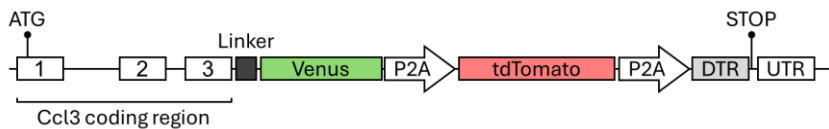


CCL3-EASER Mouse

A model for studying CCL3 expression in inflammatory processes

Invention

CCL3, also referred to as macrophage inflammatory protein 1-alpha (MIP-1α) or Scya3, is a chemokine that plays a pivotal role in immune regulation and inflammatory processes. It is a key mediator of chemotaxis, directing the migration of immune cells – particularly natural killer (NK) cells, T lymphocytes, and myeloid cells – to sites of inflammation or infection. In addition to its role in cellular trafficking, CCL3 is essential for modulating intercellular communication within the immune system and shaping the inflammatory microenvironment.



Knock-in model of the CCL3-EASER Mouse. ATG: Start Codon; P2A: 2A peptide; DTR: Diphtheria Toxin Receptor; UTR: Untranslated region

As such, the ability to monitor and understand CCL3 expression *in vivo* is fundamental for advancing research in immunology, infection biology, and the development of targeted therapies. The CCL3-EASER (ErAse, SEnd, Receive) mouse is a genetically engineered knock-in model designed to provide unprecedented *in vivo* resolution of CCL3 expression and signaling dynamics. This innovative model integrates three key components into the endogenous Ccl3 locus:

- **Ccl3-Venus:** a fluorescent CCL3 fusion protein that is secreted and can be tracked upon uptake by recipient cells.
- **tdTomato:** a cytoplasmic fluorescent reporter that indicates Ccl3 transcriptional activity.
- **DTR:** the diphtheria toxin receptor that enables inducible and selective ablation of CCL3-expressing cells upon binding to the diphtheria toxin.

These elements are separated by P2A self-cleaving peptides, ensuring the independent expression of each protein while preserving regulation by the native Ccl3 promoter.

Commercial Opportunities

Dual Readout Capability: Simultaneous tracking of Ccl3 transcription (tdTomato) and translation/secretion (Ccl3-Venus).

Ligand Recipient Mapping: Enables detection of cells that have internalized or sensed secreted CCL3 (Venus⁺/tdTomato⁻).

Dynamic Regulation Unveiled: Reveals tissue- and infection-dependent regulation of CCL3 translation, modulated by Type I interferons.

Auto-/Paracrine Circuitry Discovery: Demonstrates NK cells as both primary producers and key recipients of CCL3, highlighting feedback activation loops.

Functional Depletion: DTR allows ablation of CCL3-producing cells for causal, cell-type-specific functional analysis.

Current Status

Infection Models: Viral (e.g. mCMV), bacterial, fungal.

Tumor Immunology: Track chemokine-mediated infiltration and signaling.

Vaccine Response Studies: Analyze CCL3 involvement in adjuvanticity.

Autoimmune & Inflammatory Disease: Decipher chemokine circuits and immune misfiring.

Relevant Publications

J. Exp. Med. 2024 Vol. 221 No. 7

An invention from the University Hospital of Bonn.

Advantages

- Dual Readout Capability of Ccl3 transcription and CCL3 translation/secretion
- Ligand Recipient Mapping of CCL3
- Dynamic Regulation Unveiled of CCL3 translation
- Auto-/Paracrine Circuitry Discovery of CCL3 dependent cells
- Functional Depletion of CCL3-producing cells

Technology Readiness Level

1 2 3 4 5 6 7 8 9

System prototype demonstration in operational environment

Sector(s)

- Immunology
- Infection biology
- Research & development of targeted therapies

Ref.-No.

7305



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