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Letter

Plasmodium: Yet More Don'ts

Miles B. Markus[1,2,*]

I agree with Geoffrey McFadden that terminological communication in regard to *Plasmodium* and malaria needs to be more accurate [1]. His advice is especially pertinent given that despite his 'lecture' [2] on why there is no such noun as '*Plasmodia*' (except in particular biological circumstances related to the nonitalicized word 'plasmodia' [2]), this linguistic delusion still crops up in publications. By contrast, it should be noted that use of the adjective 'plasmodial' is entirely in order, and even desirable. The malariological acceptability or otherwise of the two words should not be confused – as has happened unfortunately, albeit rarely. McFadden advises us to 'eschew lazy language' [1]. Accordingly, I draw attention here to some additional traps for the unwary.

Mosquitoes

'Anopheline' is both an adjective ('anopheline mosquito') and a noun. Don't use an upper case 'A', except at the beginning of a sentence; and do not italicize the word as if it is a Latinized genus name.

We Don't 'Treat' Hypnozoites

It is not unusual to come across 'treat' or variations thereof in reference to hypnozoites, as in this hypothetical sentence: 'Primaquine was administered to treat hypnozoites in the liver'. The hypnozoites are not ill, however. There is nothing wrong with them, so they do not require treatment. They need to be 'eliminated', 'inactivated', or 'killed', not 'treated'.
For that matter, we do not 'treat *Plasmodium vivax*'. It is '*Plasmodium vivax* malaria' that is treated.

'Infection' Happens Once

I have occasionally seen 'infection' used to describe a malarial recrudescence or relapse [3]. This is incorrect. A person can become 'infected' only once. In the absence of superinfection or reinfection taking place, subsequent bouts of parasitemia or clinical attacks should not be called 'infections' because the patient is already infected. We can, though, speak of a 'recrudescing infection' or a 'recrudescent infection'. Likewise, 'relapsing infection' and 'relapsed infection' are correct, but 'relapse infection' is not. The difference is subtle.

Use Correct Parasite Stage Names

The terms 'bradyzoite' and 'tachyzoite' cannot be applied to *Plasmodium*, as has been done inadvertently. They refer exclusively to bradyzoic merozoites and tachyzoic merozoites of tissue cyst-forming coccidia such as *Toxoplasma* [4]. The correct plasmodial terms are 'bradysporozoite' and 'tachysporozoite' [5]. Bradysporozoites inoculated into a primate host by a mosquito are thought to become hypnozoites [6].

'Malaria' Is Not the Causative Organism

'Malarias' makes sense if it refers specifically to the infections caused by different parasite species, because 'malaria' is the name for a disease, as McFadden emphasizes [1]. This plural usage is uncommon, though, and is perhaps not to be recommended. However, when 'malarias' is used as shorthand for parasites *per se* (instead of for the disease), we have a semantic problem. Here is a quotation from the preface to a well-known book [7]: 'the fact that lower primates . . . harbor malarias infective to man, and which produce disease in him, is a relatively new concept'. The disease name 'malaria' has often been stretched like this to cover the causative organism(s) as well, and certainly subsequent to the publication of the cited book [7]. But it is not correct, and frequent repetition in the literature does not make it correct. In the example provided above, 'harbor malarias infective to man' should have read, for instance: 'harbor plasmodial parasites infective to man'. Alternative phrasing that would also have been suitable (and perhaps this is what the authors actually meant) is: 'harbor malaria parasite species that can infect man'.

As an aside, whereas we can get away with 'malaria parasite' as an abbreviation for 'malaria-causing parasite' (the previous sentence and the titles of two books serve as examples [8,9]), that is about as far as we can go without becoming unscientifically imprecise. See McFadden's explanation as to why various other non-disease-associated words should not be used in conjunction with 'malaria' [1].

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Concluding Remarks

McFadden says that 'good science needs accurate communication' [1]. The merits of this statement can hardly be contested.

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Forum

Revisiting Trypanosome Mitochondrial Genome Mysteries: Broader and Deeper

Sara L. Zimmer [1,*]

What do the products of a genome do, and when and why are they needed? For the protein products of the trypanosomatid parasites' mitochondrial genomes, the total expressed protein repertoire and the identities of the more difficult-to-characterize products have been challenging to acquire. Comparative genomics and new technologies may resolve that.

The Trypanosomatid Mitochondrial Genome

Trypanosomatids are protists that often parasitize the digestive tracts of insects. Studies exploring their basic biology have been richly rewarded. With their vast evolutionary distance from that of 'model' eukaryote species, unique means to execute proper gene expression and basic cellular functions have been discovered in trypanosomatids. For instance, the trypanosomatid single mitochondrion harbors a unique mitochondrial DNA structure with equally one-of-a-kind processes to facilitate maturation of its RNAs [1]. Typically its genome harbors two rRNA and 18 mRNA loci, but no tRNAs [2]. Protein products of mitochondrial genomes most often have roles within the organelle, most being subunits of the electron transport chain (ETC). Genomes may also contain proteins necessary for the generation or assembly of their encoded products. Most of the trypanosomatids' mitochondrion-encoded protein products have clear homologues in the mammalian system: at least eight NADH dehydrogenase (complex I) subunits (three actually encoded in the mammalian nucleus), a cytochrome bc_1 subunit, the three core cytochrome oxidase subunits, and one ATP synthase subunit. One product is a small subunit ribosomal protein [2].

Additional putative products of mitochondrial loci are called Maxicircle Unidentified Reading Frame 2 and 5 (MURF2, 5), and C (or G)-Rich 3 and 4 (CR3, 4); these very names reveal the difficulty in assigning a functional identity to these putative proteins [2]. CR3 and CR4 may be functional homologues of specific mammalian complex I subunits but do not share sequence similarity with the mammalian homologues [3,4]. ETC complexes exhibit subunit compositions that differ from the canonical eukaryotic systems [5], complex I in particular [3]. Nuclear- and mitochondrion-encoded ETC subunits must coordinate for functionality. Therefore, the sequences and expression of the subunits of mitochondrial origin cannot be ignored if we are to understand each ETC complex's biological roles and control. Investigation of the products of this mitochondrial genome has, however, proven challenging.

Current Challenges

For four reasons, the abundances, and sometimes the identities, of trypanosomatid mitochondrial genome products are uncharacterized [6]. The first is the aforementioned divergence of trypanosomatids from model eukaryotes that can make identification of homologues to some known proteins difficult, particularly those that are not core components of the ETC. Secondly, thus far the trypanosomatid mitochondrial genome has proven nonmanipulatable, so reverse genetics approaches are unavailable. Thirdly, the protein products of this genome have been notoriously difficult to detect by antibody detection or proteomics methods, although intact complexes containing these subunits can be observed. Finally, many mitochondrial mRNA loci encode cryptogenes. After these loci are transcribed, set numbers of uridylates (Us) are inserted and/or deleted in some or many positions within the mRNA. Once completed, this process of U-indel editing yields the translatable consensus mRNA [6]. Therefore, the number of functional mRNA loci in each species, or even the likely mature, translatable sequence of each cryptogene locus, cannot be elucidated from DNA alone (Figure 1).

U-indel editing begins at the most 3′ site requiring editing, and uses information