
BIOGRAPHICAL SKETCH

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NAME: **Lasfar, Ahmed, M.Sc., M.Sc., Ph.D.**

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

POSITION TITLE: Assistant Professor of Pharmacology and Toxicology Ernest Mario School of Pharmacy, Rutgers University, Associate Member of Rutgers-Cancer Institute of New Jersey

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
Paris Diderot University, France	M.Sc.	09/1989	Biochemistry
Paris Diderot University, France	M.Sc.	06/1990	Microbiology
Paris Diderot University, Pasteur Institute, France	Ph.D.	12/1997	Fundamental Immunology
CNRS, Villejuif, France	Postdoctoral	01/1999	Interferon and Viral Oncology
Rutgers – RWJMS, Piscataway, NJ	Postdoctoral	06/2002	Interferon and Cancer Immunology

A. Personal Statement

I have been always dedicated for research in cancer immunology. Currently, the research in my laboratory is particularly focused on understanding the interface between cancer cell signaling, tumor microenvironment and immune suppression. My initial training in this field started when I was a PhD student in the program of immunology at the Pasteur Institute, Paris University (France). My research project was focused on the role of type I IFN in hairy cell leukemia and multiple myeloma. After my graduation, I joined the laboratory of Viral Oncology (CNRS-Villejuif, France) in which I acquired more experience in cancer animal models and immunology approaches. After obtaining an international postdoctoral fellowship from the “French League Against Cancer”, I moved to New Jersey and continued my research on IFN and melanoma in Dr. Pestka’s laboratory. I have engineered important tools to understand the mechanisms of IFN in cancer immunity. *in vivo*. After our discovery of IFN- λ , my work, published in 2006 (highly referenced) was the first to report the role of IFN- λ in melanoma and particularly underlined the restricted expression of IFNLR1, the distinguished characteristic of this new IFN, which is still only partially understood. I have provided important insights about the difference in the mechanisms of action between IFN-alpha and IFN- λ .

My research interest in the role of leading transcription factors in melanoma resistance is expressed by my long interested on RUNX2. Our recent studies suggest that RUNX2 is involved in oncogenic signaling and immune suppression and may play a critical role in the mechanisms of resistance to BRAF inhibitors and anti-PD-1 blockade. We have important tools and research expertise to particularly address the role of RUNX2 in melanoma resistance with a mission to develop novel therapeutic strategies for patients, resistant to current therapies. In addition to original articles, reviews, editorial on melanoma, I have recently edited in 2021 a new book on melanoma (Intech, 2021, Editor, Ahmed Lasfar; Co-editor: Karine Cohen-Solal). Dr. Cohen-Solal is my long standing collaborator on melanoma (We have published more than 15 articles).

In the present application, we aim to elucidate the role of RUNX2 in the resistance mechanisms of melanoma. We also propose to use our developed *in vivo* models to test the role of a new RUNX2 inhibitor in re-sensitizing melanoma to both BRAF inhibitors and anti-PD-1 blocking antibody. We aim to understand the role of high accumulation of RUNX2 proteins in melanoma cells, resistant to PD-1 blockade. We are also very excited to elucidate the unique protein signature of RUNX2, including PD-L1, IFNLR1, IFTIM3, GBP1 and NMI. Besides PD-L1, the role of the other proteins of the signature is not yet assessed in melanoma resistance. We believe that our current proposal will exceptionally advance our understanding of the mechanisms of melanoma resistance and open novel therapeutic strategies for melanoma resistance, a relevant unmet clinical need.

Ongoing Research Support

1R01CA212171-01 A. Zloza/A. Lasfar (MPI) 07/01/2018-06/31/2023 4.8 calendar

Role of IFN-lambda in promoting breast cancer metastasis

The major goals of this project are to define and elucidate the role of IFN-lambda and the expression of its receptor (IFNLR1) in promoting distal breast cancer metastasis

Other support:

Rutgers facilities (ORED, Rutgers University) A. Lasfar (PI) 12/01/2021-11/31/2022

Tumor immunohitology analysis, Immunomarkers and tumor immunology

B. Positions, Scientific Appointments, and Honors

Positions

- 2018- Full Member. Rutgers-Cancer Institute of New Jersey, Rutgers University, New Brunswick, NJ
- 2013-2018 Associate Member. Rutgers-Cancer Institute of New Jersey, Rutgers University, New Brunswick, NJ
- 2012- Assistant Professor. Department of Pharmacology & Toxicology, Ernest Mario School of Pharmacy, Rutgers University, Piscataway, NJ
- 2004-2011 Research Associate. Department of Biochemistry & Molecular Biology, New Jersey Medical School, Rutgers University, Newark, NJ

Honors

Fellowships and awards

- 2012 Impact award (CINJ)
- 2007 Gallo and Scientific Excellence Award, New Jersey Commission on Cancer Research
- 2006 Glaxo Smith Kline Award for the Discovery of Type III Interferon Antitumor Activity
- 2006 Gallo Scientific Excellence Award, New Jersey Commission on Cancer Research
- 2002 Research Achievement Award, Robert Wood Johnson Medical School, NJ
- 2001 Travel Award, International Society for Interferon and Cytokine Research
- 1999 International Fellowship, Ligue Nationale Francaise Contre le Cancer, Paris, France
- 1993 National Fellowship, Nouvelle Association de Recherche Biomedicale, Villejuif, France

Professional Membership, Task Force and Pharmaceutical Adviser

- 2017- Scientific Advisor, Creative Biolabs
- 2016- Scientific Advisor, Lambda Pharmaceuticals
- 2013- Getting to Know Cancer Task Force (Member and scientific adviser). Role: Assessing the Carcinogenic Potential of Low-Dose Exposures to Chemical Mixtures in the Environment: Focus on the Cancer Hallmark of Evading Growth Suppression
- 1999- Member of IFN and Cytokine Research

Development of Bio-therapeutics

- IFN-alpha/beta antagonists for Hepatic ischemia (Cursio et al, Transplant Proc. 1996)
- Anti-IFNAR1 antibody antagonists for organ transplantation (Benezri et al, J Interferon Cytokine Res. 1998)
- Novel IFN-alpha products (Ongoing industrial partnership with Lambda Pharmaceuticals)

Editorial Board Member

- Frontiers Oncology (Associate editor)
- Cancers

Reviewer

International Journals

- Embo Molecular Medicine

- Science Report
- Plos One
- Journal of Interferon & Cytokine Research
- Journal of Allergy and Clinical Immunology
- Experimental cell research
- Molecular oncology

Cancer Foundations

- Belgium Foundation against Cancer (Belgium)
- kom op tegen kanker (Belgium)

National and international institutions

- National Research Institute (Poland)
- NIH/NCI: Oncoimmunology Study Section (2019)
- [-NIH/NCI: SEP-5: NCI Clinical and Translational Cancer Research \(2023\)](#)

C. Contribution to Science

1. Initial contribution to IFN and Cancer research

My initial contributions to the mechanisms of IFN action started as a graduate student. I established important antitumor mechanisms of IFN-alpha in multiple myeloma and hairy cell leukemia, and demonstrated the importance of the interactions between IFN-alpha, IL-6, TNF-alpha and IFN-gamma. Interest in solving the problems (side effects) associated with systemic IFN therapy. Evaluate alternate routes of IFN delivery in mice models of cancer and viral diseases. Developing IFN antagonists to induce immune suppression and improving organ transplantation in mice models.

- Lasfar, A**, Amirand, C, Abadie, A, Ballini, JP, Kolb JP (1993) Activation pathways triggered by interleukin-4 in the human plasmacytoma cell line RPMI-8226 - differences with resting B lymphocytes. *Eur Cytokine Network*, 4, 213-221
- Billard, C, **Lasfar, A** (1993) Production of TNF in response to IFN-gamma in hairy cell leukemia. *Leukemia*, 7, 331-332
- Lasfar, A**, Wietzerbin, J, Billard, C (1994) Differential regulation of interleukin-6 receptors by interleukin-6 and Interferons in the multiple myeloma cell lines. *Eur J Immunol*, 24, 124-132
- Eid P, Meritet JF, Maury C, **Lasfar A**, Weill D, Tovey MG (1999) Oromucosal interferon therapy: pharmacokinetics and pharmacodynamics. *J Interferon Cytokine Res*. 19, 157-69

2. Role of IFN-lambda in cancer

Since the discovery of IFN-lambda, I am particularly interested on studying its role in cancer. I have been often invited to share my expertise on IFN-lambda in important conferences and high impact journals. I have been consulted as international expert for reviewing grant applications from Europe. I also have been solicited for collaborations on IFN-lambda from the US, China, UK and France:

- I have cloned and characterized the IFN-lambda system in mice. (Cancer Res. 2006. Highly cited reference)
- I have made the first contribution for IFN-lambda in cancer research.
- I have determined the tissue specificity of IFN-lambda and suggested its advantage versus IFN-alpha.
- I have demonstrated the difference between IFN-lambda and IFN-alpha in generating innate immune response and established the role of tumor infiltrated NK cells in tumor eradication.
- I have reported the dual role of IFN-lambda in Cancer.

- Lasfar, A**, Lewis-Antes, A, Smirnov, SV, Anantha, S, Abushahba, W, Tian, B, Reuhl, K, Dickensheets, H, Donnelly, RP, Raveche, E, Kotenko, S.V. (2006) Characterization of the mouse IFN- λ ligand-receptor system: IFN-lambdas exhibit anti-tumor activity against B16 melanoma. *Cancer Res.*, 66, 4468-4477. PMID: 16618774
- Lasfar, A***, de la Torre, A, Abushahba, W, Cohen-Solal, KA, Castaneda, I, Yuan, Y, Reuhl, K, Zloza, Raveche, E, Laskin, DL and Kotenko, S (2016) Concerted action of IFN- α and IFN- λ induces local NK cell immunity and halts cancer growth. *Oncotarget*, 7 (31), 49259-49267. *Corresponding and senior author. PMID: 27363032

- c. **Lasfar, A***, Gogas, H., Zloza, A., Kaufman, HL and Kirkwood, J (2016). IFN-lambda Cancer Immunotherapy-New Kid in the Block. *Immunotherapy* 8, 877-88. *Corresponding author. PMID: 27381684
- d. **Lasfar, A***, Zloza, A., Silk, A.W., Lee, L.Y. and Cohen-Solal, K.A. (2019) Interferon Lambda: Toward a Dual Role in Cancer. *J Interferon Cytokine Res*, 39, 22-29. PMID: 30020822

3. Role of RUNX2 in melanoma cell signaling. We were the first group to report the role of RUNX2 in melanoma progression and to suggest its involvement on melanoma resistance. Our current results provide the insight mechanisms of RUNX2, involved in melanoma, cell migration and invasion. For the first time, we identify RUNX2 as a regulator of receptor tyrosine kinases and PD-L1, thereby contributing to melanoma progression and resistance to targeted therapy.

- a. Boregowda, R.K., Olabisi, O. O., Abushahba, W., Jeong, B.S., Haenssen, K. K., Chen, W., Chekmareva, M., Lasfar, A., Foran, D. J., Goydos, J. S. and **Cohen-Solal, K. A.** RUNX2 is overexpressed in melanoma cells and mediates their migration and invasion. *Cancer Letters* (2014) 348. 61-70. PMID: PMC4041161
- b. **Cohen-Solal K.A.**, Boregowda R.K. and Lasfar A. RUNX2 and the PI3K/AKT axis reciprocal activation as a driving force for tumor progression. *Molecular Cancer* (2015) 14:137-146
- c. Boregowda R.K., Medina D.J., Markert E., Bryan M.A., Chen W., Chen S., Rabkin A., Vido M.J., Gunderson S.I., Chekmareva M., Foran D.J., Lasfar A., Goydos J.S., **Cohen-Solal K.A.** (2016) The transcription factor RUNX2 regulates receptor tyrosine kinase expression in melanoma. *Oncotarget* DOI 10.18632/oncotarget.8822.
- d. **Cohen-Solal K.A.**, Kaufman H.L. and Lasfar A. Transcription Factors as Critical Players in Melanoma Invasiveness, Drug Resistance and Opportunities for Therapeutic Drug Development. *Pigment Cell and Melanoma Res.* (2018) 31:241-252.

4. Other contributions to cancer research

I have directed and edited several research topic and books on cancer. I have been member of task force and adviser for cancer development. I believe on research collaborations. My lab continues to establish national and international collaborations on Cancer Immunology. We provide KO animals, agents and advices...

Edited Books and Editorial:

- a. **Liver Cancer** (Editor: **Lasfar. A**): November 2018. DOI: 10.5772/intechopen.73806. ISBN: 978-1-78984-449-8
- b. **Tumor Progression and Metastasis** (Editor: **Lasfar. A.** and co-editor: Cohen-Solal. K). April 2020. DOI: 10.5772/intechopen.77832. ISBN 978-1-78985-349-0
- c. **Melanoma** (Editor: Lasfar. A. and co-editor: Cohen-Solal. K). May 2021. DOI: 10.5772/intechopen.91524 ISBN: 978-1-83880-879-2
- d. **Tumor Microenvironment and Resistance to Current Therapies** (Lead Editor of Topic: **Lasfar, A***) (Editorial: **Lasfar, A*** et al. *Front Oncol.* 2019; 9: 1131.)

5. Patents

- a. Rutgers patent (Protein Clustering Technology: Patent # 62/353,465. Inventor: Ahmed Lasfar)
- b. Patent application on IFN-lambda/Cancer (Rutgers Docket 2015/25)

Complete List of Published Work in My Bibliography:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1NwiYNsWr3vAS/bibliography/49472714/public/?sort=date&direction=ascending>