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Guide to the Nomenclature of Kinetoplastid RNA Editing: A Proposal

Uridine insertion/deletion RNA editing in kinetoplastid mitochondria involves the participation of a number of ribonucleoprotein complexes which contain multiple proteins. There are currently multiple names to designate the major editing complex and the polypeptide components, which has led to confusion and lack of communication both within and outside this field. We urge that the field adapt a more unified nomenclature for the complexes and the component polypeptides and we present possible options.

Introduction

Uridine insertion/deletion RNA editing is a post-transcriptional RNA modification process that occurs in the mitochondria of kinetoplastid protists (Simpson et al. 2003, 2004; Stuart et al. 2005). It has been mainly studied in the trypanosomatids, *Trypanosoma brucei* and *Leishmania tarentolae*. Uridines are inserted and occasionally deleted at precise sites usually within coding regions to create open reading frames that encode translatable mitochondrial proteins. The enzymatic machinery involves a precise endonuclease cleavage mediated by a partially complementary guide RNA (gRNA), followed by the addition or deletion of U's from the 3′ end of the 5′ fragment and religation (Blum et al. 1990; Kable et al. 1996; Seiwert et al. 1996). In some cases, the edited mRNA sequence can then be used as the target of another specific gRNA which mediates editing of the second block (Maslov and Simpson 1992). This process can then proceed further 5′ by the use of additional gRNAs.

It has been shown that the process is mediated by a multiprotein complex which sediments at around 20-24S and migrates as a single band in a native gel (Hernandez et al. 2008; Osato et al. 2009; Peris et al. 1997; Rusche et al. 1997; Stuart et al. 2002). The complex is resistant to RNase digestion (Aphasizhev et al. 2003a). The precise stoichiometry of the approximately 18-20 polypeptide components remains to be fully characterized, but, outside REL1 (Aphasizhev et al. 2003a) and REN1 (Hernandez et al. 2008) (and perhaps REL2), most components are most likely present in a single copy. A compositional heterogeneity has, however, been reported in regard to the three RNase III endonucleases, REN1, REN2 and REN3. Three classes of the complex, which vary in relative abundance, differ by the specific editing endonuclease and a few associated proteins (Carnes et al. 2008; Panigrahi et al. 2006).

Several additional usually substoichiometric multi-protein complexes have been identified which are linked to the core complex by RNA (Aphasizhev et al. 2003a). These include the MRP1/2 complex (Aphasizhev et al. 2003b; Schumacher et al. 2006; Zíková et al. 2008), the GRBC complex (Weng et al. 2008) and the MRB1 complex (Acestor et al. 2009; Hashimi et al. 2008, 2009; Panigrahi et al. 2007, 2008). These complexes appear to contain overlapping proteins and the situation is not yet entirely clear. There are currently a plethora of names for both the various complexes and the associated proteins, which has led to confusion and a lack of communication both within and, more importantly, outside the editing field. The core complex has been variously termed the "20S complex" (Panigrahi et al. 2001), "∼20S editing complex" (The actual S value of the core complex is between 20-25S, thereby leading some authors to use the ∼20S designation.) (Cruz-Reyes 2007; Hernandez et al. 2008), "∼20S complex" (Cruz-Reyes et al. 1998),

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"editosome" (Worthey et al. 2003), "20S editosome" (Stuart et al. 2005), "~20S editosome" (Law et al. 2007; Tarun et al. 2008), and L-complex (contains the REL1 RNA ligase) (Peris et al. 1997). The term "editosome" in the *T. brucei* editing literature was probably initially intended to be analogous with the term, "spliceosome" in the RNA splicing literature. But in RNA splicing, the term "spliceosome" includes the entire high molecular weight complex containing up to 300 proteins and appearing as a particle the size of a ribosome (Lührmann and Stark 2009; Nilsen 2003), and is a name in flux as more components are discovered. We propose that "editosome" be likewise reserved for the entire yet to be defined editing holoenzyme consisting of the core complex and several yet not completely defined RNA-linked multiprotein complexes.

The polypeptide components of the *T. brucei* core complex were initially labeled MP, for Mitochondrial Protein, and were numbered by the approximate apparent molecular weights. Another relative size labeling system for seven of these polypeptides was Band I-VII (Huang et al. 2001). The components of the *L. tarentolae* complex were labeled LC-1, LC-2, etc., referring to the polypeptide bands in terms of their approximate decreasing size and to the fact that RNA ligase has been used as an enzymatic marker for this complex (Aphasizhev et al. 2003a). Another, more rational system for the *T. brucei* system was also devised (Stuart et al. 2005), in which proteins were labeled KRE (Kinetoplast RNA Editing) followed by P for protein of unknown function, L for ligase, T for TUTase, etc. In recent publications, this terminology has been compressed to a single letter (Ernst et al. 2009). Both of these systems have problems. The MP naming system uses apparent molecular weights for the *T. brucei* proteins but the homologous proteins in *Leishmania* mostly have different molecular weights, and the names have no relevance to the functions. The KREP system is a more rational attempt at nomenclature, but the names are difficult to remember and distinguish, even for workers in this field. We urge the adaption of a single species-independent and hopefully rational terminology for both the editing complexes and the associated proteins and we present some suggestions. We realize that this will necessarily be a compromise which may not be completely acceptable to everyone in the field, but our proposal may act as a starting point for further discussions of this important problem. Our suggested unified nomenclature is presented in Table 1. Following is a discussion with justifications for these names.

1. The 20S complex be named the RNA Editing Core Complex or RECC or REC-complex. A "K" prefix could also be added to indicate a kinetoplast origin. The three known core complexes differing by a few distinct endonuclease-associated components (Carnes et al. 2008; Ernst et al. 2009; Panigrahi et al. 2006) be called RECC1, RECC2, RECC3. Sequential numbers will be used for other classes if discovered. We realize that there is ongoing discussion as to the nature of this complex (i.e. static [Li et al. 2009] or dynamic [Golas et al. 2009]), but there is general agreement that there is a major editing complex containing 18-20 proteins sedimenting in a glycerol gradient around 20-24S and migrating as a single band in native gels. The use of the term, REC-complex, does not imply anything other than a handle for ease of discussion. The species indication could also be added as a prefix (e.g. LtREC-complex, TbREC-complex).
2. The proteins of established function have already been given the prefix, RE. (e.g. REL1, REL2, etc.) for RNA Editing A "K" prefix could be added to more uniquely designate the protein in the database, and the species indication could also be added (e.g. LtREL1, TbREL1).
3. The RNA-binding proteins and proteins of yet unknown function be operationally designated by the original *T. brucei* MP numbers (Worthey et al. 2003), with the realization that these apparent molecular weights may not be accurate and may vary between species. These designations are already widely used in this field. The species indication be added if necessary. This is a temporary operational naming system that will be replaced by functional names as the data is obtained.

We propose not to address the terminology of the various RNA-linked complexes at this time since the situation is yet unclear. But it is important to rename these proteins and complexes as soon as there is some resolution. A few proteins already have generally accepted names: MRP1/MRP2 (Mitochondrial RNA-Binding Protein) (Aphasizhev et al. 2003b), RET1 (RNA Editing TUTase 1) (Aphasizhev et al. 2002), REH1 (RNA Editing Helicase 1) (Missel et al. 1997), KPAP (Kinetoplast PolyA Polymerase) (Etheridge et al. 2008) (see Table 1).

Table 1. Proposed and accepted names.

Proposed name	Function (demonstrated or perceived at this time)	LC number (*L. tarentolae*, *L. major*)	MP number (*T. brucei*) (Proposed)	KREP (*T. brucei*)	
REX1	3′-5′ U-specific exonuclease	LC-2	MP100	KREPC1	RECC proteins with established functions
REX2	3′-5′ U-specific exonuclease	LC-3	MP99	KREPC2	RNA Editing…
REL1	RNA ligase (U-deletion?)	LC-7A	MP52	KREL1	
REL2	RNA ligase (U-insertion?)	LC-9	MP48	KREL2	
RET2	3′ TUTase	LC-6B	MP57	KRET2	
REN1	U-deletion endonuclease	MP90	MP90	KREPB1	
REN2	U-insertion endonuclease	LC-6A	MP61	KREPB3	
REN3	COII U-insertion endonuclease	MP67	MP67	KREPB2	
MP81		LC-1	MP81	KREPA1	RECC RNA-binding proteins and those of unknown function
MP63		LC-4	MP63	KREPA2	
MP49	RNA binding	LC-7C	MP49	KREPB6	
MP47		MP47	MP47	KREPB7	
MP46	RNA binding	LC-5	MP46	KREPB4	
MP44		LC-8	MP44	KREPB5	
MP42		LC-7B	MP42	KREPA3	
MP41		MP41	MP41	KREPB8	
MP24	RNA binding	LC-10	MP24	KREPA4	
MP18	RNA binding	LC-11	MP18	KREPA6	
RET1	3′ TUTase	RET1	MP116	KRET1	
KPAP1	Mitochondrial PAP	KPAP1	KPAP1		Kinetoplast Poly(A) Polymerase
MRP1	RNA binding Annealing/ Matching	Lt26	gBP21		Mitochondrial RNA binding Proteins
MRP2	RNA binding Annealing/ Matching	Lt28	gBP25		
REH1	RNA helicase	mHel61	mHel61		RNA Editing Helicase 1

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