Circulating cell death biomarker TRAIL is associated with increased organ dysfunction in sepsis

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Online Data Supplement

Assay details:

TRAIL (R & D systems Human TRAIL Quantikine® ELISA (DTRL00)):

Assays were performed in duplicate. The intra-assay precision ranges from 2.8-5.6% and the inter-assary precision ranges from 4.4-7.5%. The assay range is from 15.6 -1,000 pg/ml. The average recovery for plasma is 103%. The % expected return, as a measure of linearity was 106% (101-110%) for the 1:2 dilution used for this assay. The mean minimum detectable dose (MDD) per the manufacturer's specification is 2.86 pg/ml with a range of 0.57-7.87 pg/ml. The detection wavelength is 450nm.

RIPK3 (Cusabio Human RIPK3 ELISA (CSB-EL019737HU)):

Assays were performed in duplicate. The intra-assay precision CV% is <8% and the inter-assay precision CV% <10%. The % expected return, as a measure of linearity was 99% (96-106%) for the 1:10 dilution used for this assay. The average recovery for plasma is 98%. The assay range is between 15.6 and 1,000 pg/ml. The assay sensitivity is 3.9 pg/ml. The detection wavelength is 450nm.

Cohort details:

WCM:

Study subjects were adults (≥18 years old) hospitalized in the MICU of New York-Presbyterian Hospital-Weill Cornell Medical Center (WCM), New York, USA (enrollment started on 10/2014), IRB 1405015116A005. Subjects were recruited regardless of underlying diagnosis and were approached within 24 hours of ICU admission for enrollment and whole blood (10 mL) was drawn from each patient into EDTA-coated blood collection tubes (BD Pharmingen, San Jose, CA) within 48 hours. Samples were stored at 4°C and centrifuged within 4 hours of collection. Plasma was separated and divided into aliquots and kept at -80°C. Patients were excluded if they were moribund, unwilling to provide blood for research, if informed consent could not be obtained, unwilling to be transfused, or with a hemoglobin level of <7 g/dL with active bleeding.

BWH RoCI:

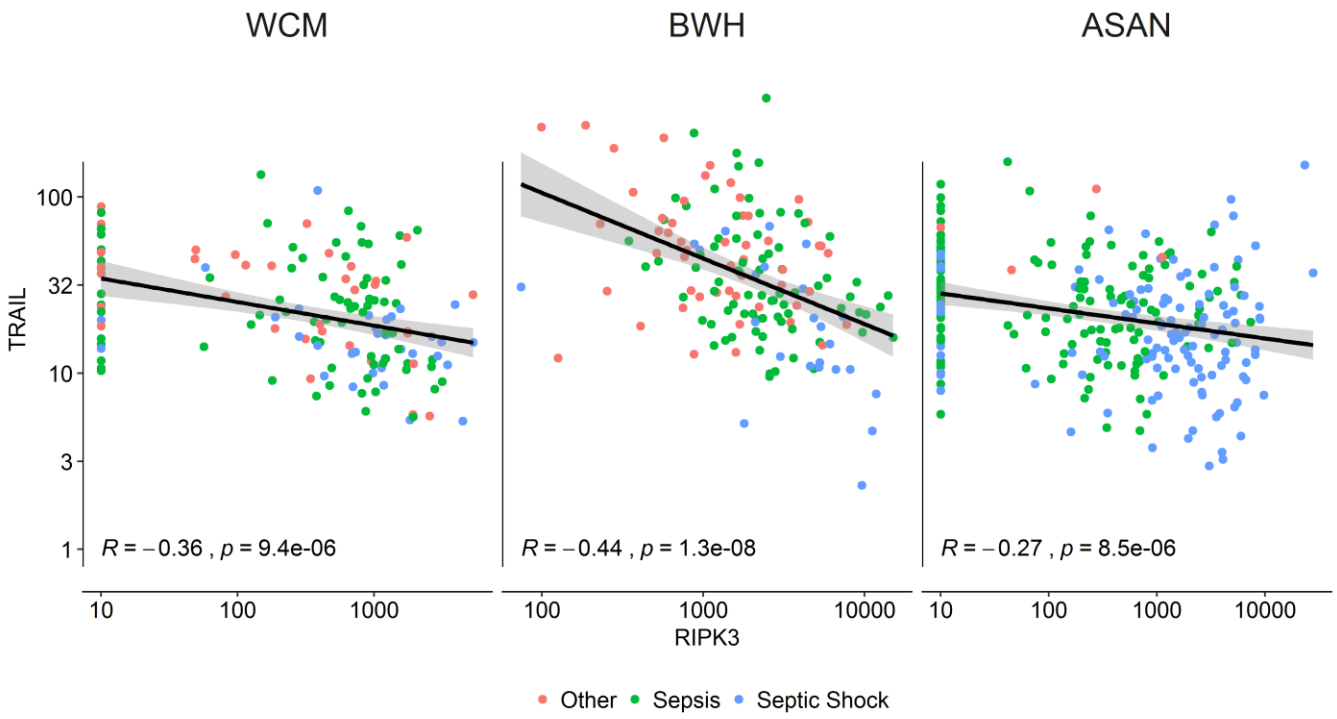
Study subjects were adults admitted to the MICU of Brigham and Women's Hospital (BWH), Boston, USA (enrollment started 2008, IRB 2008-P-000495). Any MICU patients were available for recruitment. Subjects were recruited Blood samples were drawn within 24 hours of enrollment to the biobank registry in EDTA-coated Vaccutainer tubes (BD Pharmigen, San Jose, CA). Specimen are processed within 4 hours of collection and centrifuged at 480g. Plasma aliquots are stored at -80°C for future analysis. Patients were excluded if they were moribund upon arrival, unwilling to provide blood for research, if informed consent could not be obtained, unwilling to be transfused, or with a hemoglobin level of <8 g/dL.

ASAN:

Critically ill adults were enrolled within 24 hours of their admission in medical ICU. Recruitment was restricted to those patients who had a concern for infection at the time of admission. The following exclusion criteria were applied: inability to provide informed consent (or lack of an appropriate legal representative to do so), moribund status. Within 48 hours after ICU admission, plasma was obtained.

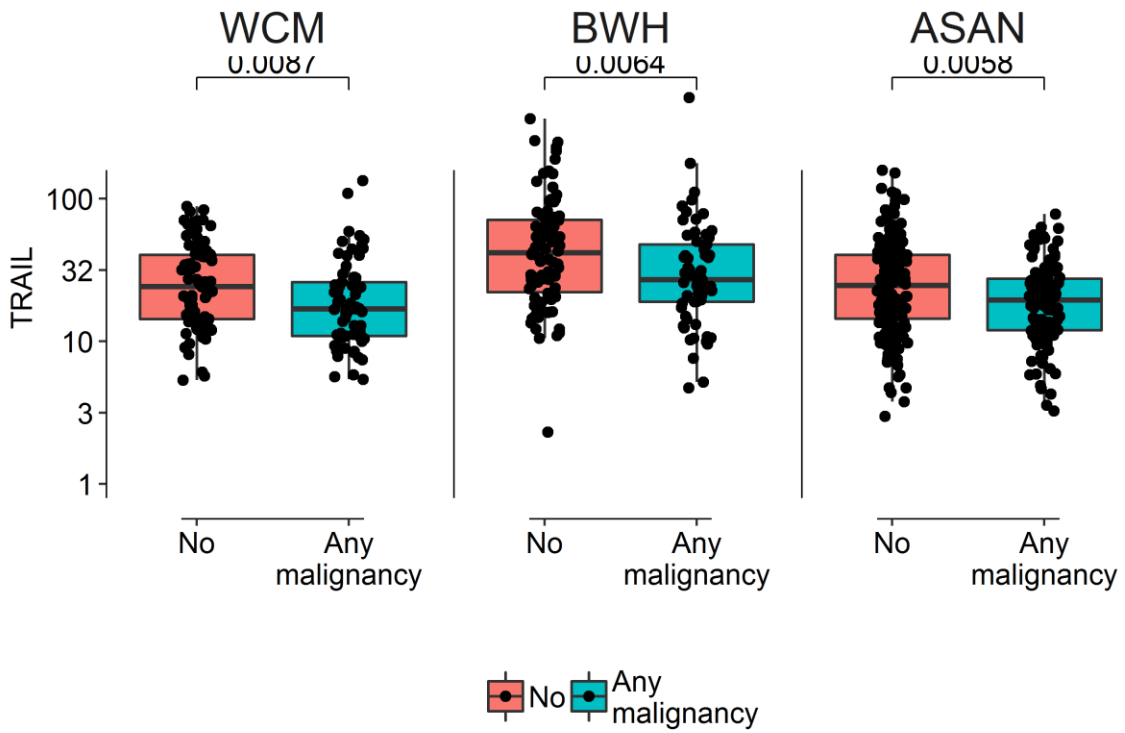
Whole blood was drawn from each patient into EDTA-coated blood collection tubes. The samples were centrifuged within 4 hours. Plasma was kept frozen at -80°C until further analysis.

Supplemental Figure 1:



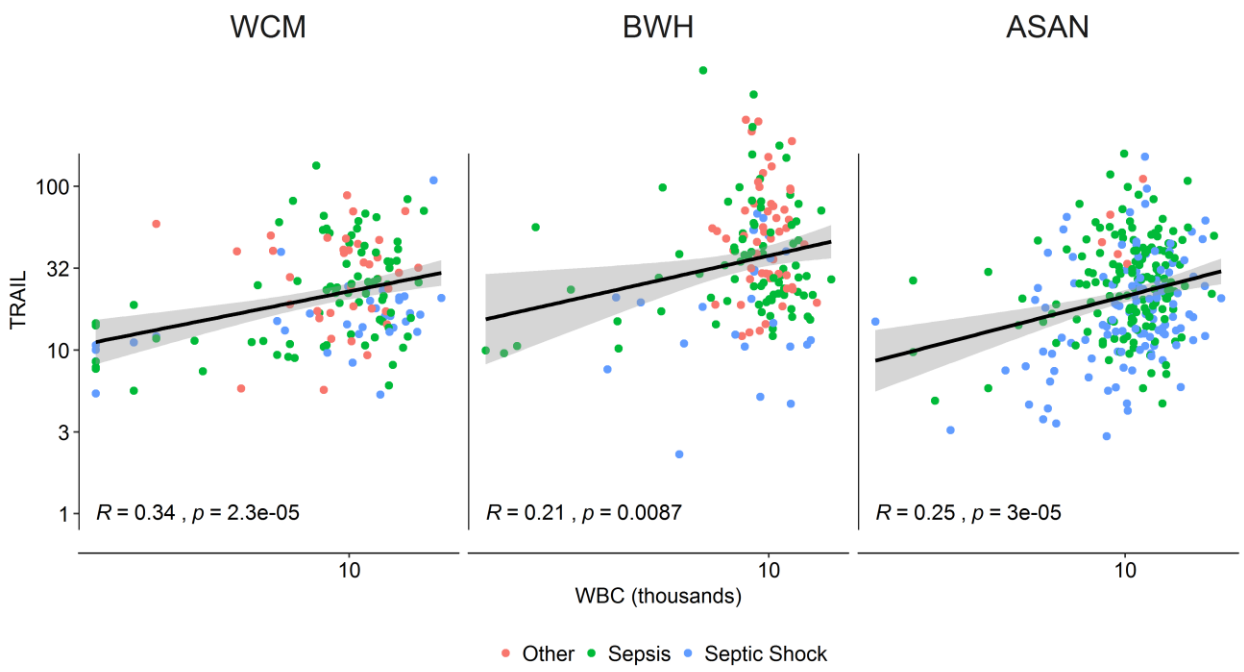
Supplemental Figure 1: Association between TRAIL and RIPK3 levels in each cohort. Linear regression of TRAIL association with RIPK3 shown in black line, with shaded area representing 95% pointwise confidence interval. Patients with non-sepsis critical illness (pink) dots, sepsis (green) dots and septic shock (blue) dots. WCM = Weill Cornell Medicine, BWH = Brigham and Women's Hospital, ASAN = Asan Medical Center

Supplemental Figure 2:



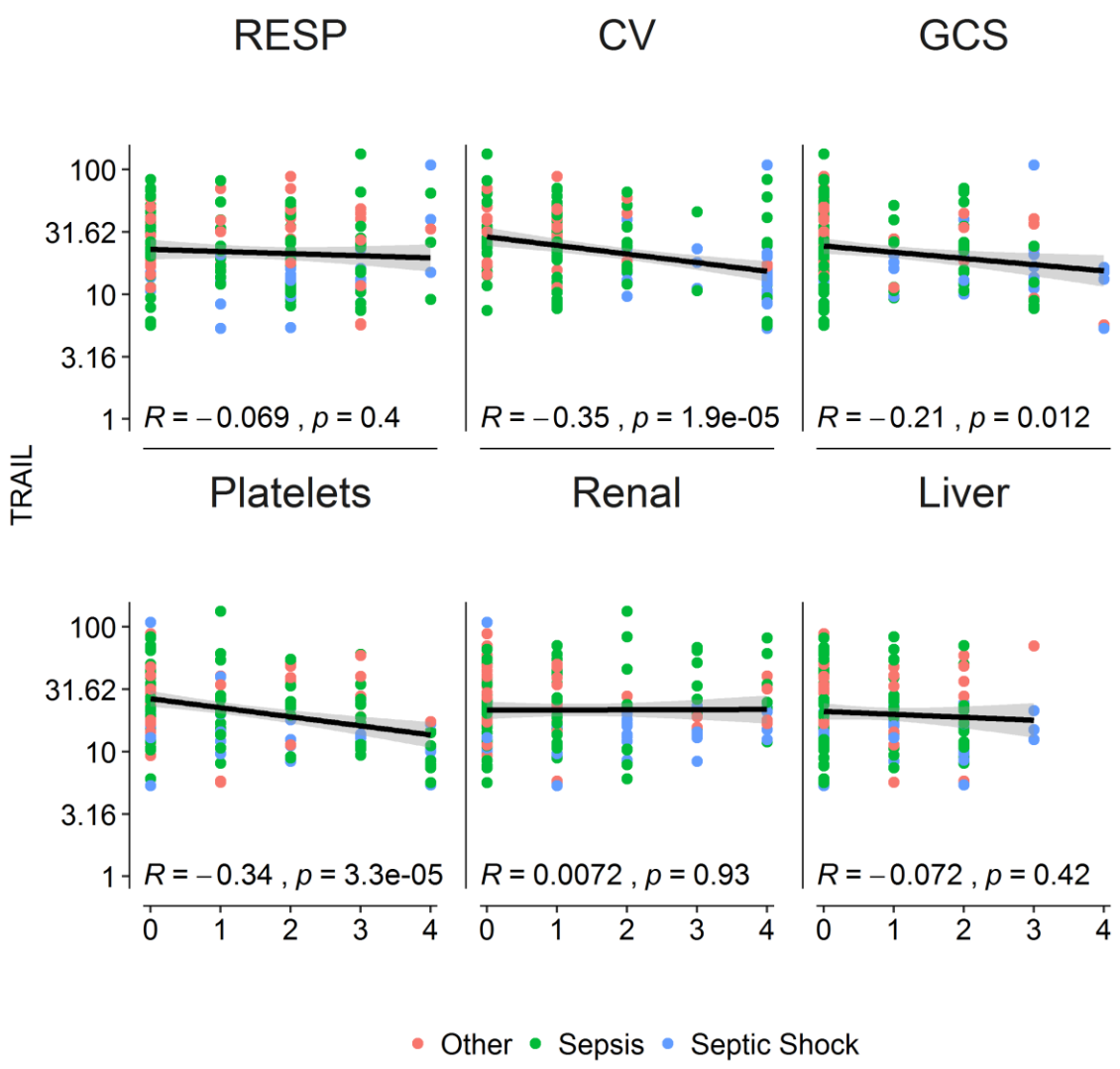
Supplemental Figure 2: TRAIL levels of patients with no active malignancy (pink) and active malignancy (blue).TRAIL levels are presented as median value (black line), interquartile range (box), and 95% (whiskers). P-values are Kruskal-Wallis non-parametric comparisons. WCM = Weill Cornell Medicine, BWH = Brigham and Women's Hospital, ASAN = Asan Medical Center

Supplemental Figure 3:



Supplemental Figure 3: Association between TRAIL levels and white blood cell count (WBC) in each cohort. Linear regression of TRAIL association with RIPK3 shown in black line, with shaded area representing 95% pointwise confidence interval. Patients with non-sepsis critical illness (pink) dots, sepsis (green) dots and septic shock (blue) dots. WCM = Weill Cornell Medicine, BWH = Brigham and Women's Hospital, ASAN = Asan Medical Center

Supplemental Figure 4:



Supplemental Figure 4: Association between TRAIL level and individual SOFA components. Resp=Respiratory, CV=Cardiovascular, GCS=Neurologic, Platelets=Hematologic, Renal, and Liver=Hepatic organ systems in all cohorts. Linear regression modelling of TRAIL association with each SOFA component shown in black line, with shaded area representing 95% pointwise confidence interval.