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Methods and Compositions for Treating Inflammatory Diseases

Tech ID: 33049 / UC Case 2019-199-0

BACKGROUND

Immune responses are crucial in fighting against infections. An uncontrolled immune response, however, can be deadly. Sepsis is one such inflammatory disease that can lead to organ failure and death, so it is crucial to develop new sepsis therapies. Long noncoding RNAs (IncRNAs), although not translated into proteins themselves, can regulate gene expression in biological processes. Studies have shown that IncRNAs can regulate immune responses, which leads to substantial interest in implicating IncRNAs in inflammatory diseases.

TECHNOLOGY DESCRIPTION

This invention involves inhibitors of gastric adenocarcinoma predictive long intergenic noncoding (GAPLINC) RNA, a type of lncRNA, and is based on UC Santa Cruz researchers' discovery that GAPLINC plays a role in regulating inflammation. GAPLINC knockdown studies suggested that GAPLINC negatively regulates the inflammatory response. Depleting GAPLINC increased expression of immune response genes. Furthermore, in response to endotoxic shock, *Gaplinc* knockout mice showed 100% survival, whereas wild type mice showed 0% survival after 2 days. By inhibiting GAPLINC, treatment for sepsis can start to go beyond supportive care.

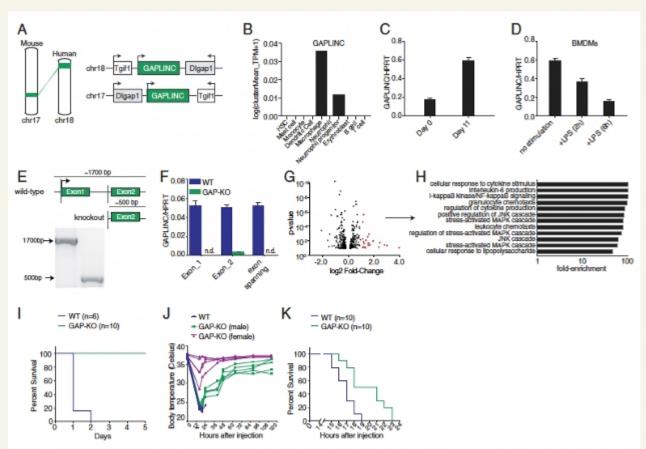


Fig. 3. GAPLINC is conserved in mice and regulates response to endotoxic shock. (A) GAPLINC is conserved in synteny. GAPLINC is located on Chr 18 in humans and on Chr 17 in mice, between protein-coding genes DIgap 1 and Tgif1. DIgap 1 is not expressed in macrophages. (B) MCA shows distribution of Gaplinc levels in various immune cell types (BM). (C) qPCR analysis of Gaplinc expression in BM cells and BMDMs; these data (mean ± SD) are representative of three independent experiments. (D) qPCR analysis of Gaplinc expression in BMDMs stimulated with LPS (200 ng/mL) for 6 it; these data (mean ± SD) are representative of three independent experiments. (E) Schematic of Gaplinc locus before and after CRSPR/Cas9 mediated deletion. Dashed lines indicate the approximate region of deletion. Gel represents PCR amplification of genomic data. Amplicon lengths are compared for WT and Gaplinc KO mice. (F) qPCR analysis of Gaplinc expression in WT and Gaplinc-KO BMDMs using a combination of primers to detect Exon1, Exon2, and exon-spanning regions of the Gaplinc transcript; these data (mean ± SD) are representative of three independent experiments. (G) RNA-Seq analysis in BMDMs from WT and Gaplinc KO mice (n = 3). Results are represented in a volcano plot. Significantly up-regulated genes with a fold change ≥ 2 are shown in red. (H) GO-Term analysis on significantly up-regulated genes. (I and J) Survival data of WT and Gaplinc KO mice are shown in response to E. coli LPS challenge (S mg/kg/mice) (n = 6 to 10). The statistical test of differences was calculated using the log-rank (Mantel-Cox) test. ***P < 0.001. Changes in body temperature of WT and Gaplinc KO mice were recorded at the indicated time points. (K) Survival data of WT and Gaplinc KO mice are shown in response to E. coli LPS challenge (20 mg/kg/mice) (n = 10). The statistical test of differences was calculated using the log-rank (Mantel-Cox) test. ***P < 0.001.

Permalink

CONTACT

Jeff M. Jackson jjackso6@ucsc.edu



INVENTORS

- Carpenter, Susan
- Covarrubias, Sergio
- ► Vollmers, Apple

OTHER INFORMATION

KEYWORDS

long noncoding RNA, inflammation, GAPLINC, innate immunity, sepsis,

p65

CATEGORIZED AS

- ▶ Medical
 - Disease: Autoimmune and Inflammation
 - ▶ Therapeutics

RELATED CASES

2019-199-0

- therapeutic intervention
- sepsis treatment
- ► RNA therapeutics
- novel drug development

ADVANTAGES

unmet need

INTELLECTUAL PROPERTY INFORMATION

Country	Туре	Number	Dated	Case
United States Of America	Published Application	20210087563	03/25/2021	2019-199

RELATED MATERIALS

A conserved long noncoding RNA, GAPLINC, modulates the immune response during endotoxic shock - 02/10/2021

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ Hek293 Cell Line Producing Murine GM-CSF
- ▶ CRISPRware

University of California, Santa Cruz

Industry Alliances & Technology Commercialization

Kerr 413 / IATC,

Santa Cruz,CA 95064

Tel: 831.459.5415

innovation@ucsc.edu

https://officeofresearch.ucsc.edu/

Fax: 831.459.1658

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