BMC Bioinformatics

MEETING ABSTRACT Open Access

Meta-analysis of genes within QTLs of group A streptococcal sepsis and their expression QTLs reveal pathways modulating host differential response to streptococcal sepsis

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From 11th Annual UT-ORNL-KBRIN Bioinformatics Summit 2012
Louisville, KY, USA. 30 March - 1 April 2012

Complex host–pathogen interactions modulate differential responses to group A streptococcal (GAS) sepsis systemic disease [1,2]. We previously found that host HLA-II allelic variations are associated with differential response to severe GAS sepsis [3]. In addition, using mouse models of GAS sepsis we found other host genetic factors contribute to disease severity by modulating inflammatory responses [4,5]. We applied systems genetics approaches and analyzed variations in disease severity phenotypes using advance recombinant inbred (ARI) BXD strain panel. We mapped quantitative trait loci (QTLs) associated with differential host response to severe GAS sepsis to mouse Chr2 and X [5]. The focus of the current study is to identify regulating genes within QTLs associated with differential GAS sepsis. To do so, we explored differences in expression and nsSNPs of genes within mapped QTLs using expression data sets of relevant tissues. We selected spleen, leukocytes and lung expression data sets deposited in GeneNetwork as most relevant data sets for GAS sepsis disease severity. Collectively, integration of QTL mapping of sepsis phenotypes with expression QTLs uncovered pathways that modulate differential susceptibility to severe GAS sepsis, underscoring the complexity of traits modulating severe GAS sepsis. Approaches used in our study provide a powerful, unbiased genetics approach for analyzing interactive traits modulating the outcomes of infectious diseases.

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Published: 31 July 2012

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doi:10.1186/1471-2105-13-S12-A6
Cite this article as: Abdeltawab *et al.*: Meta-analysis of genes within QTLs of group A streptococcal sepsis and their expression QTLs reveal pathways modulating host differential response to streptococcal sepsis. *BMC Bioinformatics* 2012 **13**(Suppl 12):A6.

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