## BIOGRAPHICAL SKETCH

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NAME: Fitzgerald-Bocarsly, Patricia A.

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

POSITION TITLE: Professor, Pathology and Laboratory Medicine

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 California, Los Angeles | B.S. | 1976 | Biochemistry |
| UC Davis, Davis, CA | M.A. | 1977 | Microbiology/Immunology |
| Boston University, Boston, MA | Ph.D. | 1980 | Microbiology/Immunology |
| Sloan-Kettering Institute, NY | Post. Doc. | 1980-1982 | Immunology |

### A. Personal Statement

I currently serve both as Professor and Vice-chair for research of Pathology and Laboratory Medicine and as the Scientific Director of the Flow Cytometry and Immunology Core Laboratory. Effective 9/15/18, I was appointed Provost of Rutgers Biomedical and Health Sciences Newark Campus; this is a half-time position, with half of my time dedicated to research and scholarly activity. My laboratory specializes in studying innate and adaptive immunity, and in particular, responses of human plasmacytoid and myeloid dendritic cells to viral infections and their contribution to T cell activation. We were among the first to describe the "natural interferon-$\alpha$ producing cells", now known as pDC, and were the first to define them as dendritic cells. We were also the first to characterize their constitutive high-level expression of IRF-7 and its translocation to the nucleus upon viral stimulus and were the first to report pDC dysfunction in HIV-infected individuals, which we have continued to characterize over the last two decades. We have also pioneered studies in the use of Imaging Flow Cytometry to study nuclear translocation, endosomal co-localization, and monitoring of autophagy in pDC and other rare cell populations. My interest in aging initiated during my graduate studies where I investigated aging of what were then newly described cells, the natural killer cells, as well as T cells in a mouse model. Our recent studies have focused on the premature senescence and immune activation of pDC in HIV-infected subjects that is further exacerbated with age in HIV-infected individuals, even in the context of virus suppression, as well as senescence of immune cells in normal aging and in COVID infection. Most recently, we have been collaborating with the Herbig laboratory to detect senescent immune cells in human peripheral blood and human tissues and to understand the cellular and molecular mechanisms of immune senescence. In addition, in collaboration with Mark Gluck from Rutgers Newark, we are collaborating to understand the contribution of immune senescence to cognitive decline leading to Alzheimer's Disease. Our lab has extensive experience in working with human PBMC and cell isolation, cell sorting, multi-parameter flow cytometry, imaging flow cytometry, SeaHorse, metabolic reprogramming and cellular and molecular analysis of human immune cells populations. I am excited to participate as a member of CINJ in this recompetition.

Ongoing and recent funded research projects that I would like to highlight Include:

2UM1AI069419-08 (R Gulick PI) 12/10/13 – 02/28/28
NIH Weill Cornell Medical College-New Jersey Medical School AIDS Clinical Trial Unit

The goal of this project is to provide a framework for HIV Clinical Trials. (Grant was renewed 12/20)
Role: Co-investigator and director of the NJMS and Weill Cornell laboratory sites.

R21AG067368 (MPI: Herbig and Fitzgerald-Bocarsly) 5/15/20-4/30/2023 (additional NCE requested)
Causes of Immune Cell Senescence in Aging Humans
Major Goals: To 1) Identify PBMC subsets that increasingly undergo cellular senescence with advancing age in humans, 2) characterize the transcriptome and epigenome of 2 PBMC subsets (bulk CD8+ T cells and bulk CD4+ T cells), and 3) characterize features of cellular senescence of the 2 PBMC subsets as well as test whether SASP factors secreted from cultured senescent human cells promote paracrine senescence.

R21AG067368-S1 (MPI: Herbig and Fitzgerald-Bocarsly) 8/21-4/23 (Additional NCE has been requested)
The impact of Alzheimers Disease neuropathology on immune cell senescence in older African Americans.
Major goal: Studies carried out with Dr. Mark Gluck from Rutgers, Newark will be carried out with elderly African American subjects to align their immune senescence and neuropathology.

Rutgers Covid Center for COVID-19 Response and Pandemic Preparedness Grant. (MPIs Fitzgerald-Bocarsly and Herbig)
Immune cell senescence in COVID-19 6/15/20-12/31/23 (currently one year NCE)
The goal of this project is to understand T cell and pDC senescence in immune response to COVID-19.

NIA R01AG053961S2 (M. Gluck, PI, PFB, co-I) 4/21-3/23
Cognitive, neural, and immunological consequences of COVID-19 in oder African Americans and how they relate to risk for Alzheimer's Disease
P. Fitzgerald-Bocarsly: co-I and subcontract for immunological studies of T cell senescence and immune function in older African Americans with and without a history of COVID-19 co-infection.

Rutgers Facility Grant (Fitzgerald-Bocarsly and S. Singh, PI) 10/21-9/22
Luminex xMAP Intelliflex for NJMS Flow Cytometry Core laboratory

**B. Positions, Scientific Appointments and Honors**

| | |
|---|---|
| 09/82 - 07/85 | Research Associate, Sloan-Kettering Institute |
| 07/85 -06/92 | Assistant Professor, Pathology, UMDNJ-New Jersey Medical School and Graduate School of Biomedical Sciences |
| 07/92 - 06/99 | Associate Professor, Laboratory Medicine and Pathology, NJMS and GSBS |
| 1997-present | Member, Cancer Institute of New Jersey |
| 7/99 -6/13 | Professor, Pathology and Laboratory Medicine, UMDNJ- NJMS and GSBS |
| 8/07- present | Scientific Director, NJMS Flow Cytometry and Immunology Core Laboratory |
| 8/11-present | Member, Center for Immunity and Inflammation, NJMS |
| 7/13- present | Professor, Pathology and Laboratory Medicine, Rutgers, New Jersey Medical School and GSBS (Merger of UMDNJ and Rutgers; NJMS is part of Rutgers Biomedical and Health Sciences) |
| 2/15-present | Vice Chair for Research Dept. of Pathology and Laboratory Medicine |
| 9/18-present | Provost, Rutgers Biomedical and Health Sciences, Newark |
| 7/21-present | Co-chair, Rutgers Biomedical and Health Sciences Womens' and GenderEquity Council |

**Other Experience and Professional Memberships**

I have served on more than 65 study sections since 1990, including being a permanent member and chair of the NIH AIDS Immunology and Pathogenesis Study Section, chair or member of ad hoc NIH study sections as well as for VA Merit Review and AHA.

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|---|---|
| 7/08-6/11 | Member, American Association of Immunologists Committee on the Status of Women |

7/09-2018 Publications Committee, Society for Leukocyte Biology
1/13- 1/18 President, Rutgers Biomedical and Health Sciences Faculty Council
2/15-7/18 Awards Committee, International Cytokine and Interferon Society
1/15- present Executive Committee, Graduate School for Biomedical Sciences
9/18-present Rutgers President's Administrative Council

**Honors/Editorial Positions**
Member, American Association of Immunologists
Editorial Board, Clin. Immunol. 4/98-12/08
Assoc. Editor, ISICR Newsletter 1998-2003
Section Editor, J. Immunology 7/02-9/06.
New Jersey Medical School Faculty of the Year Award, 2003.
Dolph Adams Award from the Soc. Leuk. Biol. 2008 for most highly-cited research article 2003-2008 in JLB.
Section Editor, J. Leuk. Biology 2009-present.
Foundation of UMDNJ Excellence in Research Award, 2011
Academic Editor, PLoS One, 8-11 – present
New Jersey Medical School Mentoring Award – 5/16
Fellow, American Scientific Affiliation 2018-present
NJMS Distinguished Career Award, 2021
Editorial Board, Frontiers in Immunology, Frontiers in Microbiology 2022-present
Fellow, American Association for the Advancement of Science, 2021

**C. Contributions to Science**

**1. Natural killer cells in human viral infections:** Early work in my laboratory and dating from my post-doctoral studies at Sloan-Kettering focused on natural killer cells responsible for the lysis of HSV-infected cells. We showed that the lysis of virus-infected cells had kinetics distinct from that of the classic NK target, K562. This NK cell activity was found to severely limit viral replication in the target cells. We further showed that in order to lyse virus-infected fibroblasts, the participation of a second HLA-DR+ cell or an activating cytokine was required. This latter finding led to our description of the cells now known as plasmacytoid dendritic cells (described in item 2, below).

a. Fitzgerald PA, Evans R, Kirkpatrick D, Lopez C: Heterogeneity of human NK cells: comparison of effectors which lyse HSV-1 infected fibroblasts and K562 erythroleukemic targets. J Immunol, 130:1663-1668, 1983.
b. Fitzgerald P, Mendelsohn M, Lopez C: Human natural killer cells limit HSV-1 replication in vitro. J Immunol 134:2666-2672, 1985.
c. Fitzgerald-Bocarsly P, Feldman M, Curl S, Schnell J, and Denny T. Positively selected Leu-11a (CD 16+) cells require the presence of accessory cells or factors for the lysis of HSV-infected fibroblasts but not HSV-infected Raji. J Immunol, 143:1318-1326, 1989.
d. Feldman, M and Fitzgerald-Bocarsly, P. Interferon dependent and independent participation of accessory cells in natural killer cell mediated lysis of HSV-1 infected fibroblasts. J Leuk Biol 52:473-482, 1992.

**2. Description of natural interferon producing cells (now known as plasmacytoid dendritic cells):** Our lab was the first to describe a lineage-/HLA-DR+ non-NK cell that produced IFN-□ during NK assays against HSV-infected cells. We went on to characterize these cells as belonging to the newly-described population of dendritic cells, and ultimately contributed to the description of these cells as plasmacytoid dendritic cells (pDC). We went on to show that these cells express high constitutive levels of IRF-7, making them immediately rapidly and robustly respond to virus stimulation with IFN-$\alpha$ production. Importantly, we discovered that pDC both produce and respond to type III IFN. Ongoing studies are investigating the mechanisms of pDC activation and regulation.

a. Siegal FP, Kadowaki N., Shodell M., Fitzgerald-Bocarsly P, Shah K., Ho S., Antonenko S, Liu Y-J. The nature of the principal type 1 interferon-producing cells in human blood. Science 284: 1835-1837, 1999. PMID: 10364556

b. Izaguirre A, Barnes BJ, Amrute S, Yeow WS, Megjugorac N, Dai J, Feng D, Chung E, Pitha PM, Fitzgerald-Bocarsly P. Comparative analysis of IRF and IFN-alpha expression in human plasmacytoid and monocyte-derived dendritic cells. J Leukoc Biol. 74(6):1125-38, 2003. PMID: 12960254 [Paper was the most highly-cited paper in J. Leuk. Biology in the period 2003-2008].

c. Deb P, Dai J, Singh S, Kalyoussef E and Fitzgerald-Bocarsly P. Triggering of the cGAS-STING pathway in human plasmacytoid dendritic cells inhibits TLR9-mediated interferon production. J. Immunology, J. Immunol. 2020, ji1800933; DOI: https://doi.org/10.4049/jimmunol.1800933

d. Hurley H, Dewald H, Rothkopf A, Singh S, Jenkins F, Deb P, De S, Barnes B, Fitzgerald-Bocarsly P. Frontline Science: AMPK regulates metabolic reprogramming necessary for interferon production in human plasmacytoid dendritic cells. 2021. J. Leuk. Biology 109:299-308. *Featured as highlighted paper: Aisenberg, LK and Chattergoon, MA. Where do pDCs find the energy?. J. Leuk. Biol. 2021,109: 283-285.*

3. **Studies of dysregulation of plasmacytoid dendritic cells in HIV infection:** Our lab was the first to demonstrate that IFN-$\alpha$ production in response to viruses is deficient in subjects with advanced HIV infection and was highly predictive of advancement to opportunistic infections. In fact, it was this observation, in part, that led us to the discovery of the natural interferon producing cells, now known as pDC. We were the first to describe these cells as belonging to the newly-defined pDC lineage. We went on to show that these cells express high constitutive levels of IRF-7, making them immediately rapidly and robustly respond to virus stimulation with IFN-$\alpha$ production. Studies investigated mechanisms of pDC activation in healthy donors and their dysregulation in HIV (AI026806) as well as the effect of aging, both in the context of HIV and without, on pDC frequency, phenotype, regulation and function (AI106125).

a. Feldman S, Stein D., Amrute S, Megjugorac N, Denny T, Garcia Z, Kloser P, Sun W, Fitzgerald-Bocarsly P. Decreased IFN-$\alpha$ production in HIV infected patients correlates with numerical and functional deficiencies in circulating type 2 dendritic cell precursors. Clin. Immun. 101:201-210, 2001. PMID: 11683579

b. Fitzgerald-Bocarsly P and Jacobs E. Plasmacytoid dendritic cells in HIV infection: Striking a delicate balance. J. Leuk. Biology, 87:609-620, 2010. PMID: 20145197.

c. Monica Macal, Yeara Jo, Simone Dallari, Aaron Y. Chang, Jihong Dai, Kyla Omilusik, Ananda W. Goldrath, Patricia Fitzgerald-Bocarsly and Elina I. Zuñiga, Self-renewal and TLR7 Signaling Sustain Exhausted Plasmacytoid Dendritic Cells Upon Chronic Viral Infection. Immunity 2018, 48(4):730-744.e5. doi: 10.1016/j.immuni.2018.03.020. PMID: 29669251.

d. Feng, Di, Denny T, Rameshwar P, Glick M, Hodder S and Fitzgerald-Bocarsly P. Turnover, mobilization and activation of circulating plasmacytoid dendritic cells in HIV infection. Submitted.

4. **Use of imaging flow cytometry to interrogate responses of dendritic cells to viruses and virus-infected cells.** pDC represent only 0.2-0.4% of the PBMC population, making traditional biochemistry studies very difficult. We collaborated with Amnis, Inc. to develop approaches using ImageStream imaging flow cytometry to interrogate pDC function. We have used the ImageStream extensively to look at transcription factor translocation in these cells (IRF-7, -5, NFKB), endosomal trafficking of TLR ligands, autophagy, apoptosis and cell:cell fusion between HIV-infected cells and DC populations. These studies have led PFB to become recognized as an expert in Imaging Flow Cytometry, and she is regularly invited to present her results at flow cytometry meetings. We regularly help other investigators to design studies utilizing imaging flow cytometry.

a. Fanning (Olshalsky) S, George T, Feldman S, Megjugorac N, Izaguirre A and Fitzgerald-Bocarsly P. Receptor cross-linking on human plasmacytoid dendritic cells leads to the regulation of IFN-alpha production. J. Immunol. 177:5829-5839, 2006. PMID: 17056507

b. Megjugorac N, Jacobs E, Izaguirre A, George T, Gupta G and Fitzgerald-Bocarsly P. Image-based study of interferongenic interactions between plasmacytoid dendritic cells and HSV-infected monocyte-derived dendritic cells. Immunol. Invest., 36:739-761, 2007. PMID: 18161527

c. George, TC, Fanning S, Fitzgerald-Bocarsly, P, Medeiros RB, Highfill S, Shimizu Y, Hall BE, Frost K, Basiji D, Ortyn W, Morrissey PJ, and Lynch, DH. Quantitative Measurement of Nuclear Translocation Events Using Similarity Analysis of Multispectral Cellular Images Obtained in Flow. J. Immunol. Methods 311:117-129, 2006.

d. Pierog P, Zhao Y, Singh J, Dai J, Yap G and Fitzgerald-Bocarsly P:, Toxoplasma gondii inactivates human pDCs by functional mimicry of IL-10. J. Immunol. 200:186-185, 2018.

**5. Senescence of human and murine immune responses.** I have a long-standing interest in senescence of the immune response, going back to my graduate work at Boston University where we investigated the effects of aging on natural killer cell and T cell responses and did bone marrow transplants between young and old mice to assess whether immune competence tracked with the host or bone-marrow derived cells. More recently, my lab has become interested in the premature aging of pDC immune responses in the context of HIV infection and were funded by an NIH R01 for 20 years on this topic. We observed shortened telomeres in pDC, increased turnover of these cells, as well as decreased numbers and function. We began our collaboration with the Herbig laboratory to try and understand whether immune senescence has the hallmarks of cellular senescence, beginning with CD8 T cells but extending to other immune cell subsets. We are about to submit a paper using ATACseq analysis of senescent vs. non-senescent T cell subsets within a single donor.

a. Fitzgerald PA, Bennett M: Aging of natural and acquired immunity of mice. I. Decreased natural killer cell function and hybrid resistance. Cancer Invest., 1:15-24, 1983.
b. Fitzgerald PA, Bennett M: Aging of natural and acquired immunity of mice. II. Decreased T cell responses to syngeneic tumor cells and parental-strain spleen cells. Cancer Invest., 1:139-150, 1983.
c. Dai J, Jacobs E, Swaminathan S, Hodder S, Singh S, Davidow A and Fitzgerald-Bocarsly P. Characterization of human plasmacytoid dendritic cells in aging and HIV-infected patients. To be submitted Spring, 2023.
d. Martínez-Zamudio R*, Dewald H*, Vasilopoulos T, Fitzgerald-Bocarsly, P** and Herbig U.** Senescence Associated β-Galactosidase Reveals the Abundance of Senescent CD8+ T Cells in Aging Humans. Aging Cell. 2021*co-first authors.**co-senior authors. PMCID: PMC8135084, DOI: 10.1111/acel.13344

**A partial list of my publications can be found at** https://www.ncbi.nlm.nih.gov/sites/myncbi/patricia.fitzgerald-bocarsly.1/bibliography/48568621/public/?sort=date&direction=ascending (since 1986) **and a full list at Scopus.**