

The Genomics of Pediatric Sepsis Database is now entering its 9th year of funding by the NIH. The goals of the database have now matured from the initial discovery and exploratory phase, to a translational and clinical application phase. Extensive details regarding the progress and achievements of the database can be found at the following website:

<http://www.cincinnatichildrens.org/research/divisions/c/critical/labs/wong/default/>

There are three main projects currently in progress:

PROJECT 1

Project 1 involves the sub-classification of pediatric shock based on a 100-gene expression signature. In a series of publications, we have described and validated 3 sub-classes of pediatric septic shock based on a specific 100-gene expression signature. Importantly, one of the 3 gene expression-based sub-classes has a higher mortality rate and higher degree of illness severity, compared to the other two sub-classes. We are now seeking to bring this sub-classification scheme closer to the bedside by using a digital RNA measurement platform capable of timely generation of clinically applicable data.

Publications related to Project 1:

1. Wong, H.R., N. Cvijanovich, R. Lin, G.L. Allen, N.J. Thomas, D.F. Willson, R.J. Freishtat, N. Anas, K. Meyer, P.A. Checchia, M. Monaco, K. Odoms, and T.P. Shanley. Identification of pediatric septic shock classes based on genome-wide expression profiling. *BMC Medicine*. 7:34, 2009.
2. Wong, H.R., D.S. Wheeler, K. Tegtmeyer, S.E. Poynter, J.M. Kaplan, R.S. Chima, E. Stalets, R.K. Basu, and L.A. Doughty. Toward a clinically feasible gene expression-based sub-classification strategy for septic shock: proof of concept. *Crit Care Med*. 38:1955-1961, 2010.
3. Wong, H.R., N.Z. Cvijanovich, G.L. Allen, N.J. Thomas, R.J. Freishtat, N. Anas, K. Meyer, P. A. Checchia, R. Lin, T.P. Shanley, M.T. Bigham, D.S. Wheeler, L.A. Doughty, K. Tegtmeyer, S.E. Poynter, J.M. Kaplan, R.S. Chima, E. Stalets, R.K. Basu, B.M. Varisco, and F.E. Barr. Validation of a gene expression-based sub-classification strategy for pediatric septic shock. *Crit Care Med*. 39:2511-2517, 2011.

PROJECT 2

Project 2 involves the development of biomarkers to diagnose/predict the development of septic shock associated renal failure. The candidate biomarkers are serum protein based, and have been derived from expression profiling experiments. A biomarker-based model will be derived to predict the development of septic shock associated renal failure and subsequently tested in a prospectively enrolled validation cohort.

Publications related to project 2:

1. Basu, R.K., S.W. Standage, N.Z. Cvijanovich, G.L. Allen, N.J. Thomas, R.J. Freishtat, N. Anas, K. Meyer, P.A. Checchia, R. Lin, T.P. Shanley, M.T. Bigham, D.S. Wheeler, P. Devarajan, S.L. Goldstein, and H.R. Wong. Identification of

candidate serum biomarkers for severe septic shock-associated kidney injury via microarray. *Crit Care*. 15:R273, 2011.

PROJECT 3

Project 3 involves sequencing the entire human matrix metallopeptidase-8 (MMP8) in a large cohort of children with septic shock. We will determine if sequence variants are associated with illness severity and outcome, as well as MMP-8 activity. The rationale for this gene sequencing project is based on the recent observation that MMP-8 may be a novel candidate target for sepsis therapeutics.

Publications related to Project 3:

- 1 Solan, P.D., K.E. Dunsmore, A.G. Denenberg, K. Odoms, B. Zingarelli, and **H.R. Wong**. A novel role for matrix metalloproteinase-8 in sepsis. *Crit Care Med*. 40:379-387, 2012.

PARTICIPATION IN THE DATABASE

We currently have 16 centers participating in the database and welcome the addition of new centers. Participating centers enroll patients with septic shock. Enrollment requires the submission of biological samples and clinical data. We cover all costs for shipping and reimburse on a per patient basis. In addition, the clinical database is web-based, thus allowing for direct data entry at the local level.

If you are interested in finding out more information regarding participation in the database, or about the database in general, please contact:

Hector R. Wong, MD
Professor of Pediatrics
Director, Division of Critical Care Medicine
Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue
Cincinnati, OH 45229
Tel: 513-636-4259
Fax: 513-636-4267
Email: hector.wong@cchmc.org