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Host-like molecules in human malarial parasites

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The human malaria parasite survives, lives and multiplies in an immunocompetent host. The parasite deploys various strategies for this purpose, i.e. fluidity in the genome, antigenic variation, molecular mimicry, acquisition of host molecules. During its asexual development in humans, the parasite exchanges a large number of molecules with the host. Deitsch et al. [1] have reported that the parasite also has the ability to import host DNA into its nucleus from the infected host cell and can express it into a protein product. In nature, the parasite has an opportunity of such host DNA import into its nucleus during liver stages as well as blood stages in case of *Plasmodium vivax*, which prefers to infect human reticulocytes rather than mature anucleated erythrocytes. This corroborates our earlier findings where we reported the presence of Alu elements in a *P. vivax* antigen [2].

The current methods of parasite purification and subsequent DNA extraction can not remove host DNA if it has either transiently been transferred to the parasite or has become part of the parasite genome. Therefore, in both cases these sequences will be detected as part of the parasite DNA. This would have resulted in the reported host sequences (Alu and LINE), deposited by several labs in the databases of the malarial genome projects. However, Deitsch et al. [3] suggest that this could be a contaminating artifact due to erroneous DNA extraction methods. We partly agree with them because sometimes the host nucleated cells are not completely removed during purification of infected erythrocytes from patient's blood. This might lead to host DNA contamination in parasite DNA preparation. But how one would get rid of the host DNA if it is present intrinsically in parasite's nucleus, either free or in integrated form, after it was horizontally transferred in nature. This possibility exists more in the field isolates for *P. vivax*.

In their experiments Deitsch et al. were unable to detect the Alu/LINE host sequences in the *P. vivax* by polymerase chain reaction (PCR) but obtained a positive signal on pulse field gel electrophoresis (PFGE) [3]. These results are contradictory to each other because one would presume that the parasites were purified from the rest of the host nucleated cells. Then why would the same parasite preparation produce negative results in PCR and positive in PFGE? In all probabilities one would expect the opposite because PCR can detect a lower level of DNA contamination than PFGE. However, caution should be taken while addressing the issue of host DNA contamination based on PCR results. This is because PCR could be inaccurate as any change (mutation) introduced in synthetic (primer) or template (host or parasite) DNA might give rise to erroneous results. Deitsch et al. [3] have used different primer sequences and DNA templates than in reference [2]. In addition, they have used blood from monkey infected with *P. vivax* rather than human patients' blood from endemic areas, a different source of control human DNA, and most importantly different primer sequences. They have used four different primers (F10+B7 and F6+B3) based on *Plasmodium falciparum* data of Cheng et al. [4] as compared to three primers used in *P. vivax* data [2] where reverse primer 12R was common (12F+12R and AF+12R).

Deitsch et al. [3] have used PFGE data to support their PCR results. The supportive data from PFGE are, however, not very convincing. Firstly, there is hybridization signal in high mol wt DNA that should have been enough to give a positive signal on PCR. Secondly, the lower mol wt DNA is run out. Therefore, these PFGE data may not rule out the transient horizontal transfer of host DNA from reticulocytes/hepatocytes to the parasite.

Deitsch et al. [3] have also pointed out the presence of these host sequences in the cultivable human malaria parasite *P. falciparum*, deposited in genome project databases and in a report [4]. While the chances of host DNA contamination are high in case of *P. vivax*, where the starting material is patient or monkey infected blood, this should be minimum or absent in case of *P. falciparum*, which is cultured in vitro using human erythrocytes free from the host nucleated cells. Then the question arises, of where do these host DNA sequences originate from, in case of *P. falciparum*, if they are not present in the parasite? It seems most likely that these host sequences are in the parasite, either in the transient state or in the integrated form.

The malaria parasite has excellent survival skills [5,6]. It can survive various drug treatments as well as the host's defense system [7]. The parasite uses host machinery to its optimum level. It imports a large number of molecules from the host either for its metabolic system or to evade the host immune system [8]. In the latter case, the parasite uses several mechanisms including molecular mimicry, i.e. presence of host sequences in parasite antigens, acquisition of antibody (IgG and IgM) molecules on the surface of knobs of the *P. falciparum* infected erythrocytes [9,10]. The presence of auto-antibodies in the malarial patients' sera also support this view [11]. However, it is possible that not all of the host molecules are imported but some are synthesized by the parasite. This seems to be possible in the light of experiments showing that the malarial parasite can import and express the host DNA [1]. Therefore, the possibility of the presence of host DNA in the parasite exists whether it is transiently acquired through horizontal transfer or is integrated in its genome. However, the clear picture of host DNA in the parasite will emerge after the completion of the parasite genome projects.

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