Table S1 Major mediators of resistance to *T. gondii* as defined by genetic knockouts in the mouse.

Immune gene	Function	Knockout Phenotype
IL-12	Soluble cytokine comprised of heterodimer (p35, p40), secreted by dendritic cells, macrophages, and neutrophils, and drives production of IFN-γ.	Acute susceptibility and failure to control parasite replication due to reduced production of IFN-γ [1, 2].
IFN-γ	Soluble cytokine produced by NK and T cells, mediates activation of cells by induction of anti-microbial gene expression, major mechanism of resistance to intracellular bacterial and protozoan pathogens.	Acute susceptibility and failure to control parasite replication [3, 4].
TNF-α	Soluble cytokine secreted by leukocytes, stimulated by LPS and IFN-γ, mediates second signal for activation of macrophages,, promotes innate NK cell responses.	Required for control of chronic toxoplasmic encephalitis in normal [5-7] and SCID mice [5].
iNOS	Inducible nitric oxide synthase, upregulated in response to endotoxin and IFN-γ, produces diffusible nitric oxide, potent antimcrobial effector.	Acute resistance is normal but animals are susceptible to chronic toxoplasmic encephalitis [8].
IGTP (IrgM3) LRG-47 (IrgM1) IIGP (Irga6)	Interferon regulated GTPases, family of GTPases strongly induced by IFN-γ and involved in pathogen resistance.	Acute susceptibility is associated with reduced anti-microbial activity [9, 10].
STAT1	Signal transducers and activator of transcription 1, phosphorylated by JAK kinases downstream of IFN-γ receptors, dimerizes, translocates to nucleus and activates gene transcription.	Acute susceptibility is associated with reduced anti-microbial activity [11 11].
STAT4	Transcription factor, phosphorylated by JAK kinases downstream of IL-12 receptors, dimerizes, translocates to nucleus and activates	Acute susceptibility is associated with a failure to produce IFN-γ [12].

	gene transcription.	
SOCS3	Suppressor of cytokine signaling 3, downregulates JAK-STAT signaling.	Acute susceptibility and failure to control parasite replication are reversed by blocking IL-6 or providing IL-12 [13].
RelB	Subunit of nuclear factor kappa-B (NFkB), downstream of MyD88, drives expression of many cytokines.	Failure to produce IFN-γ leads to susceptibility to acute infection [14].
MyD88	Common adapter for TLRs and IL-1R, signals in response to pathogen associated molecular patterns, and inflammation driven by the IL-1 family.	Required for acute resistance to *T. gondii* through production of IL-12 and also has a role in T cells [15 16].
UNC93B1	Resident ER protein, associated with regulation of TLR signaling.	Required for control of acute infection associated with a cell autonomous role in killing and the production of IL-12 [17, 18].
GBP ^{chr3}	A cluster encoding five separate guanylate binding proteins of the p65 family located on chromosome 3 in the mouse. GBP1, 2,3,5, and 7, along with a pseudogene of GBP2 are contained within this locus that was disrupted using flanking LoxP sites	Increased susceptibility to challenge with type II ME49 strain. Decreased ability to control intracellular replication in IFN-γ activated macrophages [19].

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Table S2 Host pathways altered by *T. gondii* infection

Target	Findings
Apoptosis	Infection of human foreskin fibroblasts (HFF) with type I RH strain parasites blocks multiple pathways of activating apoptosis [20]. Infection of human HL-60 or U937 cells with the type II strain NTE blocks apoptosis induced by actinomycin D, TNF-α, and cyclohexamide [21]. Infection of NIH 3T3 cells with type I RH strain parasites blocks caspase activation and inhibits apoptosis [22].
Cell cycle	Infection of HFF cells with the type I RH strain parasites stimulates G1/S transition followed by G2/M arrest, associated with sustained ERK activation[23]. Infection of human trophoblast (BeWo) and normal human dermal fibroblasts (NHDF) with the type I RH strain parasites results in G2 arrest via cyclin B1 down regulation [24].
DC maturation and trafficking	Type II PRU strain parasites preferentially infect immature murine bone-marrow derived DCs and blocks maturation induced by TLR ligands or CD40L [25]. Infection of human monocyte-derived or murine bone marrow-derived DCs with type I RH strain parasites enhances motility and barrier migration *in vitro*, and *in vivo* dissemination in the mouse with DCs pulsed with the type II strain parasite PTG [26]. DC are activated and expand in response to type II strains but this is reduced in Type I strains [27].
Host gene transcription	Infection a clone of the type II strain ME49 induces transcription of many genes in HFF cells, including immune response pathways, glycolysis, and lipid metabolism [28]; similar responses were seen in HFF cells infected with the type I RH strain [29]. Infection with type I RH strain induces Hif1a in HFF cells and this response is important for parasite growth under hypoxic conditions [30]. Induction of host EGR2 transcriptional response is due to rhoptry discharge following infection of HFF cells by the type I RH strain [31]. Differential expression of host cell transcriptional responses during infection of HFF cells by type II and III strain parasites drives development of immune responses including STATs and IL-12 [32].
P38, JNK, ERK1/2	Infection of human THP-1 monocyte cell line with type I strain RH induces phosphorylation of ERK1/2, P38, and JNKs [33]. Transient activation of MAPK pathways in murine bone marrow derived macrophages cells infected with the type I RH strain is followed by suppression of LPS triggered responses [34]. Soluble tachyzoite antigen from type I RH strain activates MAPK through TRAF6 that are required for IL-12 production [35].
NFkB	Proinflammatory cytokines triggered by LPS are blocked by inhibition of nuclear translocation of NFκB in response to infection with type I RH strain [36]. The ability of LPS to induce NFκB activation is blocked by infection of bone marrow derived murine macrophages infected with type I RH strain [37].
IL-12	IL-12 production is strongly induced by type II, but not type I or III strains in murine bone marrow derived and peritoneal macrophages [38]. Infection of bone marrow derived murine macrophages with type II strain ME49 induces higher levels of IL-12 than infection with type I RH strain [39].
IFN-γ	Induction of gene expression by treatment of HFF cells with IFN-γ is blocked by infection with each of three strain types (I,II, III) [40]. Induction of MHC I and MHC II by treatment of murine bone marrow derived macrophages cells with IFN-γ is blocked by infection with type II NTE strain [41]. Infection of murine bone marrow derived macrophages or RAW264 macrophages with the type II NTE strain down regulated induction of

	inducible nitric oxide by treatment with IFN-γ [42]. Infection of RAW264 macrophages with type I RH and type II ME49 strain parasites inhibited upregulation of MHC II by IFN-γ, but only type I RH strain parasites were able to block induction of nitric oxide production [43]
STAT1	Infection of bone marrow derived macrophages with type II NTE strain blocked IFN-γ induced transcriptional changes by altering chromatin and disrupting STAT1 binding to nuclear promoters [44].
SOCS-1	Induction of SOCS-1 expression contributes to blocking of IFN-γ signaling through STAT1 in murine BMM and RAW264 macrophages infected with type I BK strain parasites [45]. SOCS1 expression in RAW264 macrophages cells is upregulated during infection with type I strain but not type II ME49 strain parasites; this pathway independent of TLR signaling but is regulated by EGR2 and p38 Map kinase [43].
SOCS-3	Infection with type I and II strains induces SOCS3 that limits IL-6 signaling and protects from immune pathology [13].
TNF-α	Infection with type I RH strain suppresses TNF-α mediated transcription in murine BMM and this occurs through chromatin modification [46].
STAT3	Infection with live type I RH strain, but not treatment with lysates, induces STAT3 activation in murine bone marrow derived macrophages and suppresses IL-12 and TNF-α [47].

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