Potential diagnostic for dengue fever outcomes based on metabolomic profiles

February 25 2016

Dengue fever is a mosquito-borne tropical disease that can develop into the life-threatening dengue hemorrhagic fever/dengue shock syndrome. There are currently no standard biomarkers or algorithms for the prognosis of the progression to hemorrhagic fever or potentially fatal shock syndrome. In the latest issue of *PLOS Neglected Tropical Diseases* scientists from Colorado State University explore the use of small molecules in patient serum for diagnosis of dengue fever and potentially predicting progression to the severe disease.

In a collaboration with colleagues from the University of California, Berkeley, the Nicaraguan Ministry of Health, and the University of Yucatan, Mexico, the researchers analyzed serum samples from dengue patients in Mexico and Nicaragua. They used liquid chromatography and mass spectrometry to identify molecular features in patients diagnosed with dengue fever, dengue hemorrhagic fever/dengue shock syndrome or non-dengue disease groups. As per earlier studies by others, they confirmed that infection with dengue virus perturbs the human metabolome; the set of small molecule metabolites within the serum sample. They also found many metabolites had statistically significant differences in pair-wise comparisons between the three diagnostic groups.

In the Nicaraguan samples, distinct metabolic clusters were associated with the three different diagnostic groups. However this effect was not seen in the Mexican samples. The researchers suggest this may be due to much greater diversity in both the disease (two different serotypes and

no available information on immune status) and the patients in Mexico, who had a larger age distribution compared with the pediatric-only Nicaraguan samples. It is clear that metabolic profiles for the disease will differ between region, patient age, genetic background, and disease status, nonetheless, similar trends were found for many metabolites that differentiated disease outcomes in the two groups.

In order to explore whether differences in the metabolome might be used to predict dengue outcomes, the researchers studied 31 samples from Nicaragua. 16 of these patients progressed from dengue fever to hemorrhagic fever/dengue shock syndrome while the remaining 15 did not. 65 metabolites were found that differentiated the two disease outcomes. Six of these prognostic metabolites have thus far been structurally confirmed.

By identifying and profiling molecules that differ between different forms of dengue, the researchers lay the foundations for finding biomarkers present at early-stage dengue that are able to predict disease development. An early predictor of dengue hemorrhagic fever/dengue shock syndrome would allow appropriate triaging of patients for management and treatment. An understanding of the metabolic profile of infected patients also provides insights into the intracellular pathways instrumental in dengue infection, replication and pathogenesis.

"Metabolomics provides new opportunities and a powerful approach to investigate potential viral, host, pathogenic and immunological determinants of dengue infection and pathogenesis," explains Dr. Barry Beaty, from the Colorado State University. The research team is currently conducting a prospective clinical study in Nicaragua to further identify small molecule biomarker "biosignatures" for efficient diagnosis and prognosis of dengue.

More information: *PLOS Neglected Tropical Diseases*,