Collaborative Cross mice and their power to map host susceptibility to *Aspergillus fumigatus* infection

Supplemental file S1

Candidate Genes under QTLs

The most significant QTL is *Asprl*1 on chr 8, containing two promising candidates: interferon regulatory factor 2 (*Irf2*) and glycoprotein m6a (*Gpm6a*). Interferon is involved in host response to infectious diseases (Harada et al. 1989; Masumi et al. 2009). Homozygous mutants of *Gpm6a* have increased percentages of total body fat and fat mass (Baumrind et al. 1992; Fronz et al. 2008). Mice with high fat may be more susceptible to infectious diseases (Faggioni et al. 2001). Merge analysis identified associated SNPs in or near *Irf2* (logP = 5.63), *Stox2, Cldn22 and Wwc2*. Thus, *Irf2* is the most consistent candidate for this QTL.

Two distinct QTL *Asprl2* and *Asprl4* were mapped on chr 10. *Asprl4* contains several *a priori* candidates: (i) BCL2-associated transcription factor 1 (*Bclaf1*); mice homozygous for a knock-out allele exhibit postnatal lethality, impaired lung development, and T cell and B cell homeostasis (McPherson et al. 2008) (ii) *Btg1* (B-cell translocation gene 1, anti-proliferative), which is involved in B-cell expression (Rouault et al. 1993; Ling et al. 2009) (iii) suppressor of cytokine signaling 2 (*Socs2*) (Bradford and Famula 1984; Newton et al. 2010), which has an important role in cytokine expression and regulation, all of which are important in host response to infectious diseases. However, merge analysis implicated a different set of genes: *Aig1*, *Nmbr*, *Raet1d*, *Slc2a12*, *ENSMUSG00000075292*, *Tcf21* and *Eya4*. Strong *a priori* candidates under *Asprl2* include tumor necrosis factor alpha-induced protein 3 (*Tnfaip3*) (Kawai et al. 2001), interleukin 20 receptor alpha (*Il20ra*) (Tewari et al. 1995), interleukin 22 receptor alpha 2 (*Il22ra2*) (Wolk et al. 2007) and interferon gamma receptor 1 (*Ifngr1*) (Kohlmeier et al. 2010), which all play important roles on host response to infectious diseases. Merge analysis failed to identify any genes.

The *a priori* candidates under *Asprl3* on chr 15 include lysosomal-associated protein transmembrane 4B (Laptm4b) (Kawai et al. 2001) and heat-responsive protein 12 (*Hrsp12*) (Samuel et al. 1997). These are supported by merge analysis, which identified a run of sequence variants at logP = 6.18 with the strain distribution pattern WSB/EiJ vs others encompassing *Laptm4b* and *Hrsp12* as well as *Matn2, Rp130, BC030476*, and *Pop1*.

There were no *a priori* candidates under *Asprl5* on chr 18 or *Asprl6* on chr 3, but merge analysis suggests variants in or near *Gata6* and *Rbbp8* for *Asprl5*, and *Frrs1* and *Agl* for *Asprl6*. Finally, under *Asprl7* on chr 2, three *a priori* candidate genes were identified; Trans-acting T-cell-specific transcription factor *Gata3*, interleukin 2 receptor, alpha chain (*Il2ra*), and interleukin 15 receptor, alpha chain (*Il15ra*). *Gata3* is involved in fetal liver hematopoiesis and T cell development is impaired when the locus is conditionally inactivated during this process (Zon et al. 1991; Oohashi et al. 1999). T cells are important in host response mechanism to infectious diseases, including aspergillosis. Interleukin genes are also involved in host response to infectious diseases. Mice homozygous for a targeted null mutation in *Il2ra* exhibit massive proliferation of polyclonal T and B cells as adults and develop autoimmune disorders including inflammatory bowel disease and hemolytic anemia with age (Grigorieva et al. 2010). Mutations of *Il15ra* result in the absence of NK cell production in spleen and bone marrow (Ortega et al. 1984; Giri et al. 1995; Carninci et al. 2005). However, merge analysis does not support these candidates, instead favouring *Taf3, Kin, Atp5c1, Itih2, Itih5*