TRAIL as a biomarker for viral infections in febrile children

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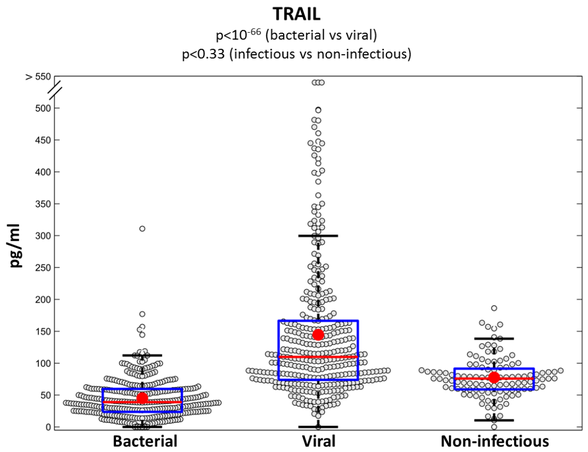
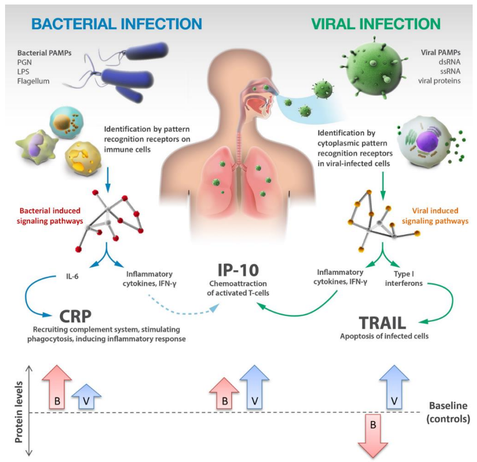
Background and design

1. TRAIL can serve as a useful biomarker for distinguishing between bacterial and viral infections when computationally combined with CRP and IP-10

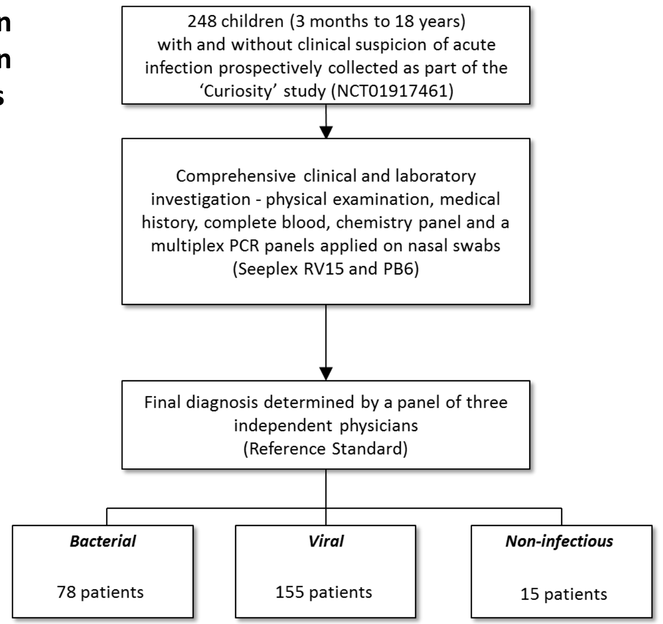




Oved et al. PLOS ONE 2015

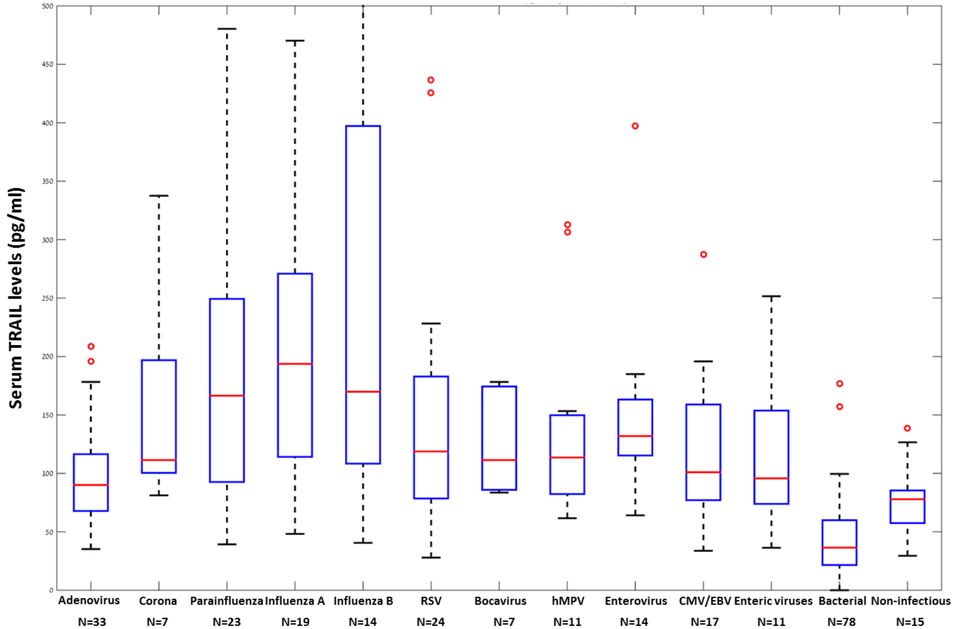
2. We evaluated TRAIL levels in children with various viral infections as well as in bacterially infected children and controls

Here we describe a sub-study of the 'Curiosity' study that was conducted prospectively between August 2009 and November 2013 at two Medical Centers in Israel (NCT01917461; Oved et al. PLOS ONE 2015; Eden et al JOI 2016). We studied 233 febrile children and 15 non-infectious controls. Patient etiology (78 bacterial and 155 viral) was determined by majority adjudication of three independent physicians based on comprehensive clinical and laboratory investigation. Bacterial and viral strains were detected using multiplex-PCR applied to nasal swabs [Seeplex-RV15/PB6]). Serum TRAIL levels were measured using ELISA (MeMed).



Results and conclusion

3. TRAIL levels were increased in all viral strains tested and decreased in bacterial patients



Blue boxes present first to third quartiles. Red line corresponds to group median. RSV - Respiratory syncytial virus; hMPV – human Metapneumovirus; Enteric viruses include: Rota Virus, Astrovirus, Enteric Adenovirus, Norovirus G I and G II. TRAIL levels were increased in viral patients and decreased in bacterial patients (average±SD [pg/ml]: bacterial 44±32; viral 153±110; controls 78±29). The difference between TRAIL levels in viral and bacterial patients was statistically significant for all evaluated strains (ttest p-value<0.001).

TRAIL expression increases in patients infected with a wide range of viral strains. While induction of TRAIL levels in response to viral disease was statistically significant for all viral strains examined, some strain specific variability was observed. For example, Influenza disease, which manifests as an acute febrile illness with variable degrees of systemic symptoms, ranging from mild fatigue to respiratory failure and death, induced the highest TRAIL elevation. In contrast, Adenovirus, which is known to trigger a bacterial-like inflammatory host response with clinical manifestation including prolonged fevers, leukocytosis and elevated CRP, exhibited the lowest induction. Although TRAIL is induced less by adenovirus, the opposing dynamics of TRAIL in response to bacterial versus viral infections may assist in distinguishing between adenovirus and bacterial infections that induce similar clinical symptoms.