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Short communication

Relationships between the major kinetoplastid paraflagellar rod proteins: a consolidating nomenclature $\stackrel{\diamond}{\sim}$

Catarina Gadelha^{a,b}, Jonathan H. LeBowitz^c, Jerry Manning^d, Thomas Seebeck^e, Keith Gull^{a,*}

^a Sir Willian Dunn School of Pathology, University of Oxford, South Parks Road, Oxford OX1 3RE, UK ^b Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil

^c Purdue University, West Lafayette, IN, USA

^d University of California, Irvine, CA, USA

^e University of Bern, Bern, Switzerland

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The Kinetoplastida comprise a family of flagellated microbes that are defined by the presence of a network of concatenated mitochondrial DNA called the kinetoplast and a range of other unique features. One such is the paraflagellar rod (PFR), which has an essential role in cell motility [1–3], an intricate sub-structural arrangement [4,5] and an interesting phylogenetic distribution [6,7].

Although the complete composition of the PFR is still unknown, the major structural components have been described in several species of Kinetoplastida. The first biochemical description in kinetoplastids identified the two major PFR proteins, PFR1 and PFR2, in Crithidia fasciculata [8]. In that paper, PFR1 was defined as the protein with the slower migration in SDS-PAGE gels while the faster migrating band was called PFR2. Since then, other descriptions of major PFR proteins in trypanosomatids have been made, including those of Herpetomonas megaseliae [9], Trypanosoma species [10,11] and Leishmania species [12,13]. At the time of many of these publications the correlation between major PFR proteins of different species was unclear and nomenclatures developed that were peculiar to each species and did not reflect the homologies amongst the proteins (see Table 1). However, with the increasing availability of DNA and protein sequences, we have now been able to define the levels of homology between PFR proteins (Fig. 1) and this reveals that the disconnected nomenclature

for the different species that has persisted is inaccurate and misleading.

As the genome projects of some of the cited species (namely, *Trypanosoma brucei*, *Trypanosoma cruzi* and *Leishmania major*) are nearing completion, we wish to introduce a consistent nomenclature for the major PFR proteins and genes in order to avoid confusing or misleading annotation. We advocate a standard nomenclature for the major PFR components, based on points listed below:

- 1. Major components of the PFR should be assigned the three-letter code 'PFR'. This is in keeping with the names used for the majority of PFR sequences available in public databases such as GenBank and EMBL. It is also useful to distinguish this structure from the paraxial rod (PAR) structure found in dinoflagellates [14], which is phylogenetically and morphologically distinct to the paracrystalline structure of the PFR in kinetoplastids and euglenoids.
- 2. The two most abundant proteins of the PFR should be named PFR1 and PFR2.
- 3. The major PFR proteins already described in *T. brucei*, *T. cruzi*, *Leishmania mexicana* and *L. major* should be numbered on the basis of molecular mass, with the protein of higher molecular mass being numbered PFR1. This is in agreement with the original description of the major PFR components in Kinetoplastida [8] and is in keeping with systems of nomenclature commonly used elsewhere in biochemistry. It also groups the proteins according to their inferred phylogeny (see Fig. 1).
- 4. New descriptions of PFR1 and PFR2 proteins in other species should be numbered in accordance with

 $^{^{\}diamond}$ *Note: Crithidia fasciculata* sequence data reported in this paper are available in the GenBank under the accession numbers AY568293 (*PFR2*) and AY568294 (*PFR1*).

^{*} Corresponding author. Tel.: +44-1865-285455;

fax: +44-1865-285691.

E-mail address: keith.gull@path.ox.ac.uk (K. Gull).

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Table 1 Major proteins of the PFR of Kinetoplastida

Species	PFR1 orthologues	PFR2 orthologues	References
Crithidia fasciculata Trypanosoma brucei Trypanosoma cruzi Leishmania mexicana Leishmania major	PFR1 PFRC PAR3 PFR1 PFR1	PFR2 PFRA PAR2 PFR2 PFR2 PFR2	[17] [10,18] [11,19] [12,20] [21]

homology regardless of their migration in SDS-PAGE or their predicted molecular mass.

- 5. PFR1 and PFR2 genes should be designated as *PFR1* and *PFR2*, respectively, as directed by the genetic nomenclature for *Trypanosoma* and *Leishmania* [15].
- 6. Multiple copies of genes should be distinguished by hyphenated numbers (again as in [15]), for example *PFR1-1*, *PFR1-2*, etc. If tandemly repeated, the genes should be numbered sequentially in the direction of transcription.

We believe that this nomenclature, consolidated across all species in the Kinetoplastida, provides a clear, coherent nomenclature for the major PFR components and the authors have updated their entries on public databases accordingly. Of course, alongside these major structural com-



Fig. 1. Phylogenetic analysis of PFR sequences of Kinetoplastida. The neighbour-joining unrooted phylogram shown was inferred from protein alignments. Topology support from 1000 bootstrap replicates using either neighbour-joining or maximum parsimony methods is shown as percentage next to nodes (NJ/MP). Brackets show new suggested names for the respective proteins.

ponents, there are many other proteins that are associated with the PFR (see [16]), most of which have yet to be characterised. We are not extending the nomenclature proposed here to any 'minor' components of the PFR already described, since their nomenclatures are largely established, unambiguous and consistent between species. This in no way prevents researchers assigning other components of this structure with the prefix 'PFR'. However, we believe that in future this prefix should be reserved for proteins whose localisation has been rigorously demonstrated to be in the paraflagellar rod.

References

- Hunger-Glaser I, Seebeck T. Deletion of the genes for the paraflagellar rod protein PFR-A in *Trypanosoma brucei* is probably lethal. Mol Biochem Parasitol 1997;90:347–51.
- [2] Santrich C, Moore L, Sherwin T, et al. A motility function for the paraflagellar rod of *Leishmania* parasites revealed by PFR-2 gene knockouts. Mol Biochem Parasitol 1997;90:95–109.
- [3] Bastin P, Sherwin T, Gull K. Paraflagellar rod is vital for trypanosome motility. Nature 1998;391:548.
- [4] Fuge H. Electron microscopic studies of the intraflagellar structures of trypanosomes. J Protozool 1969;16:160–6.
- [5] Farina M, Attias M, Souto-Padron T, de Souza W. Further studies on the organization of the paraxial rod of trypanosomatids. J Protozool 1986;33:552–7.
- [6] Cachon J, Cachon M, Cosson MP, Cosson J. The paraflagellar rod: a structure in search of a function. Biol Cell 1988;63:169–81.
- [7] Bastin P, Matthews KR, Gull K. The paraflagellar rod of Kinetoplastida: solved and unsolved questions. Parasitol Today 1996;12: 302–7.
- [8] Russell DG, Newsam RJ, Palmer GCN, Gull K. Structural and biochemical characterization of the paraflagellar rod of *Crithidia fasciculata*. Eur J Cell Biol 1983;30:137–43.
- [9] Cunha NL, De Souza W, Hasson-Voloch A. Isolation of the flagellum and characterization of the paraxial structure of *Herpetomonas megaseliae*. J Submicrosc Cytol October 1984;16:705–13.
- [10] Schlaeppi K, Deflorin J, Seebeck T. The major component of the paraflagellar rod of *Trypanosoma brucei* is a helical protein that is encoded by two identical, tandemly linked genes. J Cell Biol 1989;109:1695–709.
- [11] Fouts DL, Stryker GA, Gorski KS, et al. Evidence for four distinct major protein components in the paraflagellar rod of *Trypanosoma cruzi*. J Biol Chem 1998;273:21846–55.
- [12] Moore LL, Santrich C, LeBowitz JH. Stage-specific expression of the *Leishmania mexicana* paraflagellar rod protein PFR-2. Mol Biochem Parasitol 1996;80:125–35.
- [13] Ismach R, Cianci CM, Caulfield JP, Langer PJ, Hein A, McMahon-Pratt D. Flagellar membrane and paraxial rod proteins of *Leishmania*: characterization employing monoclonal antibodies. J Protozool 1989;36:617–24.
- [14] Maruyama T. Fine structure of the longitudinal flagellum in *Ceratium tripos*, a marine dinoflagellate. J Cell Sci 1982;58:109–23.
- [15] Clayton C, Adams M, Almeida R, et al. Genetic nomenclature for *Trypanosoma* and *Leishmania*. Mol Biochem Parasitol 1998;97: 221–4.
- [16] Moreira-Leite FF, de Souza W, da Cunha-e-Silva NL. Purification of the paraflagellar rod of the trypanosomatid *Herpetomonas megaseliae* and identification of some of its minor components. Mol Biochem Parasitol 1999;104:131–40.
- [17] Gadelha C, Wickstead B, Gull K. Direct submission. 2004 [AY568293 and AY568294].

- [18] Deflorin J, Rudolf M, Seebeck T. The major components of the paraflagellar rod of *Trypanosoma brucei* are two similar, but distinct proteins which are encoded by two different gene loci. J Biol Chem 1994;269:28745–51.
- [19] Beard CA, Saborio JL, Tewari D, Krieglstein KG, Henschen AH, Manning JE. Evidence for two distinct major protein components, PAR 1 and PAR 2, in the paraflagellar rod of *Trypanosoma*

cruzi—complete nucleotide sequence of PAR 2. J Biol Chem 1992;267:21656–62.

- [20] Maga JA, Sherwin T, Francis S, Gull K, LeBowitz JH. Genetic dissection of the *Leishmania* paraflagellar rod, a unique flagellar cytoskeleton structure. J Cell Sci 1999;112:2753– 63.
- [21] http://www.sanger.ac.uk/Projects/L_major.