Curriculum Vitae
Matthew Fisher

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Contact Information
Matthew Fisher
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Education
2011 B.S. Biology (May 2011) Sacred Heart University, Fairfield, CT (Dean's Scholarship)
2017 PhD. Biochemistry and Molecular Biology (May, 2017) University of Maryland, Baltimore

Funding
2017 Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral Fellowship (Parent F32). **Impact Score**: 17, **Percentile**: 4

Research Experience During my time in Dr. Richard L. Eckert's laboratory, I studied the role of transglutaminase 2 (TG2) in epidermal cancer stem cells. I utilized various cellular and molecular biology techniques to elucidate a novel TG2 driven stem cell survival pathway in epidermal cancer stem cells. As part of this work I identified a number of novel interacting partners of TG2, particularly in the basement membrane, utilizing a biotin ligase fusion protein and Co-Immunoprecipitation. Employing inhibitor studies, siRNA transfections and CRISPR mediated knockouts, I demonstrated the importance of these TG2 interactions in driving signaling pathways involved in regulating stemness and tumor growth. This work was the first report showing that TG2 could regulate the Hippo signaling pathway component LATS1, a potent tumor suppressor. This was also the first time TG2 had been shown to induce the stem cell survival protein ΔNp63α. These efforts culminated in a manuscript published in Cancer Research. Additionally, I showed TG2, independent of NFκB, is capable of stimulating a cancer stem cell phenotype (Molecular Cancer Research, 2015) and Epithelial to Mesenchymal Transition (Oncotarget, 2015) as measured by spheroid formation, invasion and migration. This represented a novel mechanism of TG2 induced Epithelial to Mesenchymal Transition, as previous reports indicated a dependence on NFκB. This work is of high importance, as the incidence of squamous cell carcinoma continues to rise and survival rates of recurrent disease remain below 30%.

In addition to my work with squamous cell carcinoma, I also worked with melanoma. In this regard, I identified a diet derived compound, sulforaphane, as a potential therapeutic for targeting melanoma cancer stem cells. I demonstrated that sulforaphane treatment reduces expression of polycomb group proteins, which have been implicated in drug resistance and metastasis. This work provides important insight, as sulforaphane may be useful in preventing melanoma metastasis (Molecular Carcinogenesis, 2015). As drug resistance is a major problem in melanoma treatment, I also developed a number of drug resistant cell lines to elucidate novel signaling mechanisms employed by cells to confer resistance to $BRAF^{V600E}$ inhibitors, where I identified the Hippo pathway transducers YAP and TAZ as playing a major role in drug resistance. This work is the first to demonstrate that the YAP inhibitor, Verteporfin, is a potential therapeutic for patients who have developed $BRAF^{V600E}$ inhibitor resistant melanoma, as it sensitizes cells to $BRAF^{V600E}$ inhibitor treatment, and reduces tumor volume. In addition to my research, I have mentored several students in the Eckert Lab. This experience has expanded my desire to pursue teaching opportunities in the laboratory and classroom.

Career Goals Currently, I am a postdoctoral fellow in the laboratory of Alea Mills at Cold Spring Harbor Laboratory. My work focuses on identifying novel p63 regulated chromatin remodelers that are critical for the survival of the cancer stem cell population in Head and Neck Squamous Cell Carcinoma.

My long term goals include heading a laboratory at a research-intensive university or non-profit research institute to continue my efforts in cancer research while training the next generation of scientists. My laboratory will focus on elucidating novel signal transduction pathways involved in driving cancer stemness, metastasis and drug resistance, and determining how these pathways can be targeted in epithelial cancers.

Manuscripts

Adhikary G, Grun D, Kerr C, Balasubramanian S, Rorke EA, Vemuri M, Boucher S, Bickenbach JR, Hornyak T, Xu W, **Fisher ML**, Eckert RL. Identification of a population of squamous cell carcinoma cells with enhanced potential for tumor formation. **PLoS One** 8, 12, : e84324, 2013

Fisher ML, Keillor JW, Xu W, Eckert RL, Kerr C. Type II Transglutaminase is required for epidermal squamous cell carcinoma stem cell survival. **Molecular Cancer Research** 7, 1083-1094, 2015

Fisher ML, Adhikary G, Xu W, Kerr C, Keillor JW, Eckert RL. Type II transglutaminase stimulates epidermal cancer stem cell epithelial-mesenchymal transition. **Oncotarget** 24, 20525-20539, 2015

Eckert RL, **Fisher ML**, Grun D, Adhikary G, Xu W, Kerr C. Transglutaminase as a cancer stem cell survival factor. **Molecular Carcinogenesis** 10, 947-958, 2015

Fisher ML, Adhikary G, Grun D, Kaetzel DM, Eckert RL. Ezh2 is necessary for the aggressive phenotype of melanoma cancer stem cells, and is a target of diet-derived sulforaphane. **Molecular Carcinogenesis** 55, 2024-2036, 2016

Kerr C, Szmacinski H, **Fisher ML**, Nance B, Lakowicz JR, Akbar A, Keillor JW, Wong TL, Godoy-Ruiz R, Toth EA, Weber DJ, Eckert RL. Transamidase site-targeted compounds alter the conformation of transglutaminase to reduce GTP binding activity and cancer stem cell survival. In Press, **Oncogene** 36, 2981-2990, 2017

Fisher ML, Kerr C, Adhikary G, Xu W, Keillor J, Eckert RL, Transglutaminase interacts with α6/β4-integrin to stimulate hippo dependent ΔNp63α stabilization leading to enhanced epidermal cancer stem cell survival. **Cancer Research** 76, 24, 7265-7276, 2016

Saha K, **Fisher ML**, Adhikary G, Grun D, Eckert RL. Sulforaphane suppresses PRMT5/MEP50 function in epidermal squamous cell carcinoma leading to reduced tumor formation. In press, **Carcinogenesis** 2017

Fisher ML, Grun D, Adhikary G, Eckert RL. Sulforaphane reduces YAP/ΔNp63α signaling to reduce cancer stem cell survival and tumor formation. In press, **Oncotarget**, 2017

Fisher ML, Grun D, Adhikary G, Kerr CL, Eckert RL. Transglutaminase (TG2) is a direct target of YAP-TAZ—Reply. In press, **Cancer Research** 2017

Fisher ML, Grun D, Adhikary G, Eckert RL (2016) YAP1 and TAZ as therapeutic targets in BRAF inhibitor-resistant melanoma. Submitted, **Cancer Research**

Scientific Presentations

Fisher ML, Keillor, JW, Xu W, Eckert RL Transglutaminase 2 is necessary for cancer stem cell survival in squamous cell carcinoma. Sixth Annual Maryland Stem Cell Research Fund Symposium, Annapolis, 2013

Fisher ML, Xu W, Adhikary G, Kerr C, Eckert R Transglutaminase 2 is required for cancer stem cell survival in epidermal squamous cell carcinoma. UMSOM Stem Cell Center Retreat, Baltimore, October 2013

Fisher ML, Xu W, Adhikary G, Kerr C, Eckert R Transglutaminase 2 is required for cancer stem cell survival in epidermal squamous cell carcinoma. Maryland Stem Cell Research Fund - Johns Hopkins University, Baltimore, December, 2013

Fisher ML, Xu W, Adhikary G, Kerr C, Eckert R Transglutaminase 2 is required for cancer stem cell survival in epidermal squamous cell carcinoma. 3rd Annual Biochemistry and Molecular Biology Departmental Retreat, Baltimore, January, 2014.

Fisher ML, Xu W, Adhikary G, Kerr C, Eckert R Transglutaminase 2 Regulates Epidermal Cancer Stem Cell Epithelial-Mesenchymal Transition. 4th Annual Biochemistry and Molecular Biology Departmental Retreat, Baltimore, January, 2015.

Fisher ML, Adhikary G, Grun D, Xu W, Eckert RL Ezh2 is necessary for the aggressive phenotype of Melanoma Cancer Stem Cells, and is a Target of Diet-Derived Sulforaphane. 4th Annual Biochemistry and Molecular Biology Departmental Retreat, Baltimore, January, 2015

Fisher ML, Xu W, Adhikary G, Kerr C, Eckert RL Type II transglutaminase is an epidermal squamous cell carcinoma stem cell survival protein. AACR Annual National Meeting, Philadelphia, PA, April, 2015

Fisher ML, Xu W, Adhikary G, Kerr C, Eckert RL Transglutaminase 2 is necessary for cancer stem cell survival in squamous cell carcinoma. Greenebaum Cancer Center Annual Research Day, Baltimore, MD, May, 2015

Fisher ML, Adhikary G, Xu W, Eckert RL Transglutaminase interacts with $\alpha 6/\beta 4$ –integrin to stimulate hippo-dependent $\Delta Np63\alpha$ stabilization leading to enhanced epidermal cancer stem cell survival. 5th Annual Biochemistry and Molecular Biology Departmental Retreat, Baltimore, January, 2016

Fisher ML, Adhikary G, Xu W, Eckert RL Transglutaminase stimulates YAP-dependent $\Delta Np63\alpha$ stabilization leading to enhanced epidermal cancer stem cell survival. Greenebaum Cancer Center Annual Research Day, Baltimore, MD, May, 2016

Fisher ML, Adhikary G, Xu W, Eckert RL Transglutaminase-dependent epidermal cancer stem cell survival and epithelial-mesenchymal transition requires GTP binding but not transamidase activity, and does not require NFκB signaling. "Transglutaminases in Human Disease Processes" **Gordon Research Conference**, Girona, Spain, July, 2016

Fisher ML, Grun D, Adhikary G, Eckert RL YAP1 and TAZ as therapeutic targets in BRAF inhibitor-resistant melanoma. PanAmerican Society for Pigment Cell Research Meeting, Baltimore, Maryland, October 2016 **Oral Presentation** (T. Hornyak)

Fisher ML, Adhikary G, Grun D, Xu W, Eckert RL Ezh2 is necessary for the aggressive phenotype of Melanoma Cancer Stem Cells, and is a Target of Diet-Derived Sulforaphane. PanAmerican Society for Pigment Cell Research Meeting, Baltimore, Maryland, October 2016 (T. Hornyak)

Teaching Service – Mentoring & Training

University of Maryland Student Training - Mentoring

2014 Rajkumar Baldeosingh (UMSOM Molecular Medicine MS Program)
2014 Prarthana Ravishankar (UMSOM Molecular Medicine MS Program)
2016 Nicholas Ciavattone (UMSOM Molecular Medicine PhD Program)
2016 Louis Born (UMSOM Molecular Medicine MD/PhD Program)

Undergraduate Research Trainees (3 Month Summer Research Rotations) - Mentoring

2013 Sara Siddiqui (Student - University of Maryland Baltimore County Student)
2015-2016 Bailey Nance (Intern - University of Maryland Baltimore County - Meyerhoff Minority Res Prog)
2017 Sean Connelly (Undergraduate Research Program – Cold Spring Harbor Laboratory)

Awards

Travel Fellowship, 2016 **Gordon Research Conference** - Transglutaminases in Human Disease Processes, Girona, Spain
Best Poster Presentation, 2016 PanAmerican Society for Pigment Cell Research Meeting, Baltimore, Maryland

Research Experience

Sacred Heart University, Fairfield, CT, Dept. of Biology
Undergraduate research, mentor: Nicole M. Roy, Ph.D.
Cardiac defects due to the phenylpyrazole pesticide, Fipronil, in the developing zebrafish embryo

Sacred Heart University, Fairfield, CT, Dept. of Biology
Undergraduate research, mentor: Nicole M. Roy, Ph.D.
bli-4 knockdown in Caenorhabditis elegans via RNAi.

Baltimore VA Medical Center, Baltimore, MD, Dept. of Neurology
Graduate research assistant, Principe Investigator, Paul Fishman, M.D., Ph.D.
TAT and TET peptides for the Delivery of Proteins to the CNS

University of Maryland, Baltimore, MD, Dept. of Biochemistry
PhD Candidate, Principle Investigator, Richard Eckert, Ph.D.
Transglutaminase 2 role in epidermal squamous cell carcinoma cell survival

Internships

Maryland Venture Fund (Department of Business and Economic Development)
Life Sciences intern, mentor: Alastair Mackay, Ph.D.
Analysis of Maryland biotech and pharmaceutical companies' pipeline products and competitive landscape

Jerome Stevens Pharmaceuticals Incorporated, Bohemia, NY
Research intern, mentor: Daniel Akeson, M.A.
Granulation, compounding and composite sampling of pharmaceuticals Levothyroxine and Digoxin

References

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