Disease-resistant genes: New approaches towards the control of parasitic diseases

Populations infected with various parasites have been estimated as 270 million for malaria, 200 million for schistosomiasis, 90 million for filariasis, 18 million for Chagas diseases and 12 million for leishmaniasis[1]. Drug research is a top priority in many countries though drug use has many disadvantages. The various drugs and their toxic effects toward host system make drug use a threat to humans. Drug researchers are aware of the side effects and increasing drug resistance of the pathogens.

Recent studies have resulted in remarkable findings in identifying several disease-resistant loci in mice. These are identified as *Lsh*, *Ify* and *Bcg*, denoting resistance to *Salmonella typhimurium*, *Leishmania donovani*, *Mycobacterium bovis*[2–5]. These genes are located on the chromosome 1. Later studies have identified and selected several such genes in mouse[6–10] for a variety of pathogenic infections (Table 1). How these genes confer resistance towards pathogenic infections is not known. Cloning of these genes and their expression in other mammalian systems will give an understanding of how to combat parasitic diseases. Even though the hypothesis of one-gene : one-disease for hereditary diseases cannot be applicable in this context, one can think of polygenic localization of such disease-resistant factors. Recent progress in the isolation and characterization of candidate genes and new microsatellite-based markers for family linkage studies of the whole genome is at its frontiers. However, genome scanning approaches to gene mapping for infectious diseases are in preliminary stages in the case of parasitic diseases. This approach will be a fair play to overcome parasitic diseases and to tackle problems of drug use and its associated hazards.

Table 1. Various genes/loci identified in mammals have impact on pathogenesis resistance or susceptibility

Gene/locus	Chromosome	Function encoded	Disease/pathogen
MHC class II	17	Membrane glycoprotein presents antigen to $CD4^+$ T cells	Malaria Leprosy
MHC class I	17	Membrane glycoprotein antigen to $CD8^+$ T cell	*T. gondii*
MHC class I-b	17	Non classical MHC antigen presentation to $CD8^+$ T cell	Listeria
TAP	17	Peptide transporters located in ER	Intracellular infections
LMP	17	Proteasomes: degradation of protein, antigen representation	Intracellular infections
Bcg/Ity/Lsh	1	Enhancement of APC function	*Mycobacteria, Leishmania Salmonella*
Vβ5	6	Response to superantigen	*T. gondii*
Vβ6	6	Response to viral superantigen	Polyoma virus
Vβ8	6	Response to superantigen	Staphylococcus, *T. gondii*
VI(γ)δ subset	13	Response to Mycobacterial super-antigen	*Mycobacteria, Leishmania*
TNF-α	17	Glycoprotein	*T. gondii*, Malaria
IL-4	11	Prototypic Th2 cytokine	*Leishmania*, Leprosy
INF-γ	10	Th1 cytokine	*Leishmania, Mycobacteria*
Cryp	8	Cell defense	*T. gondii, Salmonella*
NOS2	11	No synthase; control pathogen multiplication	*Mycobacteria, Salmonella Leishmania*
Mx 1	16	75 kDa Mx 1 protein	Influenza
Anth 2	2	Control pathogenesis	*Bacillus anthracis*
Bcga	12	Anergy to DTH	*Mycobacterium bovis*
HC	2	Pulmonary clearance of bacteria	*Staphylococcus aureus*
Lsr I	2	Bacterial multiplication	*Listeria monocytogenes*
Rict (Era 1, Api 1, Flu 1)	5	Control pathogenesis	*Rickettsia tsutsugamushi*
Ld	17	Brain parasite burden	*T. gondii*
Sc 11	8	Resolution of cutaneous lesions	*Leishmania tropica major*
Sc 12	4	Resolution of cutaneous lesions	*Leishmania maxicana maxicana*
Cmv 1	6	Virus replication in spleen	Cytomegaloma virus
Fv 1	4	Splenomegaly	Friend virus
Fv 2	9	Splenomegaly	Friend virus
Hv 2	7	Infection of macrophages and neurons	Mouse hepatitis virus 4
Rmc 1	1	Infectively retardation	Mink cell focus forming virus
Rmc f	5	Infectively retardation	Mink cell focus forming I
Rmp 2	2	Survival	Mouse pox
Tmevd 1	6	CNS demyelination	Theiler's encephelomyelitis virus
Tmevd 2	3	CNS demyelination	Encephelomyelitis
Rmv 1, 2	1	Viremia	Malaney virus I

Mouse genes and their location on chromosomes have been described, however, human homologous genes have also been identified and many more will be identified within coming decades.
CNS, central nervous system; ER, endoplasmic reticulum; T, *Toxoplasma*.

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