BIOGRAPHICAL SKETCH

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NAME: Brossay, Laurent

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

POSITION TITLE: Professor

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
Rennes University, France	B. S.	1986	Biochemistry
Laval University, Quebec, QC, Canada	Ph. D.	1994	Microbiology
UCLA & LIAI, CA	Postdoctoral	1999	Immunology

A. Personal Statement

My laboratory is interested in understanding the molecular mechanisms controlling the development and activation of both Natural Killer (NK) and non-classical T cells. We use an animal model to determine the contribution of these innate-like cells during the immune response to infections, including murine cytomegalovirus (MCMV). During the last 25 years, we have generated several tools including an anti-CD1d antibody, an anti-KLRG1 antibody, the KLRG1 tetramer, and immunodeficient animals such as Qa-1 deficient mice and KLRG1 deficient mice. Most reagents are shared freely or/and donated to Jackson lab or NIH tetramer facility

I have served on numerous NIH study sections (~30) and I was a member of the *Immunity and Host Defense* study section. I also served as a Section Editor and Associate Editor for the *Journal of Immunology* and I am currently an Associate Editor for *Frontiers in NK Cell Biology*. I have been continuously funded by the NIH since 2000.

I was the chair of the Molecular Microbiology & Immunology Department from 2009 to 2021. As a chair, I recruited 6 tenure track Assistant Professors. They have been awarded NIH RO1s, NIH R21s, NIH K99, DARPA award, DOD discovery awards, SEARLE award, and a multitude of local grants. Most of them have been project leaders on NIH COBRE grants. Papers published by these junior members are *Immunity*, *Nature Immunology, Cell Host and Microbes, PloSPathogens* etc. Finally, I am the mentor for several successful Assistant Professors from other departments.

I have graduated 14 graduate students and I am currently training two, several of whom won presentation and/or poster awards at national or international conferences such as the American Association of Immunologist Conference or Keystone conferences. Six graduate students from my laboratory were awarded an NIH F31 fellowship. Most of the graduate students I trained have published papers in top-tier journals as a first-author. Overall, I am committed to mentoring my trainees and helping them to become successful and visible immunologists.

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

RO1 AI173163, 1-5
Brossay (PI)
05/12/23 - 06/30/28
Immune response to MCMV infection in the salivary glands

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2011-2021 Chair, Department of Molecular Microbiology & Immunology
2009-2011 Acting chair, Department of Molecular Microbiology & Immunology
2014-Present Professor, Brown University, Providence, RI

2006-2014 Associate Professor, Brown University, Providence, RI
2000-2006 Assistant Professor, Brown University, Providence, RI
1997-2000 Research Scientist, La Jolla Inst. for Allergy & Immunology, San Diego, CA
1994-1997 Postdoctoral fellow, Department of Microbiology & Immunology, UCLA, Los Angeles, CA

Scientific Appointments

2025 Ad Hoc Reviewer ANR France
2020 Ad hoc Reviewer NIH, IHD Study Section, June 2020
2020 Ad Hoc Reviewer NIH NIAID ZRG1 IMM Study Section
2016-2019 Member of Finance Committee, American Association of Immunologists
2019 ZRG1-IMM-j03-2019 Study Section, ad hoc reviewer, July 2019
2018 Ad hoc Reviewer NIH, IHD Study Section, October 2018
2018 Ad hoc Reviewer, Belgian Foundation against Cancer,
2017 Ad hoc Reviewer NIH, IHD Study Section, October 2017
2017-Present NEIC steering committee
2016 Ad Hoc Reviewer for NIH NIAID ZRG1 IDM (December) Study Section
2016 Ad Hoc Reviewer for NIH NIAID ZRG1 IDM (April) Study Section
2015 Ad hoc Reviewer NIH, IHD Study Section, February 2015
2011-present Associate Editor for *Frontiers in NK Cell Biology*
2010-2014 Section Editor: *J. of Immunology*
2014 Ad Hoc Reviewer for NIH NIAID ZRG1 IMM Study Section
2013 Ad Hoc Reviewer for NIH NIAID Phase 1 Immune Mechanisms of Virus Control (U19)
2010-2014 Ad Hoc Reviewer ANR France
2009-2013 NIH IHD Study Section Member
2007-2010 Associate Editor: *J. of Immunology*
2009 Ad hoc Reviewer NIH, IHD Study Section
2009 Ad Hoc Reviewer for Stage 1 review of Challenge Grant Applications
2008 Ad Hoc Reviewer NIH, RCE Biodefense and Emerging Infectious Diseases Study Section
2008 Ad hoc Reviewer NIH, IHD Study Section
2004-2009 Ad Hoc Reviewer Belgium Fund Research
2008 Ad hoc Reviewer NIH, Program Project
2007 Ad hoc Reviewer NIH, Program Project
2004 Ad hoc Reviewer NIH, Program Project
2003 Ad hoc Reviewer NIH, Special Emphasis Study Section
2003 Ad hoc Reviewer NIH, Program Project
2002 Ad hoc Reviewer Swiss National Foundation and Irish Health Research Board
2002 Ad hoc Reviewer Swiss National Foundation and Irish Health Research Board
2002 Ad hoc Reviewer NIH, Special Emphasis Study Section
2001 Ad hoc Reviewer NIH, Special Emphasis Study Section
1999-Present Ad hoc Reviewer*: J. Exp. Medicine, Nature Immunology, Science Immunology, J. of Clinical Investigation, Elife, PloS Pathogens, PNAS, European J. of Immunology, Blood, Nature Medicine, Nature Communications etc*

Honors

2015 American Association of Immunologist Laboratory Travel Award
2015 American Association of Immunologist career in Immunology Fellowship Award
2013 American Association of Immunologist Laboratory Travel Award
2009 American Association of Immunologist Faculty Mentor Travel Award
2004 American Association of Immunologist Junior Faculty Travel Award

C. Contribution to Science

1. NK cell response and non-classical T cell response during MCMV infection

We first characterized KLRG1 as a marker of recently activated NK and $CD8^+$ T cells. This is now widely accepted and this marker is used in many critical studies, which aim to understand the development of memory $CD8^+$ T cells. We then demonstrated that in response to MCMV, NK cells follow a kinetic parallel to $CD8^+$ T cells. In this system, we showed that NK cells undergo accelerated phenotypic maturation, expand, and contract. This work has been in part the foundation of a novel concept called *memory NK cells* developed by

several investigators. We also identified Qa-1 as a restricting element for non-classical $CD8^+$ T cells during MCMV infection. These cells can compensate for the absence of conventional T cells and protect against MCMV induced lethality.

- Anderson CK, Reilly EC, Lee AY, **Brossay L**. Qa-1-Restricted $CD8^+$ T Cells Can Compensate for the Absence of Conventional T Cells during Viral Infection. *Cell Reports*. 2019 Apr 9;27(2):537-548.e5. doi: 10.1016/j.celrep.2019.03.059. PubMed PMID: 30970256; PubMed Central PMCID: PMC6472915.
- Hogan M.J., N. Maheshwari, B.E. Begg, A. Nicastri, E.J. Hedgepeth, H. Muramatsu, N. Pardi, M.A. Miller, S.P. Reilly, **L. Brossay**, K.W. Lynch, N. Ternette, and L.C. Eisenlohr. 2023. Cryptic MHC-E epitope from influenza elicits a potent cytolytic T cell response. *Nature Immunol*. doi: 10.1038/s41590-023-01644-5
- Reilly SP, Smith ML, Borys SM, Fugère C, Demers D, Hogan MJ, Zemmour D, **Brossay L**. 2025. Unconventional CD8+ T cell surveillance of cytomegalovirus via Qa-1/HLA-E-restricted epitope recognition. *Science Advances*. Dec 19;11(51):eaea8707. doi: 10.1126/sciadv.aea8707.

2. Identification of the KLRG1 ligands and role of KLRG1 as a checkpoint inhibitor

Using a reporter cell line and the KLRG1 tetramer, we identified E, and N-cadherin as ligands for KLRG1. The KLRG1 tetramer has been made available to the scientific community at the NIH tetramer facility. The KLRG1 deficient animals have been donated to Jackson laboratories.

- Tessmer, M. S., C. Fugère, F. Stevenaert, O. V. Naidenko, G. Leclercq, and **L. Brossay**. 2007. KLRG1 binds cadherins and preferentially associates with SHIP-1. *International Immunol*. 19: 391-400.
- Banh, C., C. Fugere and **L. Brossay**. Immunoregulatory functions of KLRG1 Cadherin interactions are dependent on forward and reverse signaling. 2009. *Blood*. 114: 5299-5306 PMCID: PMC2796135
- Tata, A., G. Dodard, C. Fugère, C. Leget, M. Ors, B. Rossi, E. Vivier and **L. Brossay**. 2021. Combination blockade of KLRG1 and PD-1 promotes immune control of local and disseminated cancers. *Oncoimmunology* 2021, VOL. 10, NO. 1, e1933808.

3. NK cell like behavior of iNKT cell during infection

iNKT cells are unique T cells that can respond within minutes to specific antigens mostly agonist such as α-GalCer. In the absence of specific antigen, iNKT cells have been shown to contribute directly or indirectly to the immune response to several pathogens leading to a second model of iNKT cell activation, which involves both TCR engagement and inflammatory cytokines. We hypothesized that in some cases such as viral infection, iNKT cells may not need TCR engagement to be activated. Using the MCMV system, we demonstrated that iNKT cell activation is mostly TCR-independent. Therefore, iNKT cells essentially behave like NK cells during MCMV infection. These findings were confirmed by others using TCR reporter mice. In fact, the current view of iNKT cell activation during pathogen infection has shifted to a more important role of cytokine-mediated activation than TCR-mediated activation during infections.

- Wesley, J., M. S. Tessmer, D. Chaukos, and **L. Brossay**. 2008. NK cell-like behavior of Va14i NK T cells during MCMV infection. *Plos Pathogens*. 4(7):e1000106. PMCID: PMC2442879
- Anderson, C. K. Reilly S. P. and **L. Brossay**. 2021. The Invariant NKT Cell Response Has Differential Signaling Requirements during Antigen-Dependent and Antigen-Independent Activation. *J. Immunol.* PMCID: PMC7855310

4. Role of phosphatases during NK cell and NKT cell development

NK cell and NKT cell inhibitory receptors associate predominantly with SHP-1 or SHP-2, which are thought to dephosphorylate key players of cellular activation. Using mice deficient for SHP-1, SHP-2 or SHIP1, we have defined the roles of these phosphatases during NK and iNKT cell development.

- Banh, C., S. Miah S.M., G. Kerr, and **L. Brossay**. 2012. The development and maturation of NK cells are differentially regulated by SHIP-1. *Blood, 120:* 4583-4590 PMCID: PMC3512235
- Anderson, C. K., A. I. Salter, L. E., Toussaint, E. C. Reilly, C. Fugere, N. Srivastava, W. G. Kerr, and **L. Brossay**. 2015. Role of SHIP1 in iNKT cell development and functions. *J. Immunol.* 195*:* 2149-2156. PMCID: PMC4546909
- Miah SMS, Jayasuriya CT, Salter AI, Reilly EC, Fugere C, Yang W, Chen Q, **Brossay L**. Ptpn11 Deletion in CD4+ Cells Does Not Affect T Cell Development and Functions but Causes Cartilage Tumors in a T Cell-Independent Manner. *Frontiers in immunology*. 2017;8:1326. Epub 2017/11/01. doi: 10.3389/fimmu.2017.01326. PubMed PMID: 29085371; PMCID: PMC5650614.

- Niogret C, Miah SMS, Rota G, Fonta NP, Wang H, Held W, Birchmeier W, Sexl V, Yang W, Vivier E, Ho PC, ***Brossay L**, *Guarda G. Shp-2 is critical for ERK and metabolic engagement downstream of IL-15 receptor in NK cells. *Nature communications*. 2019; 10(1):1444. PubMed PMID: 30926899 PMCID: PMC6441079. *Corresponding authors

5. Unique population of NK cells and T cells in the salivary glands

NK cells are critical effector cells during the immune response to viral infections, yet despite their presence in the salivary glands, several viruses persist in this organ for several weeks to months. We demonstrated that salivary gland NK cells have a unique phenotype with reduced effector functions. New findings in the laboratory indicate that this mucosal tissue harbors several subsets of NK cell-like cells. We are currently testing the hypothesis that although NK cells cannot clear viral infections in this organ, NK cell response is sufficient to prevent viral reactivation while limiting tissue injury**.** We also recently demonstrated that NK cells regulate $CD8^+$ T cell number and frequency in the salivary glands.

- Tessmer M. S., Reilly E. C., and **L. Brossay**. Salivary gland NK cells are phenotypically and functionally unique. 2011. *Plos Pathogens*. 7(1):e1001254 PMCID: PMC3020929
- Erick, T. K., C. K. Anderson, E. C. Reilly, J. R. Wands and **L. Brossay**. 2016. NFIL3 expression distinguishes tissue-resident NK cells and conventional NK-like cells in the mouse submandibular glands. *J. Immunol*. 197. 2485-2491 PMCID: PMC5010994
- Dodard G., Tata, A., Erick, T.K., Jaime D., Mia S. M.S., Quatrini, L., Escaliere B, Ugolini S., Vivier E., and **L. Brossay**. 2020. Inflammation-Induced Lactate Leads to Rapid Loss of Hepatic Tissue-Resident NK Cells. *Cell Reports,* doi:10.1016/j.celrep.2020.107855. PubMed PMID: 32640221; PMCID: PMC7383148.
- Borys, S.M., S.P. Reilly, I. Magill, D. Zemmour, and **L. Brossay**. 2024. NK cells restrain cytotoxic $CD8^+$ T cells in the submandibular gland via PD-1—PD-L1. *Science Immunology.* 9:eadl2967

Link to the full list of 80 peer-reviewed publications:

http://www.ncbi.nlm.nih.gov/sites/myncbi/laurent.brossay.1/bibliography/40347211/public/?sort=date&direction=descending.