BIOGRAPHICAL SKETCH

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NAME: BIRGE, RAYMOND B.

eRA COMMONS USER NAME (credential, e.g., agency login): RBIRGE

POSITION TITLE: Professor and Vice Chair

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Connecticut	BS	05/1983	Biology
University of Connecticut	PhD	05/1989	Biochemical Toxicology
The Rockefeller University	Postdoc	1994	Molecular Oncology

A. Personal Statement:

I have been a Principal Investigator for almost 30 years, beginning as an Assistant Professor at The Rockefeller University from 1994-2000, and for the ~past 20+ years at Rutgers University (legacy University of Medicine and Dentistry of New Jersey). My current position is Professor and Vice Chair in the Department of Microbiology, Biochemistry, and Molecular Genetics, and I hold a full membership at The Cancer Institute of New Jersey (CINJ). I also serve as Director of the Center for Cell Signaling (CCS) at Rutgers, Biomedical and Health Sciences on the Newark campus. Scientifically, my laboratory focuses on (i) understanding the mechanisms by which normal cells become malignant through the activation of oncogenes, and (ii) the mechanisms by which tumor cells evade immune responses and metastasize. We employ multidisciplinary approaches to tackle these problems, including molecular biology, genetics & animal models, biochemistry, and structural biology. As a PI, I have successfully administered funded research projects (including staffing, research training, budgets), and successfully collaborated with diverse researchers to produce original research papers. Over the past 25 years as a PI, I have successfully administered funded research projects (staffing, research training, budgets), and successfully collaborated with diverse researchers to produce original research papers. I am also very committed to PhD and postdoctoral training and have several projects in cancer biology that focus on oncogenes, signaling, and cancer immunology. My current NIH funded research projects anticipate the frequent use of several shared resources at CINJ and Rutgers, and the maintenance and acquisition of state of the art facilities is essential for the success of the my research as well as the training of junior scientists in their early careers.

Ongoing and recently completed projects that I would like to highlight include:

Current:
NIH REACH Program (U01HL150852)
PI's: Birge/Kotenko MPI
11/15/22-05/15/24
Development of Interferon fusion proteins as broad-spectrum antivirals:
The goal of this project is to develop and characterize chimeric phosphatidylserine-targeting interferons to target enveloped viruses as potential therapeutics for acute respiratory diseases involving influenza and SARS-Cov-2.

R01 CA260137-01A1 (**MPI: Birge/Kotenko**)
02/01/22-01/31/27
Targeting a phosphatidylserine/TAM receptor/PD-L1 axis as a vulnerability in cancer
The goal of this project is to investigate the role of Mertk (a phosphatidylserine receptor) as a driver of immune evasion in breast cancer.

New Jersey Commission on Cancer Research
COCR21RBG011(**MPI: Birge/Kotenko**)
05/01/21-04/30/23
"Targeting a phosphatidylserine/TAM receptor/PD-L1 axis as a vulnerability in cancer"
*T*he goal of this bridge project is to develop a knock-in mouse model to express human Mertk in the C57 Bl/6 background and assess Mertk expression in human archived breast cancer tissues.

Gladiator Therapeutics **(PI: Birge)**
08/01/20-08/01/23
Sponsored Research
Phosphatidylserine-dependent Cell Penetrating Activity of GLA and GLA-based Fusion Proteins:
The goals of this project will evaluate a series of PS targeting biologicals that target the tumor microenvironment for immune-oncology applications.

Completed:

Busch Biomedical Research Grant (**co-PI: Lutz/Birge**)
09/01/19-09/01/22
Sponsored Research
PS-mediated TAM receptor activation in lung cancer cells stimulates PGE_2 production to encourage an immunosuppressive and pro-tumorigenic phenotype
The goals of this project set are to investigate how activation of Mertk on macrophages induces resolving prostaglandins and immune-modulatory cytokines.

New Jersey Commission on Cancer Research
01/01/17-12/31/18
(PI: Calianese/Mentor: **Birge**)
Cloning anti-PS antibodies from HIV-infected individuals for cancer immunotherapy
The goals of this mentored pre-doctoral fellowship set out to clone a series of anti-PS Mabs from memory B cells of HIV-1-infected patients and engineer these antibodies into cancer therapeutics.

R01 CA165077 **(PI: Birge)**
07/01/12-06/30/18
NIH NCI CA165077-06
Non-canonical signal pathway for Crk in breast cancer
The goals of this project were to explore the structure and function of Crk oncogene in breast cancer invasion and metastasis.

B. Positions, Scientific Appointments, and Honors

Positions:

2019-present: Director, Center for Cell Signaling, Rutgers Biomedical and Health Science (RBHS) 1994-
2014-present: Vice Chair, Department of Microbiology, Biochemistry, and Molecular Genetics. RBHS
2014-present: Member, Cancer Institute of New Jersey, New Brunswick Campus
2013-2017: Member, New Jersey Medical School Cancer Center, Newark Campus
2013-present: Tenured Professor, Department of Biochemistry and Molecular Biology. Rutgers-Biomedical and Health Sciences (RBHS)
2009-present: Professor, Department of Biochemistry and Molecular Biology. University of Medicine and Dentistry of New Jersey-New Jersey Medical School.
2000-2009: Associate Professor, Department of Biochemistry and Molecular Biology, UMDNJ-NJMS
1998-2000: Acting Head, Laboratory of Molecular Oncology, The Rockefeller University
1998: Assistant Professor, The Rockefeller University

Scientific Appointments:

2022-: Scientific Founder, Targeron Therapeurtics, LLC (with R. Toddywala and S. Kotenko)
2019-: Scientific Founder. TamRx Biotechnology, LLC (with W. Welsh and Y. Peng)
2017-: Editor-in-Chief: *Cell Communication & Signaling*
2010-: Member, American Society of Cancer Research (AACR)
2008-: Member, American Society of Biochemistry and Molecular Biology (ASBMB)
2008-2016 Editorial Board. *Cell Communication & Signaling* (2008-2016)
2008-2018: Editorial Board. *The Journal of Biological Chemistry*
2006-2010: Scientific Advisory Board; GliaMed Biotechnology (2006-2010)
2004-: Board of Directors, The International Cell Death Society

Honors

2022: Springer Nature: Top Editor-in-Chief for Cell Communication and Signaling.
2022: International Cell Death Society Prize
2021: New Jersey Commission on Cancer Research Dr. Jonathan Yavelow Mentor Award
2017: New Jersey Medical School Mentoring Award
2004-2007: Johnson and Johnson Focused Giving Merit Award
1999-2001: Muscular Dystrophy Association Research Fellow
1994-1996: James A. Shannon Directors Award, General Medical Sciences, NIH
1991-1992: NIH Postdoctoral F32 Individual Fellowship F32, Molecular Oncology
1989-1991: American Cancer Society Postdoctoral Fellow

C. Contribution to Science:

My early publications focused on the structure and function of oncogenes, with a primary emphasis on the Crk and Src oncogenes. I was part of the original work defining the structure and function of the Src Homology 2 (SH2) domain, as well as studies elucidating the biology of how SH2 domains achieve binding specificity. I have continued to publish extensively on the Crk oncogene and tyrosine phosphorylation (40 peer-reviewed papers), including more recent studies that elucidate how Crk promotes cell migration, cell invasion, metastasis, and chemo-resistance.

- G.Waksman, D.Kominos, S.C.Robertson, N.Pant, D.Baltimore, **R.B.Birge**, D.Cowburn, H.Hanafusa, B.J.Mayer, M.Overduin, M.D.Resh, C.B.Rios, L.Silverman, and J. Kuriyan. (1992). Crystal structure of the phosphotyrosine recognition domain SH2 of v-Src complexed with tyrosine-phosphorylated peptides. *Nature* 358:646-653. (PMID 1379696)
- Z. Songyang, S.E.Shoelson, M.Chaudhuri, G.Gish, T.Pawson,W.G. Haser, F.King, T.Roberts, S.Ratnofsky, R.J. Lechleider, **R.B.Birge**, J.E.Fajardo, M.M.Chou, H.Hanafusa, B.Schaffhausen, and L.C.Cantley. (1993). SH2 domains recognize specific phosphopeptide sequences. *Cell* 72:767-778. (PMID 7680959)
- S. Kumar, V. Davra, A. Obr, K. Geng, T. L. Wood, M S. De Lorenzo, and **R. B. Birge** (2017). Crk oncogene promotes PD-L1 expression, EMT and immune evasion in a triple-negative murine model of breast cancer. *Oncoimmunology*: e1376155. (PMID 28296536)
- S. Kumar, B. Lu, V. Davra, P. Hornbeck, K Machida, and **R B. Birge** (2018). Crk Tyrosine Phosphorylation Regulates PDGF-BB-inducible Src Activation and Breast Tumorigenicity and Metastasis. *Molecular Cancer Research.* 2017 Oct 3. 1158/1541-7786. (PMID 28974561)

My laboratory has also made contributions in the field of apoptosis and apoptotic cell clearance (a term called efferocytosis is recent years). Initially, we focused on the identification and characterization of phosphatidylserine (PS) receptors (such as αvβ5 integrin, TAM receptors, and TIM receptors) and showed these receptors triggered efferocytosis by activating an evolutionarily conserved module (Ced2/Ced5/Ced10) to stimulate Rac1. Our research on efferocytosis has also led to the identification of novel ligands and receptors that control these processes, including the identification of urokinase plasminogen activator receptor (UPAR) as an unconventional phagocytic receptor on phagocytes, and the characterization of high molecular weight kininogen, externalized glycolytic enzymes (TPI-1 and Enolase) and autophagy proteins as novel ligands on apoptotic cells.

- ML. Albert, J-I. Kim, and **R.B. Birge** (2000). The αvβ5 integrin recruits the Crk/Dock180 molecular complex for phagocytosis of apoptotic cells. *Nat. Cell Biol.* 2:899-906. (PMID 11146654).
- V. D'mello, S. Singh, Y Wu, and **R. B. Birge** (2009). Urokinase plasminogen activator receptor (uPAR) promotes efferocytosis of apoptotic cells. *J. Biol. Chem*, 284:17030-17038. (PMID: 18039660)
- I. Teplova Lozy F, Price S, Singh S, Barnard N, Cardiff RD, **R. B. Birge**, Karantza V. (2013). ATG proteins mediate efferocytosis and suppress inflammation in mammary involution. *Autophagy*. 9:459-75. (PMID: 23380905)
- P. K. Mishra, M. Palma, B. Buechel, J. Moore, V. Davra, C. Niansheng, A. Millman, N. J. Hallab, T. Kanneganti, **R. B. Birge**, E. M. Behrens, A. Rivera, K. S. Beebe, J. Benevenia, and W. C. Gause (2019). Sterile particle induced inflammation is mediated by macrophages releasing Il-33 through a Bruton's tyrosine kinase-dependent pathway. *Nature Materials* 18 (3) 289-297. (PMID: 30664693).

Most recently, we have shown that PS and PS receptors (most notably Mertk) are dysregulated in the tumor environment and have important roles in immune escape. From these studies, we have received a new R01 to further investigate how PS receptors drive inhibitory receptors to foster an immunosuppressive signal in the tumor microenvironment that prevents a host anti-tumor immune response. We anticipate the frequent use of several shared resources at CINJ and Rutgers, and the maintenance and acquisition of state of the art facilities is essential for the success of the my research as well as the training of junior scientists in their early careers.

- Kasikara C*, Kumar S, Kimani S, Tsou WI, Geng K, Davra V, Sriram G, Devoe C, Nguyen KN, Antes A, Krantz A, Rymarczyk G, Wilczynski A, Empig C, Freimark B, Gray M, Schlunegger K, Hutchins J, Kotenko SV, **Birge RB** (2017). Phosphatidylserine Sensing by TAM Receptors Regulates AKT-Dependent Chemoresistance and PD-L1 Expression. *Mol Cancer Res*. doi: 10.1158/1541-7786.MCR-16-0350. *(*Awarded among most cited papers at the 2019 annual AACR meeting in Atlanta, GA)* (PMID 28184013)
- Kimani SG, Kumar S, Bansal N, Singh K, Kholodovych V, Comollo T, Peng Y, Kotenko SV, Sarafianos SG, Bertino JR, Welsh WJ, **Birge RB** (2017). Small molecule inhibitors block Gas6-inducible TAM activation and tumorigenicity. Sci Rep. 7:43908. doi: 10.1038/srep43908. (PMID 28172423)
- C. Kasikara, V. Davra, D. Calianese, K. Geng, T. Spires, M. Quigley, M. Wichroski, G. Sriram. L. Suarez-Lopez, M. B. Yaffe, S. V. Kotenko, M. S. De Lorenzo, and **R. B. Birge**; (2019). Pan-TAM tyrosine kinase inhibitor BMS-777607 enhances responsivity to anti-PD-1 mAb checkpoint therapy in a murine model of triple negative breast cancer. *Cancer Research* 79(: 2669-2683*).* (PMID 30877108)
- V. Davra, S. Kumar, K. Geng, D.Calianese, D. Mehta, V. Gadiyar, C. Kasikara, K. Lahey, S.Desind, Y.Chang, M. Wichroski, C. Gao, M. S. De Lorenzo, S.V. Kotenko T.Bergsbaken, P. K. Mishra, W. C. Gause, M.Quigley, T. E. Spires, and **R B. Birge**. (2021) Axl and Mertk receptors cooperate to promote breast cancer progression by combined oncogenic signaling and evasion of host anti-tumor immunity. Nov 25; canres.2066.2020. doi: 10.1158/0008-5472.CAN-20-2066. (PMID 33239426)

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