LAIR-1 is a negative regulator of SIV-specific CD8 T cells during chronic SIV infection

Vijayakumar Velu, PhD.

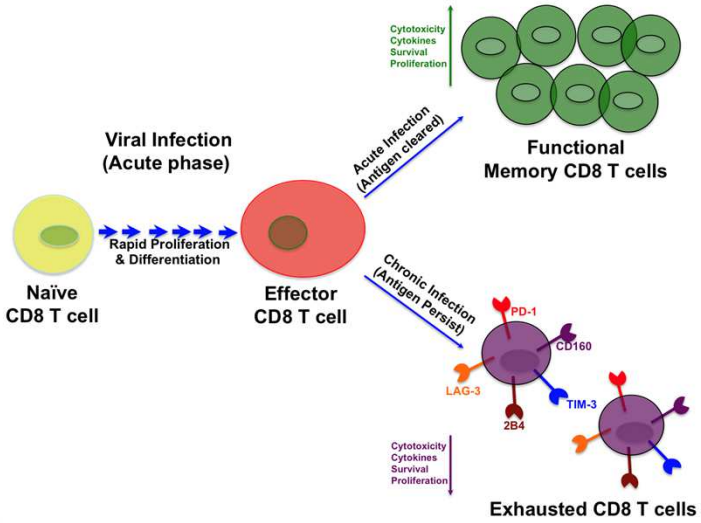
Assistant Professor

Department of Pathology & Laboratory Medicine, Emory School of Medicine
Division of Microbiology & Immunology, Emory National Primate Center
Emory University, Atlanta, Georgia, USA, 30329.

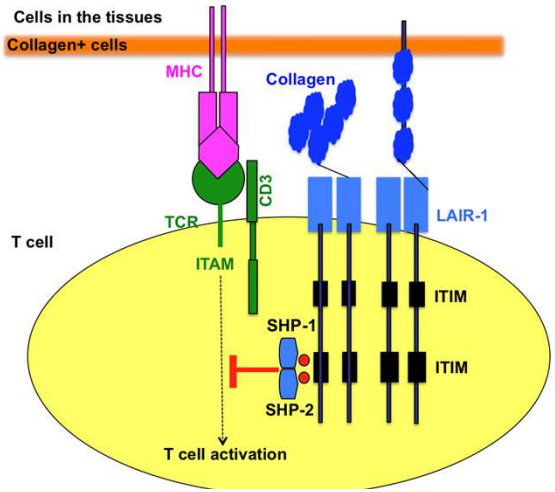
The authors declare no conflicts of Interest

Background

CD8 T cell differentiation during Acute vs Chronic Viral infection



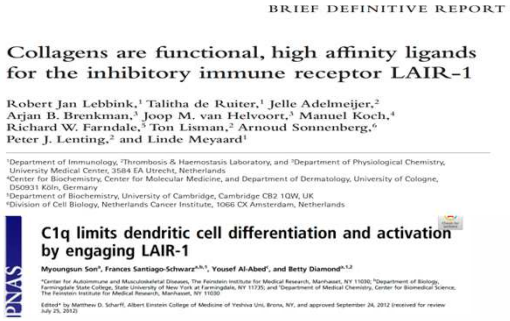
LAIR-1 mediated signaling



Leukocyte-associated Ig like receptor (LAIR-1)

- Leukocyte-associated Ig like receptor (LAIR-1) is a member of the Ig superfamily
- Expressed on the majority of human PBMCs, including NK, B, T, dendritic cells, and monocytes
- The inhibitory potential of LAIR-1 was initially demonstrated in human NK cells
- LAIR-2 is a secreted protein but lacks the transmembrane and cytoplasmic domains

Collagens are functional ligands for LAIR-1


BRIEF DEFINITIVE REPORT

Collagens are functional, high affinity ligands for the inhibitory immune receptor LAIR-1

Robert Jan Lebbink,[1] Talitha de Ruiter,[1] Jelle Adelmeijer,[2] Arjan B. Brenkman,[3] Joop M. van Helvoort,[3] Manuel Koch,[4] Richard W. Farndale,[5] Ton Lisman,[2] Arnoud Sonnenberg,[6] Peter J. Lenting,[2] and Linde Meyaard[1]

[1]Department of Immunology, [2]Thrombosis & Haemostasis Laboratory, and [3]Department of Physiological Chemistry, University Medical Center, 3584 EA Utrecht, Netherlands [4]Center for Biochemistry, Center for Molecular Medicine, and Department of Dermatology, University of Cologne, D50931 Köln, Germany [5]Department of Biochemistry, University of Cambridge, Cambridge CB2 1QW, UK [6]Division of Cell Biology, Netherlands Cancer Institute, 1066 CX Amsterdam, Netherlands

PNAS

C1q limits dendritic cell differentiation and activation by engaging LAIR-1

Myoungsun Son[a], Frances Santiago-Schwarz[a,b,1], Yousef Al-Abed[c], and Betty Diamond[a,1,2]

[a]Center for Autoimmune and Musculoskeletal Diseases, The Feinstein Institute for Medical Research, Manhasset, NY 11030; [b]Department of Biology, Farmingdale State College, State University of New York at Farmingdale, NY 11735; and [c]Department of Medical Chemistry, Center for Biomedical Science, The Feinstein Institute for Medical Research, Manhasset, NY 11030

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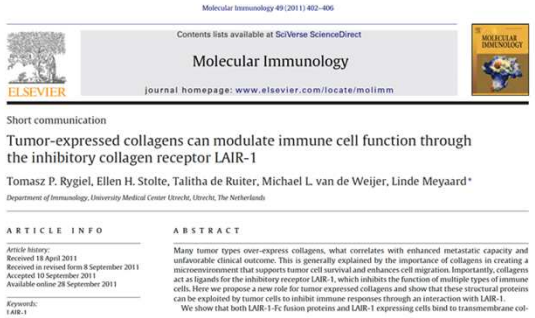
Role of LAIR-1 in Cancer/Infectious disease models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Short communication

Tumor-expressed collagens can modulate immune cell function through the inhibitory collagen receptor LAIR-1

Tomasz P. Rygiel, Ellen H. Stolte, Talitha de Ruiter, Michael L. van de Weijer, Linde Meyaard*

Department of Immunology, University Medical Center Utrecht, Utrecht, The Netherlands

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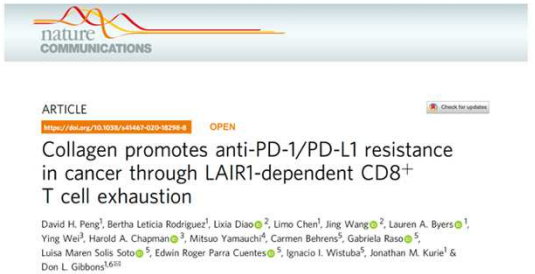
ABSTRACT

Many tumor types over-express collagens, what correlates with enhanced metastatic capacity and unfavorable clinical outcome. This is generally explained by the importance of collagens in creating a microenvironment that supports tumor cell survival and enhances cell migration. Importantly, collagens act as ligands for the inhibitory receptor LAIR-1, which inhibits the function of multiple types of immune cells. Here we propose a new role for tumor expressed collagens and show that these structural proteins can be exploited by tumor cells to inhibit immune responses through an interaction with LAIR-1.

We show that both LAIR-1-Fc fusion proteins and LAIR-1 expressing cells bind to transmembrane col-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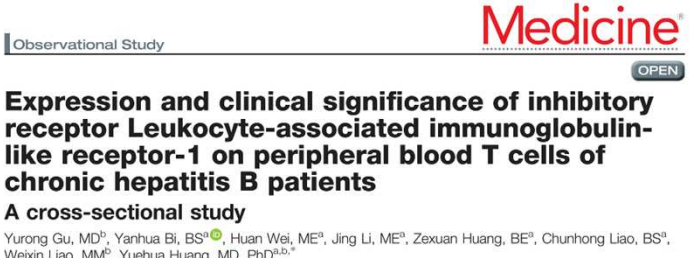
Collagen promotes anti-PD-1/PD-L1 resistance in cancer through LAIR1-dependent CD8+ T cell exhaustion

David H. Peng[1], Bertha Leticia Rodriguez[1], Lixia Diao[2], Limo Chen[1], Jing Wang[2], Lauren A. Byers[1], Ying Wei[3], Harold A. Chapman[3], Mitsuo Yamauchi[4], Carmen Behrens[5], Gabriela Raso[5], Luisa Maren Solis Soto[5], Edwin Roger Parra Cuentes[5], Ignacio I. Wistuba[5], Jonathan M. Kurie[1] & Don L. Gibbons[1,6✉]


Observational Study

Medicine

OPEN

Expression and clinical significance of inhibitory receptor Leukocyte-associated immunoglobulin-like receptor-1 on peripheral blood T cells of chronic hepatitis B patients

A cross-sectional study

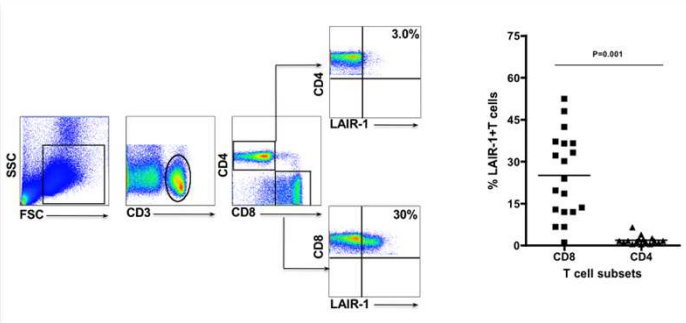
Yurong Gu, MD[b], Yanhua Bi, BS[a], Huan Wei, ME[a], Jing Li, ME[a], Zexuan Huang, BE[a], Chunhong Liao, BS[a], Weixin Liao, MM[b], Yuehua Huang, MD, PhD[a,b,*]

Chronic Hepatitis B model – LAIR-1 inhibit T cell function

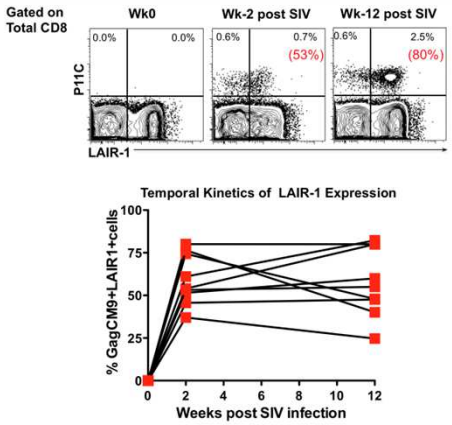
What happens in SIV naive animals?

What happens during SIV infection ?

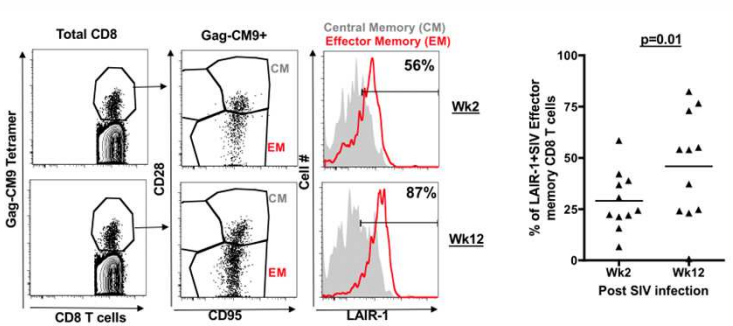
LAIR-1 is highly expressed on CD8 T cells compared to CD4 T cells



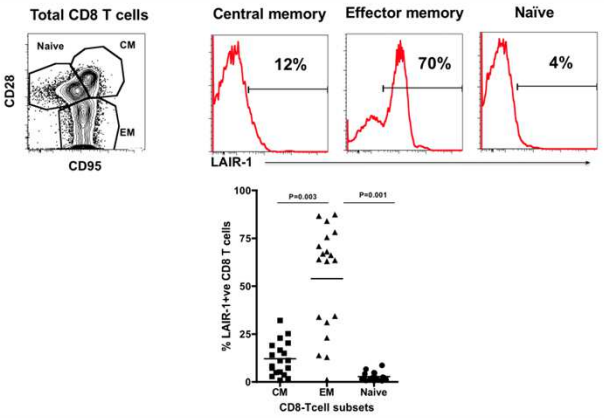
LAIR-1 is highly elevated on SIV-specific CD8 T cells following SIV infection



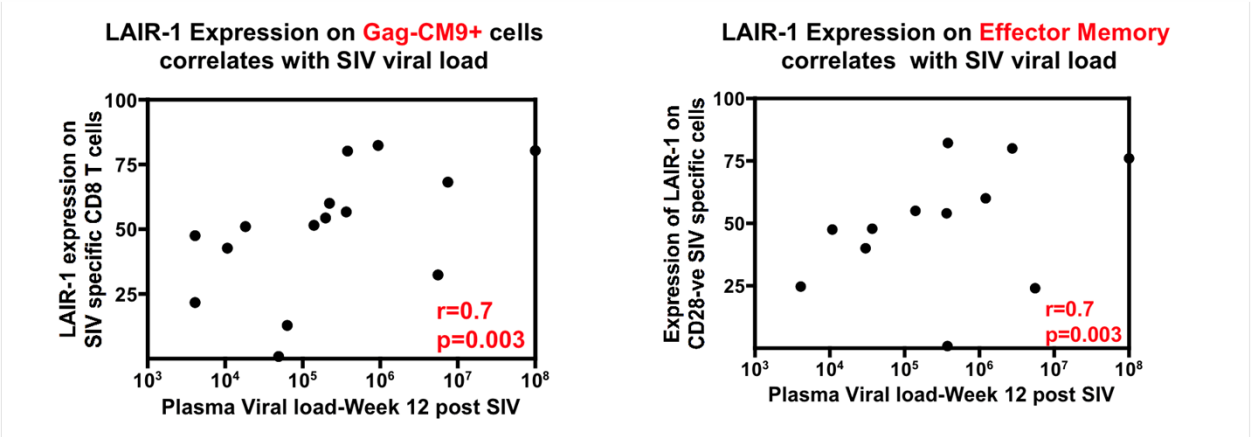
LAIR-1 is highly elevated on SIV-specific effector memory CD8 T cells following SIV infection



Effector Memory CD8 T cells express higher levels of LAIR-1 compared to Central memory CD8s

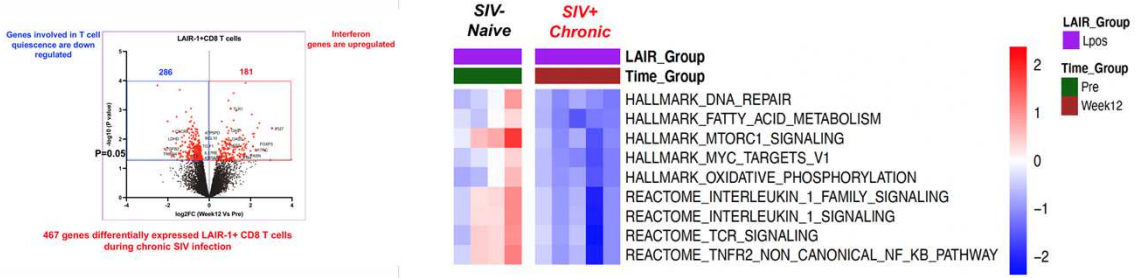


Higher levels of LAIR-1 expression on SIV-specific CD8 T cells correlates directly with plasma viral RNA levels



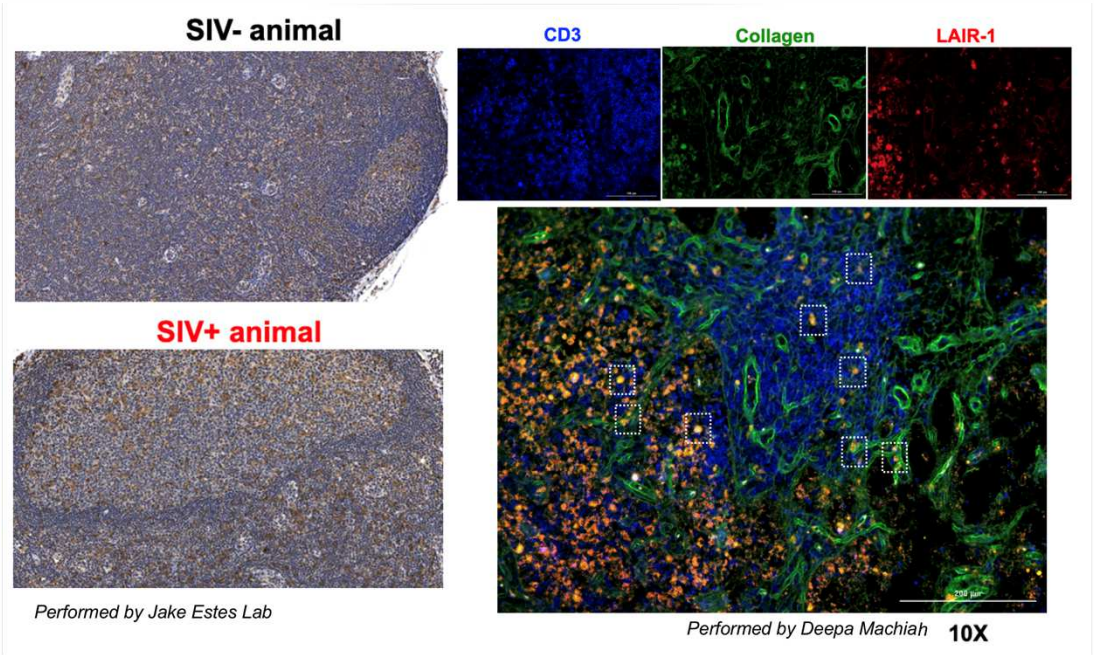
Transcriptomic Profile of LAIR-1+ CD8 T cells

Reduced TCR signaling, Cell cycle signaling and Cell metabolism pathways in LAIR-1+ CD8 T cells during chronic SIV infection



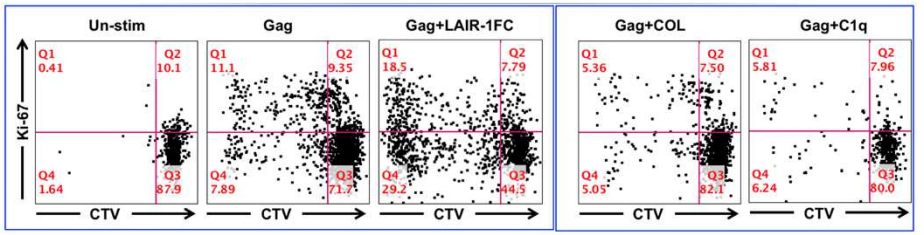
Immunohistochemistry

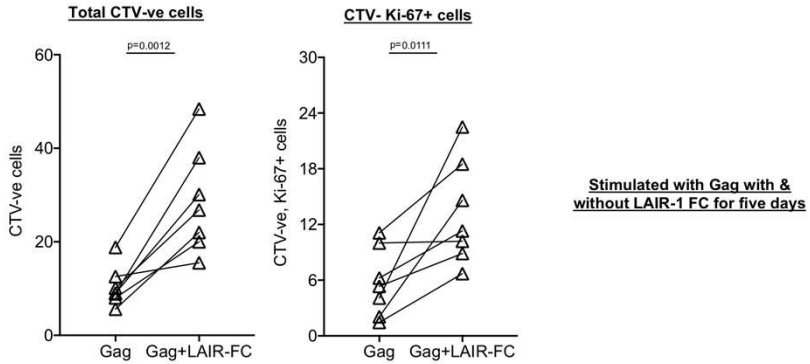
LAIR-1 expression is increased in the lymph node during chronic SIV infection



In vitro blockade of LAIR-1

In vitro blockade of LAIR-1 results in enhanced proliferation of SIV-specific CD8 T cells during chronic SIV infection

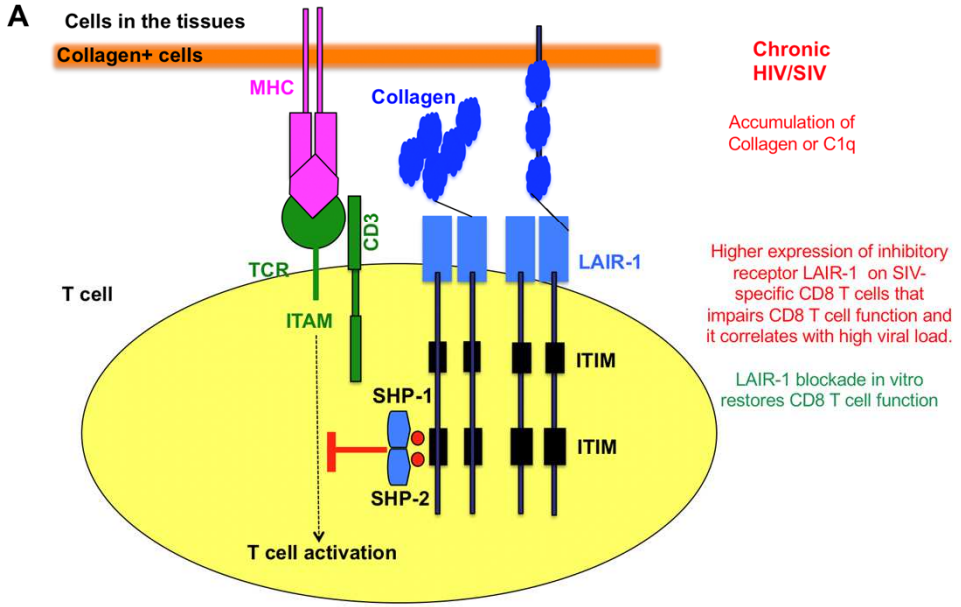




LAIR-1 expression on SIV-specific CD8 T cells inhibits CD8 T cell proliferation and function:

Thus support testing for the safety and therapeutic potential of in vivo blockade of LAIR-1 to control HIV infection.

LAIR-1 mediated inhibition of CD8 T cells during chronic SIV/HIV infection



Key question(s)

- What is the role of LAIR-1 on SIV-specific CD8 T cells during chronic SIV infection.

Key finding(s)

- LAIR-1 expression on SIV-specific CD8 T cells inhibits the proliferation and function of SIV-specific CD8 T cells during chronic SIV infection and correlates with disease progression.

What are the next steps?

- These data supports the testing for the safety & therapeutic potential of LAIR-1 blockade in vivo : If it works there is a posibility to combine this with another co-inhibitory receptor blockade (or) therapeutic vaccine for HIV cure strategy

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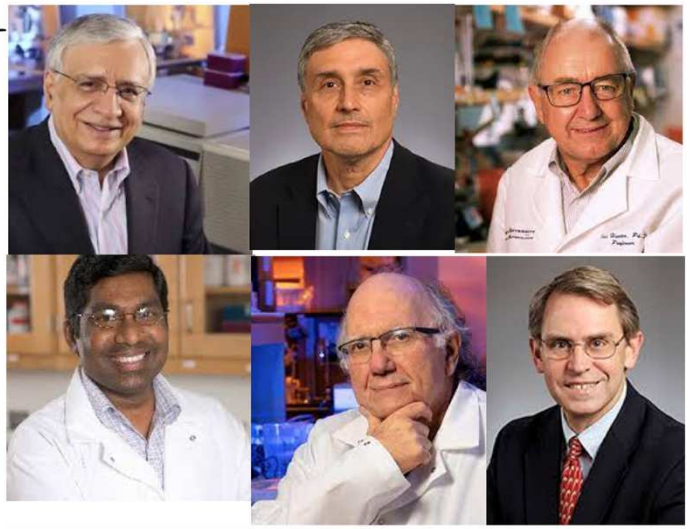

Team Work