Co-infection between tuberculosis and malaria: a consideration on interaction of molecules and pathogenesis

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Human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) and malaria are counted as worst diseases for the following: (i) together cause 4 million deaths every year; and (ii) pregnant women are at high risk of developing anaemia and infection of placenta. Children born to co-infected mother are in low birth weight. AIDS may increase the risk of severe malaria and antimalarial drugs are less effective. Virus that cause AIDS replicate more readily. A common infection in a patient with AIDS is tuberculosis.

Malaria and tuberculosis are endemic in many regions of the world, and co-infection with the two pathogens is common. The interaction between both infections within a co-infection episode is an interesting topic in infectious medicine. The public health importance of TB/malaria is highlighted in this paper. Page et al. said that tuberculosis-induced potentiation of type 1 immune responses is associated with protection against lethal murine malaria. The protective process is believed to relate to gamma interferon induction. This induction of cellular immune responses is related to ATP-binding protein (ATPBP) of Plasmodium species. Zheng et al. found that heat shock protein 70 (HSP70) from Mycobacterium tuberculosis was associated with the induction of a strong humoral and cellular response directed against Plasmodium falciparum.

During the co-infection, the protective effect between each other was noted and has been studied for a few years. However, a study on the proteins’ expression in an episode of co-infection is warranted. To study the interaction between both infections, the new development in bioinformatics can be applied. Here, the author used a new gene ontology technology to predict the molecular function of HSP70 and ATPBP in an episode of co-infection.

The database PubMed was used for data mining of the amino acid sequence for HSP70 and ATPBP. Prediction of molecular function and biological process of HSP70 and ATPBP was performed using a novel gene ontology prediction tool, GoFigure. GoFigure is a computational algorithm tool which is recently developed in gene ontology. The tool accepts an input DNA or protein sequence, and uses BLAST to identify homologous sequences in GO annotated databases. The approach is to use a BLAST search to identify homologues in public databases that have been annotated with gene ontology terms. These include SwissProt, Flybase (Drosophila), the Saccharomyces Genome Database (SGD), Mouse Genome Informatics (MGI) and Wormbase (Nematode). The contents of the results will show results for molecular function as well as biological process of the studied protein. The prediction of molecular function was presented and compared.

Sequence of LIPF in different Mycobacterium species from searching of the database, sequence of HSP70
and ATPBP can be derived and used for further study. Using GoFigure server, the molecular functions in HSP70 and ATPBP were predicted and are presented in Figs. 1 and 2, respectively.

New developments have forced a reevaluation of our understanding on tropical infections. Both malaria and tuberculosis are important tropical infectious diseases. The co-occurrence between these two diseases can be expected. A large proportion of people with latent tuberculosis live in malaria-endemic areas, so co-infection with these two organisms is likely to be common. Aberration in pathogenesis of infection in an episode of malaria and tuberculosis co-occurrence is interesting and becomes a new focus in tropical medicine. The aberration in immunological process is believed to be important part in the pathogenesis of co-infection.

In the present study two key documented molecules corresponding to the pathogenesis of malaria-tuberculosis co-infection were studied. The gene ontology technique that was used is a new concept and used in some recent molecular biological studies.

Of interest, HSP70 and ATPBP share a common molecular function as ATP binding resulting from purine nucleotide binding. Therefore, a competitive antagonist effect between both molecules can be expected. Indeed, in an animal model, co-infected mice were less able to contain growth of \textit{M. tuberculosis} in lung, spleen and liver. This finding can be a good explanation for the protective effect between each other in malaria-tuberculosis co-infection. Indeed, the structural homology between both studied molecules was reported in a recent study by Garsia \textit{et al}. However, further experimental studies are needed before making a conclusion on this topic. The finding in this study not only supports the previous knowledge on malaria and tuberculosis but also gives
the new view on the pathogenesis of co-infection.

References


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