL<sup>+</sup> B-ALL (Witkowski et al. <i>J Exp Med</i> 2017).</li></ul>	2011-2015
<b>Walter and Eliza Hall Institute of Medical Research</b> Research Assistant; Advisors: Anne Verhagen, PhD, Douglas Hilton, PhD	2009-2010
<b>University of Melbourne, Department of Genetics</b>	2009

Undergraduate Research Assistant; Advisors: Christopher Cobbett, PhD

### **TEACHING EXPERIENCE**

- 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**

- Children's Oncology Group Active Member** 2018-Present  
Laboratory Science Discipline
- Significant Contributor**  
Venetoclax Development  
Walter and Eliza Hall Institute, Melbourne, Australia

### **CONFERENCE PRESENTATIONS**

- 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**

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

<sup>#</sup>Corresponding author

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

<sup>#</sup>Corresponding author, <sup>\*</sup>co-first author

### **PRIMARY RESEARCH PUBLICATIONS**

**Witkowski MT<sup>\*#</sup>**, Lee S<sup>\*</sup>, Wang E<sup>\*</sup>, 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<sup>#</sup>. NUDT21 limits CD19 levels through alternative mRNA polyadenylation in B cell acute lymphoblastic leukemia. *Nature Immunology* doi: 10.1038/s41590-022-01314-y. Online ahead of print. (2022)

<sup>#</sup>Corresponding author, <sup>\*</sup>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**<sup>\*,#</sup>, 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)

<sup>#</sup>Corresponding author, <sup>\*</sup>co-first author

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**, Guillaumot 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, Guillaumot 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**

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