

COMBINING VIRAL- AND BACTERIAL-INDUCED HOST PROTEINS FOR DIAGNOSING SERIOUS BACTERIAL INFECTIONS IN FEBRILE CHILDREN

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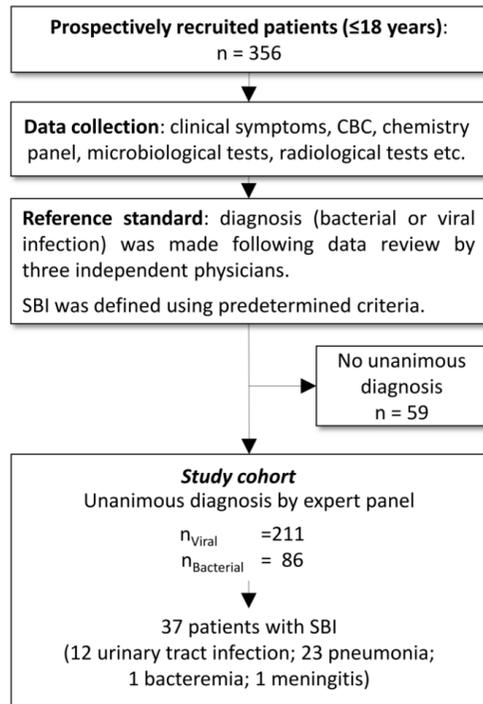
BACKGROUND AND DESIGN

Febrile children with serious bacterial infections (SBI) are at high risk for adverse outcomes. We developed a computational signature for accurately distinguishing between acute bacterial and viral infections that integrates measurements of novel viral- and traditional bacterial-induced proteins: TNF-related apoptosis-inducing ligand (TRAIL), Interferon gamma-induced protein-10 (IP-10) and C-reactive protein (CRP)¹. Here, we evaluate the sensitivity of our signature for SBIs and compare its performance to routine laboratory parameters.

We prospectively recruited 356 children (≤18 years) with a suspected acute infection. Diagnosis was determined by three independent experts on the basis of clinical and microbiological data. SBI was defined using predetermined criteria. Using the signature, a bacterial likelihood score was computed for each patient.

RESULTS

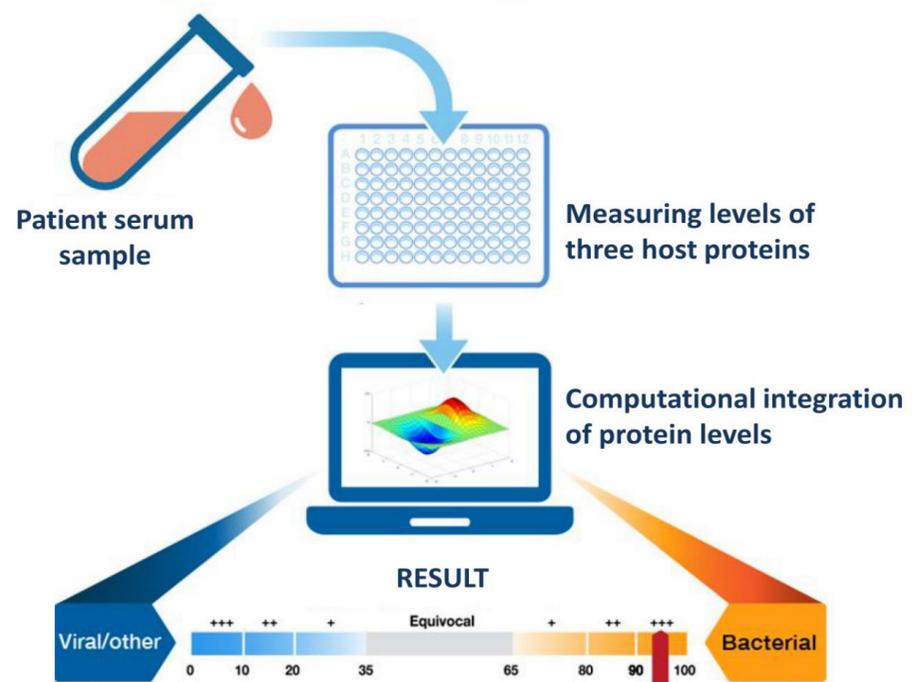
Unanimous diagnosis of the experts was attained in 211 viral and 86 bacterial patients, of whom 37 had SBI (12 urinary tract infection; 23 pneumonia; 1 bacteremia; 1 meningitis). In the remaining 59 patients unanimous diagnosis was not attained. The signature had a specificity of 0.93 ± 0.04 and sensitivity of 0.92 ± 0.06 for differentiating between bacterial and viral infections (34 patients had equivocal test results). Sensitivity of SBI detection was slightly higher than bacterial infections in general (0.94 ± 0.07 ; 4 SBI patients had equivocal test results).



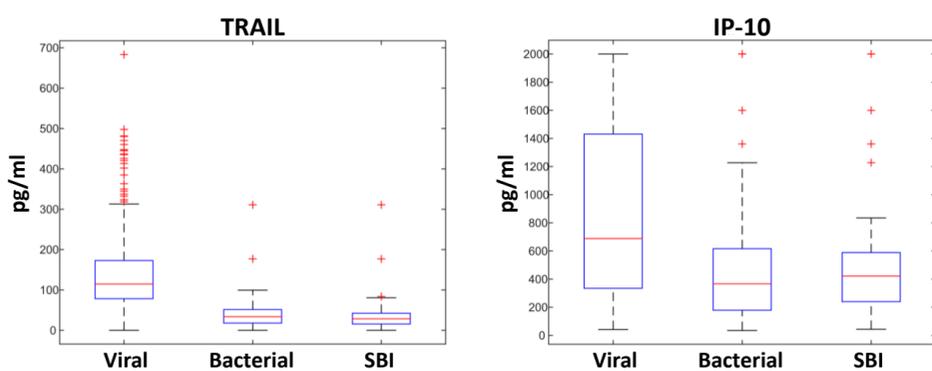
DISCUSSION

The incidence of SBI among children presenting with febrile illness at an emergency department is approximately 7%. 1 out of 4 such children are not prescribed antibiotics at initial consultation, with the delayed or missed diagnosis leading in some cases to serious medical consequences. On the other hand, 40-70% of antibiotic prescriptions are erroneously given to treat infections of viral origin. Our novel immune signature has the potential to reduce this antibiotic misuse, by aiding prompt identification of children with SBI and discriminating those children with viral infections who do not require antibiotic treatment. It provides actionable information to the clinician beyond the currently available state-of-the-art, guiding diagnosis and treatment decisions.

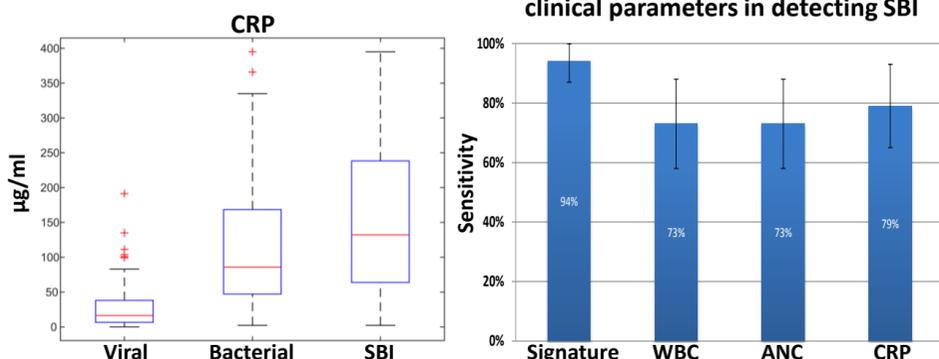
Principles of the assay:



A. The host proteins comprising the signature show complementary dynamics in response to bacterial, viral and SBI diseases

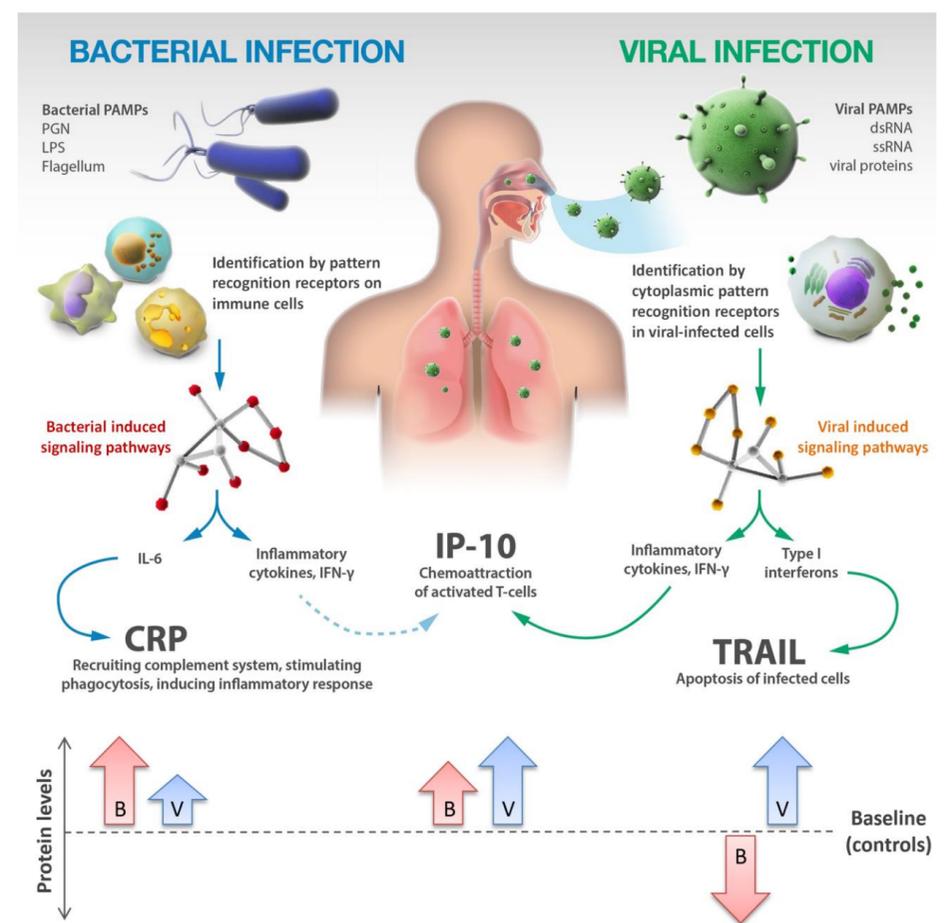


B. The signature outperforms routine clinical parameters in detecting SBI



REFERENCES

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- Craig JC, Williams GJ, Jones M, Codarini M, Macaskill P, et al. The accuracy of clinical symptoms and signs for the diagnosis of serious bacterial infection in young febrile children: prospective cohort study of 15 781 febrile illnesses. *BMJ* 2010



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