# The Evolutionary Significance of Depression in Pathogen Host Defense (PATHOS-D)

Charles L. Raison, MD[1] & Andrew H. Miller, MD[1]

[1] Department of Psychiatry and Behavioral Sciences; Emory University School of Medicine, Atlanta, GA, USA

Corresponding Author:

Charles L. Raison, MD; Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, 1365B Clifton Road, Fifth Floor, Atlanta, GA 30322; Phone (404) 712-8800, FAX (404) 727-3233; email: craison@emory.edu

**Supplementary Table 1.**

**Supplementary Table 1** provides information on host defense/immune system functionality of genes associated with depression using the genome-wide association (GWAS) methodology. To identify these genes and to examine functionality linked to host defense, the following procedure was employed.

Pubmed and Ovid searches were conducted using the key words “genome-wide association” and “major depression” (http://www.ncbi.nlm.nih.gov/pubmed). Reference lists of studies located using this approach were examined to identify any GWAS investigations not found by Pubmed search. To utilize the largest subject populations possible, studies that conducted meta-analyses of prior GWAS data and/or that employed a genome-wide association methodology on two or more independent study populations were selected for further evaluation. Using these criteria, seven publications were selected, including a recent meta-analysis conducted by Wray et al. that is discussed in the article text and in **Figure 1**. Of the other included publications that comprise **Supplementary Table 1**, six examined major depression, and the seventh (Terracciono et al. *Biol Psychiatry* 2010; 68: 811-17) examined trait level depression rather than the categorical construct of major depression. Two of the included studies (Liu et al. *Mol Psychiatry* 2011; 16: 2-6; McMahon et al. *Nat Genetics* 2010; 4: 128-31) compared allelic differences between major depression and other mood disorders (i.e. bipolar disorder), and the other five limited themselves to examining depression. Because **Supplementary Table 1** is intended to be illustrative, rather than exhaustive, we have limited our investigation to genes associated with depression at a genome-wide level of significance when such genes were identified in a given meta-analysis (indicated by a superscript “a” following the study title in the table) and for up to ten genes with the lowest p-values in studies that did not report an allele associated with depression at a genome-wide level of significance (indicated with a superscript “b” following the study title in the table).

To explore potential host defense/immune system effects of GWAS-identified genes the following approach was employed. Gene symbols as provided in each meta-analysis were entered into Pubmed. When available, Gene database information was reviewed as an initial step to familiarize ourselves with any known information about overall gene function (http://www.ncbi.nlm.nih.gov/gene/*GENE ID*). Following this, we reviewed citations identified by selecting the option entitled “See articles about gene function”. When available, we then searched the bibliography provided on the Gene database page. We repeated this process for any aliases for each gene listed in either the Gene database or on the National Center for Biotechnology Information AceView webpage (http://www.ncbi.nlm.nih.gov/IEB/Research/Acembly/av.cgi?db=human&l=*GENE SYMBOL*). To supplement these strategies, a Pubmed search was then conducted using the full name for each gene and any full name aliases. If data indicated that a given gene had an established physiological relationship with another protein or was an established member of a well-characterized biological pathway, immune system/host defense properties of the relevant proteins or pathways were examined. Any Pubmed search that returned an intractable number of hits (generally greater than 300) was narrowed down by crossing the gene symbol or name (of either the gene or related proteins/pathways) with each of the following terms separately: *host defense, immune, inflammation, interleukin, C - reactive protein, infection, viral, virus, bacteria,* and *bacterial*.