

**Name of Journal:** *World Journal of Hepatology*

**Manuscript NO:** 57110

**Manuscript Type:** REVIEW

#### 4-1BB/TRAF1 pathway on hepatitis C viral persistence and natural history

TRAF1 & HCV

##### Abstract

Hepatitis C virus (HCV) infection is an excellent immunological model for understanding the mechanisms developed by non-cytopathic viruses and tumors to evade the adaptative immune response. The antigen-specific cytotoxic T cell response is essential for keeping HCV under control, but during persistent infection, these cells become exhausted or even deleted. The exhaustion process is progressive and depends on the infection duration and level of antigenemia. During high antigenic load and long duration of infection, T cells become extremely exhausted and ultimately disappear due to apoptosis. The development of exhaustion involves the impairment of positive co-stimulation induced by regulatory cytokines, such as transforming growth factor beta 1. This cytokine downregulates tumor necrosis factor receptor (TNFR)-associated factor 1 (TRAF1), the signal transducer of the T cell co-stimulatory molecule TNFR superfamily member 9 (known as 4-1BB). This impairment correlates with the low reactivity of T cells and an exhaustion phenotype. Treatment with interleukin-7 *in vitro* restores TRAF1 expression and rescues T cell effector function. The process of TRAF1 loss and its *in*

### Match Overview

- |   |  |     |
|---|--|-----|
| 1 | <b>Crossref</b> 28 words<br>Shao-Cong Sun. "The non-canonical NF-κB pathway in immunity and inflammation", <i>Nature Reviews Immunology</i> , 2017             | 1%  |
| 2 | <b>Crossref</b> 19 words<br>Jonathan Chee, Bruce W.S. Robinson, Robert A. Holt, Jene ...<br>e Creaney. "Immunotherapy for Lung Malignancies", <i>Chest</i> , 2 | 1%  |
| 3 | <b>Internet</b> 15 words<br>crawled on 23-Aug-2020<br><a href="http://www.mdpi.com">www.mdpi.com</a>   | <1% |



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## [Natural history of hepatitis C - ScienceDirect](https://www.sciencedirect.com/science/article/pii/S0168827814004814)

<https://www.sciencedirect.com/science/article/pii/S0168827814004814>

Nov 01, 2014 · Although **hepatitis C** causes **persistent hepatitis**, the RNA **viral** genome does not integrate into the host genome and **viral** replication can be curtailed and a virological cure achieved by treatment. Accepted cure is defined as undetectable HCV RNA in serum at 12–24 weeks following completion of treatment (sustained virological response, SVR).

**Cited by:** 699**Author:** Rachel H. Westbrook, Geoffrey Dusheiko**Publish Year:** 2014

## [TRAF1 Signaling in Human Health and Disease](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6305416)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6305416>

Moreno-Cubero et al. recently examined **Hepatitis C virus** (HCV)-specific CD8 + T cells from patients with progressive infection and those with resolved infection . As with chronic HIV infection, progressive exhaustion during **persistent** infection with HCV was also associated with loss of TRAF1 measured directly ex vivo or after in vitro TCR ...

**Cited by:** 8**Author:** Maria I. Edilova, Ali A. Abdul-Sater, Tania H....**Publish Year:** 2018

## [Frontiers | TRAF1 Signaling in Human Health and Disease ...](https://www.frontiersin.org/articles/10.3389/fimmu.2018.02969)

<https://www.frontiersin.org/articles/10.3389/fimmu.2018.02969> ▼

Tumor necrosis factor receptor (TNFR) associated factor 1 (TRAF1) is a signaling adaptor first identified as part of the TNFR2 signaling complex. TRAF1 plays a key role in pro-survival signaling downstream of TNFR superfamily members such as TNFR2, LMP1, 4-1BB, and CD40. Recent studies have uncovered another role for TRAF1, independent of its role in TNFR superfamily signaling, in negatively ...

**Cited by:** 8**Author:** Maria I. Edilova, Ali A. Abdul-Sater, Tania H.



Tumor necrosis family receptor superfamily member 9/tumor necro



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## [TNFRSF12A - Tumor necrosis factor receptor superfamily ...](#)

<https://www.uniprot.org/uniprot/Q9NP84> ▾

**Receptor** for TNFSF12/TWEAK. Weak inducer of apoptosis in some cell types. Promotes angiogenesis and the proliferation of endothelial cells. May modulate cellular adhesion to matrix proteins.

## [The Role of Tumor Necrosis Factor Receptor Superfamily ...](#)

<https://www.whdl.org/role-tumor-necrosis-factor...> ▾

Zika virus (ZIKV) is a **member** of the Flaviviridae virus **family** and as of February 2016 has been declared a global public health emergency by the World Health Organization. Understanding the T cell response to ZIKV is critical in making steps towards developing vaccines and antiviral therapies. This project investigated the effect of **tumor necrosis factor receptor** (TNFR)

## [4-1BB Delineates Distinct Activation Status of Exhausted ...](#)

<https://aasldpubs.onlinelibrary.wiley.com/doi/full/10.1002/hep.30881>

We aimed to investigate costimulatory **receptor** expression, particularly 4-1BB (CD137 or **tumor necrosis factor receptor superfamily member 9**), on **tumor**-infiltrating CD8 + T cells (CD8 + **tumor**-infiltrating lymphocytes [TILs]) and its association with distinct T-cell activation features among exhausted CD8 + TILs in hepatocellular ...

**Cited by:** 6

**Author:** Hyung-Don Kim, Seongyeol Park, Seongj...

**Publish Year:** 2020

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