Heat Shock Protein in Host Parasite Interaction in Murine Malaria Infection

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Exposure of cells to a variety of stressful conditions such as elevated temperature, chemical intoxication, or infection leads to the transcription of a set of genes and subsequently, to the synthesis of a family of polypeptides called heat shock proteins (HSPs). Using HSPs, some bacteria can survive even in hot water of over 100℃ in the bottom of the sea.

For intracellular parasites, HSPs may be essential for the adaptation of those organisms to the strict environment of host cells, and for transformation of organisms to infectious form. On the other hand, HSPs synthesized by host cells as they respond to stress during certain infections may actually play a role in host defense. Thus, HSPs expressed by either host or parasite may have the potential to modulate the host-parasite interaction.

Obligate intracellular protozoa such as *Toxoplasma gondii*, *Leishmania major* or *Trypanosoma cruzi* possess different escape mechanisms each other. For example, *Toxoplasma* escapes from host macrophages by preventing fusion of phagosome with lysosome and proliferate within the phagosome. *Leishmania* escapes by changing phenotype from promastigote to agastigote. Then, they evade from the attack of lysosomal enzymes. *Trypanosoma* escapes into cytoplasm before the fusion of phagosome and lysosome. We already reported that HSP65 in host macrophages is expressed by $\gamma\delta$ T cells in infection with *Toxoplasma gondii*, NKT cells in that with *Leishmania major* or NK cells in that with *Trypanosoma cruzi*. This HSP plays crucial roles in resistance against each infection.

For malaria infection, mice prepared different effecter mechanisms in HSP expression and protection from other obligate intracellular protozoa mentioned above, although HSP65 had also an essential role in protective immunity even in this parasite. That is, against this infection, primitive cells like NK, NKT or $\gamma\delta$ T cells did not contribute to the expression of HSP65 as well as to the protective immunity but both $CD4^+$ and $CD8^+$ T cells were required for either function.

We are also investigating the role of HSP of protozoan themselves in their virulence or their escape mechanisms. Different patterns of HSP90 expression were observed between high virulent L strain and low virulent NL strains of *Plasmodium yoelii*. A high virulent L strain strongly expressed HSP90 compared with low virulent NL strain. Thus, some HSP may play some important roles in their escape mechanisms, in other wards, in their virulence.

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