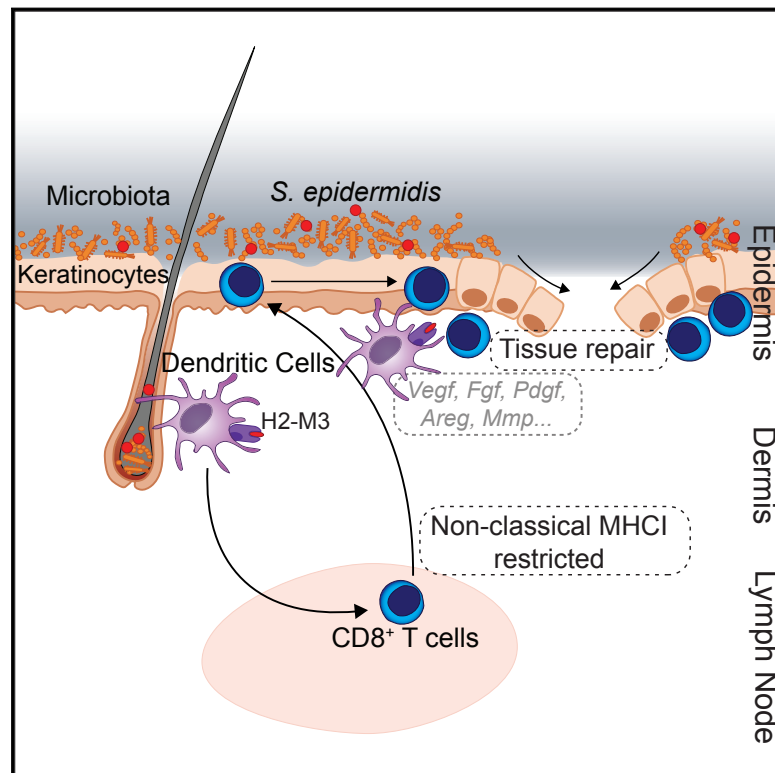


# Non-classical Immunity Controls Microbiota Impact on Skin Immunity and Tissue Repair

## Graphical Abstract



## Authors

Jonathan L. Linehan, Oliver J. Harrison, Seong-Ji Han, ..., Jason M. Brechley, John J. O'Shea, Yasmine Belkaid

## Correspondence

ybelkaid@niaid.nih.gov

## In Brief

Microbiota induce a form of adaptive immunity that couples antimicrobial function with tissue repair.

## Highlights

- Non-classical MHC class I molecules promote homeostatic immunity to the microbiota
- Commensal-specific T cells express immunoregulatory and tissue repair signatures
- Commensal-specific T cells accelerate wound closure



# Non-classical Immunity Controls Microbiota Impact on Skin Immunity and Tissue Repair

Jonathan L. Linehan,<sup>1</sup> Oliver J. Harrison,<sup>1</sup> Seong-Ji Han,<sup>1</sup> Allyson L. Byrd,<sup>1,2,3</sup> Ivan Vujkovic-Cvijin,<sup>1</sup> Alejandro V. Villarino,<sup>4</sup> Shurjo K. Sen,<sup>5</sup> Jahangheer Shaik,<sup>6</sup> Margery Smelkinson,<sup>7</sup> Samira Tamoutounour,<sup>1</sup> Nicholas Collins,<sup>1</sup> Nicolas Bouladoux,<sup>1,8</sup> Amiran Dzutsev,<sup>5</sup> Stephan P. Rosshart,<sup>9</sup> Jesse H. Arbuckle,<sup>10</sup> Chyung-Ru Wang,<sup>11</sup> Thomas M. Kristie,<sup>10</sup> Barbara Rehermann,<sup>9</sup> Giorgio Trinchieri,<sup>5</sup> Jason M. Brechley,<sup>12</sup> John J. O'Shea,<sup>4</sup> and Yasmine Belkaid<sup>1,13,\*</sup>

<sup>1</sup>Mucosal Immunology Section, Laboratory of Parasitic Diseases, NIAID, NIH, Bethesda, MD 20892, USA

<sup>2</sup>Translational and Functional Genomics Branch, NHGRI, NIH, Bethesda, MD 20892, USA

<sup>3</sup>Department of Bioinformatics, Boston University, Boston, MA 02215, USA

<sup>4</sup>Molecular Immunology and Inflammation Branch, NIAMS, NIH, Bethesda, MD 20892, USA

<sup>5</sup>Cancer and Inflammation Program, NCI, NIH, Bethesda, MD 20892, USA

<sup>6</sup>Laboratory of Parasitic Diseases, NIAID, NIH, Bethesda, MD 20892, USA

<sup>7</sup>Biological Imaging, Research Technology Branch, NIAID, NIH, Bethesda, MD 20892, USA

<sup>8</sup>NIAID Microbiome Program, NIH, Bethesda, MD 20892, USA

<sup>9</sup>Immunology Section, Liver Diseases Branch, NIDDK, NIH, Bethesda, MD 20892, USA

<sup>10</sup>Molecular Genetics Section, NIAID, NIH, Bethesda, MD 20892, USA

<sup>11</sup>Department of Microbiology and Immunology, Northwestern University, Chicago, IL 60611, USA

<sup>12</sup>Barrier Immunity Section, Laboratory of Parasitic Diseases, NIAID, NIH, Bethesda, MD 20892, USA

<sup>13</sup>Lead Contact

\*Correspondence: [ybelkaid@niaid.nih.gov](mailto:ybelkaid@niaid.nih.gov)

<https://doi.org/10.1016/j.cell.2017.12.033>

## SUMMARY

Mammalian barrier surfaces are constitutively colonized by numerous microorganisms. We explored how the microbiota was sensed by the immune system and the defining properties of such responses. Here, we show that a skin commensal can induce T cell responses in a manner that is restricted to non-classical MHC class I molecules. These responses are uncoupled from inflammation and highly distinct from pathogen-induced cells. Commensal-specific T cells express a defined gene signature that is characterized by expression of effector genes together with immunoregulatory and tissue-repair signatures. As such, non-classical MHCI-restricted commensal-specific immune responses not only promoted protection to pathogens, but also accelerated skin wound closure. Thus, the microbiota can induce a highly physiological and pleiotropic form of adaptive immunity that couples antimicrobial function with tissue repair. Our work also reveals that non-classical MHC class I molecules, an evolutionarily ancient arm of the immune system, can promote homeostatic immunity to the microbiota.

## INTRODUCTION

The immune system acts as a formidable regulator of host homeostasis to sustain and restore tissue function in the context of microbial encounters and environmental challenges.

The development of defined arms of the immune system and, more particularly, those associated with adaptive immunity has coincided with the acquisition of a complex microbiota, suggesting that a large fraction of this machinery has evolved as a means to maintain symbiotic relationships with these highly diverse microbial communities (Belkaid and Hand, 2014).

Most of what we understand today about the function of the immune system has come from the exploration of inflammatory settings or responses to pathogenic microbes. However, the vast majority of immune system-microbial encounters are those resulting from the symbiotic relationship with the microbiota. The characteristics and properties of this class of immunity remain largely unknown. Far from being ignored by the immune system as originally perceived, microbes at all barrier surfaces are tonically educating tissues for antimicrobial functions and are actively recognized by both the innate and the adaptive immune systems (Belkaid and Hand, 2014; Honda and Littman, 2016; Pamer, 2016). In the gastrointestinal tract, host-microbe communications are mediated by immunoglobulin A (IgA), T helper 17 (Th17), and regulatory T (Treg) cell responses, a dialog that can be in part explained by the unique requirement of the gastrointestinal (GI) tract for absorption (Belkaid and Hand, 2014; Honda and Littman, 2016). However, it is now becoming clear that even at more stringent barrier sites, such as the skin, the immune system is poised to sense and to respond to the microbiota (Naik et al., 2015; Scharschmidt et al., 2015). These commensal-specific responses not only control microbiota containment but also promote antimicrobial defenses via their action on both innate and epithelial cells (Ivanov et al., 2009; Naik et al., 2015; Yang et al., 2014). However, despite the extraordinary number of potential



متن کامل مقاله

دریافت فوری ←

**ISI**Articles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات