various cellular compartments and for specific classes of molecules — that are thought to help the animals survive other extreme conditions[5,12,13]. Understanding these protectants' potency outside of tardigrades has been of interest, given their potential practical uses for guarding fragile biomedical materials. But demonstrating *in vivo* roles for protectants has been a challenge. The recent development of transgenic and CRISPR techniques for tardigrades[16–18], along with RNAi by injected double-stranded RNAs[19] or by soaking siRNAs as in the recent paper[4], promises fruitful routes toward understanding *in vivo* roles for protectants and toward dissecting their mechanisms of action.

DECLARATION OF INTERESTS

The author declares no competing interests.

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Cell biology: A new dynamin superfamily protein remodels mitochondrial dynamics

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Dynamin superfamily proteins mediate mitochondrial fusion in fungi and animals. A new study expands the taxonomic reach of this superfamily and provides insights into the roles these proteins play by investigating MfnL, a family member involved in trypanosomal mitochondrial dynamics. Importantly, MfnL occurs widely in eukaryotes and prokaryotes.

The continual rearrangement of biological membranes — by bending, pinching, fission and fusion — is vital to life. However, the spontaneous curvature of membrane phospholipids is insufficient for such thermodynamically unfavorable acts of acute bending. Instead, proteins are required to orchestrate such membrane dynamics[1].

The dynamin superfamily encompasses an array of mechanochemical GTPases that catalyze various membrane-remodeling events in prokaryotes and eukaryotes[2]. The founding member,

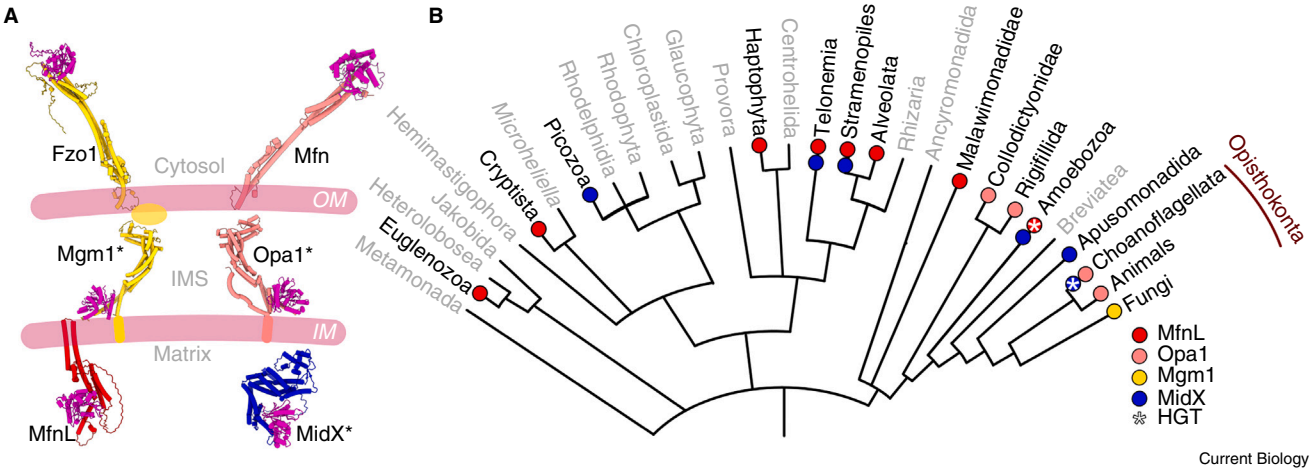

Figure 1. The repertoire of fusion dynamin superfamily proteins.
(A) Schematic representation of fusion-related, dynamin-superfamily-protein structure, membrane topology and subcompartment localization. Proteins are color coded as in (B). GTPase domains are colored in purple. Asterisks mark proteins that have a typical dynamin-related protein structure. Ugo1 (yellow oval) bridges Mgm1 and Fzo1, and unsolved transmembrane domain structures of long forms of Mgm1 (PDB accession number 6RZV)[16] and Opa1 (PDB accession number 8EFF)[17] are shown as cartoons. Only a single Mfn is depicted, although vertebrates have two paralogs[1]. OM, outer membrane; IMS, intermembrane space; IM, inner membrane. (B) Phylogenetic distribution of inner membrane and matrix-localized dynamin superfamily proteins. HGT, horizontal gene transfer. (Modified from Hashimi *et al.*[4] and Sheikh *et al.*[5].)

appropriately named dynamin, pinches off vesicles budding from the plasma membrane into the cytosol at early stages of endocytosis. Dynamin-related proteins reiterate the structure and domain architecture of dynamin (Figure 1A). However, not all members of the larger dynamin superfamily of proteins assume structures resembling those of dynamin and dynamin-related proteins. Such dynamin superfamily proteins typically have transmembrane domains, whereas dynamin-related proteins on the other hand typically interact with membranes transiently.

Mitochondria are dynamic organelles that coalesce into and dissociate from an interconnected, net-like reticulum. The presence of a broad repertoire of dynamin superfamily proteins (Figure 1A) enables mitochondrial membrane dynamics[1], including the well characterized dynamin related protein 1 (Drp1), which plays a key role in mitochondrial fission. Each of the two mitochondrial membranes, a vestige of the organelle's bacterial past, have their own dedicated fusion machinery. The dynamin-related proteins Opa1 and Mgm1 catalyze inner membrane fusion in animals and fungi, respectively. Dynamin superfamily proteins facilitate outer membrane fusion: Mfn in animals and Fzo1 in fungi.

The years since their discovery over two decades ago have seen substantial progress in understanding how these dynamin superfamily proteins act on mitochondrial membranes mechanistically and how they impact the whole cell (for example, the regulation of apoptosis[1]). But the size of the known mitochondrial dynamin-superfamily repertoire has stayed the same. Furthermore, apart from Drp1, which evidently facilitates mitochondrial fission in all aerobic eukaryotes[3], all of the known fusion dynamin superfamily proteins are restricted to Opisthokonta, a group originating from the last common ancestor of animals and fungi. Surprisingly, the dynamin superfamily proteins mediating mitochondrial fusion in animals and fungi do not share a common origin at the root of opisthokonts as would be expected based on their phylogenetic relationship[4,5] (Figure 1B). So how do other eukaryotes perform mitochondrial membrane fusion? And why does mitochondrial fusion require a dedicated set of dynamin superfamily proteins in animals, fungi, and perhaps other eukaryotes?

In this issue of *Current Biology*, Morel and colleagues have looked outside of Opisthokonta to explore the diversity of mitochondrial dynamin superfamily proteins[6]. They achieved this with a *tour de force* characterization of MfnL in *Trypanosoma brucei*, a unicellular parasite of cattle and humans that is spread by its tsetse fly vector in Africa. *T. brucei* MfnL (TbMfnL) was so named due to its ostensible similarity to Mfn (hence Mfn-like) in an earlier investigation of its possible role in the lysis of the pathogen by a factor in human blood serum[7]. While this specific aspect of trypanolysis remained open-ended, the study hinted at TbMfnL's capacity to remodel mitochondrial membranes.

Mitochondrial dynamics in *T. brucei* is different because it has only a single mitochondrion[8] (Figure 2). *T. brucei*'s Drp1 is recruited for mitochondrial scission only during cytokinesis to ensure the organelle's inheritance[9–11]. The rest of the time, Drp1 assumes the task of endocytic vesicle scission since it is the only dynamin-related protein available in trypanosomatids. So, despite involvement of the ubiquitous Drp1, the occurrence of trypanosomatid mitochondrial fission seems limited to a discrete cell-cycle stage instead of happening continuously.

But does a single mitochondrion really undergo fusion? Echoing animals and fungi, a reticulated mitochondrion is regularly observed in insect-midgut dwelling *T. brucei* and related trypanosomatids. This reticulum is more dynamic than expected, with branches perpetually splitting, extending, and fusing (!) into other branches[12]. The physiological significance of this vacillating morphology remains mysterious. However, the relatively modest branching of the

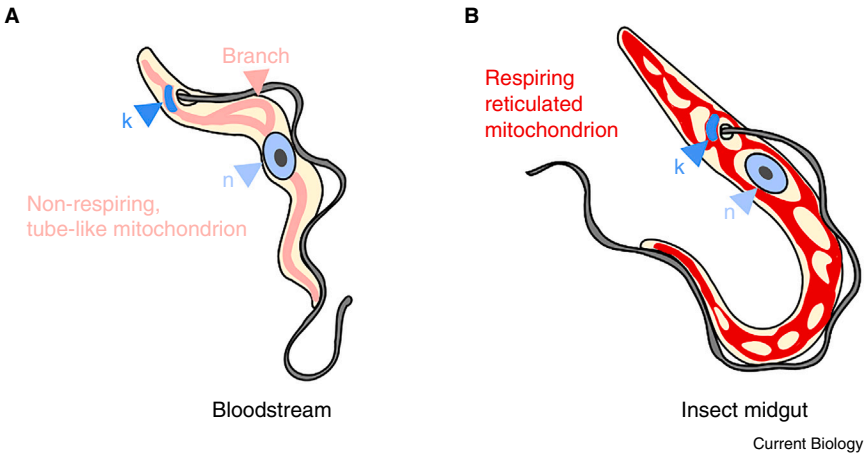

Figure 2. The difference between *Trypanosoma brucei* bloodstream-stage and insect-midgut-stage mitochondria.
Depiction of a *T. brucei* cell's single mitochondrion, with the mitochondrial genome encapsulated in the single kinetoplast (blue arrowhead marked 'k'), colored based on presence (red) and absence (pink) of cellular respiration in the bloodstream (A) and insect-midgut (B) cells. A loop captured extending from the simplified tube-like mitochondrion in the bloodstream form is marked with arrowhead. The nucleus (n), flagellum (gray), and cytosol (light peach) are also shown in addition to the large mitochondrion meandering throughout the parasite cell.

tube-shaped mitochondrion during the parasite's bloodstream life-cycle stage (Figure 2A) is hypothesized to generate adequate mitochondrial mass for equal distribution into each daughter cell[13,14].

Morel and colleagues show that TbMfnL induces branching of the reticulated form of the insect life-cycle stage mitochondrion[6]. Whereas deletion of the *TbMfnL* gene did not significantly reduce branching, overexpression of the gene product dramatically increased mitochondrial reticulation and volume. This phenotype was ameliorated when either TbMfnL's GTPase activity was ablated or its integration into the inner mitochondrial membrane was disrupted by removal of its two transmembrane domains, verifying TbMfnL's direct role in the observed branching and showing that it interacts with the membrane only via its transmembrane domains.

But more surprises were revealed upon further TbMfnL characterization. In contrast to what was observed in the insect-midgut-stage parasite, TbMfnL overexpression failed to induce mitochondrial branching in bloodstream-stage *T. brucei.* Although this could be because of different overexpression levels in the cell lines used, this observation still has an interesting implication. The degree of morphological complexity observed in the insect-stage versus the bloodstream-stage mitochondrion corresponds to the presence and absence of a respiratory chain in the respective life-cycle stages[8] (Figure 2). Therefore, the results of Morel *et al.* suggest that TbMfnL acts only on a membrane populated by cellular respiration machinery. By extension, the regulation of mitochondrial volume by branching may tune cellular respiration to the cell's immediate bioenergetic needs. TbMfnL overexpression alone does not cause mitochondrial branching in the bloodstream-stage parasite, implying that other factors in addition to or instead of TbMfnL are required to extend the mitochondrion at this stage. The observation that TbMfnL ablation alone does not significantly reduce branching suggests other redundant factors are involved.

Another surprise is the topology of TbMfnL (Figure 1A). Like Opa1 and Mgm1, TbMfnL localizes to the inner membrane via a mitochondrion-targeting presequence. But its GTPase and other domains extend into the organelle's matrix, whereas Opa1's and Mgm1's face the opposite way to initiate fusion with a colliding inner membrane[1,4]. Mfn and Fzo1 also face the cytosol from the outer membrane to access an adjacent outer membrane. Thus, the mechanism by which TbMfnL produces branch points — and perhaps fusion into branches — from the innermost chamber of the mitochondrion is an intriguing question. Perhaps this could be answered by the presence of interaction partners, like the adaptor protein Ugo1, which bridges Fzo1 and Mgm1 in the outer and inner membranes, respectively, in yeast (Figure 1A)[15]. Also, does TbMfnL act on membranes via homotypic interactions, as do other dynamin superfamily proteins like Mgm1 and Opa1[16–18]?

Finally, TbMfnL is not merely an oddity of trypanosomatids and other related euglenozoan flagellates. MfnL orthologs are found in other far-flung eukaryotic lineages such as stramenopiles (a group containing multicellular kelp and algae) and amoebozoans (Figure 1B). Remarkably, MfnL is also found in a broad spectrum of bacteria, including alphaproteobacteria. Perhaps its wide, albeit sporadic, distribution in eukaryotes implies that MfnL was the founding inner-membrane dynamin superfamily protein, later replaced in animals and fungi by Opa1 and Mgm1, respectively. By extension, maybe mitochondrial Mfn1 was inherited from the alphaproteobacterial progenitor of mitochondria, a phenomenon with precedence[19]. But acquisition of MfnL by horizontal gene transfer after mitochondria were established is equally plausible, as the amoebae likely obtained the *mfnL* gene this way from ingested bacteria[6]. What can be stated for certain is that the name 'MfnL' is a misnomer, as this novel dynamin superfamily protein is phylogenetically distinct from animal Mfn, resulting in a different predicted structure than Mfn and Fzo1 (Figure 1A).

The existence of MfnL in prokaryotes raises another question: does it really catalyze membrane fusion, since bacteria presumably do not fuse together? Bacterial dynamin-related proteins have been proposed to use their fusion activity in mediating vesicle secretion and/or septum formation between daughter cells during cell division[20]. Answering what MfnL does in bacteria is of not only intrinsic value, but also added value in informing how mitochondrial Mfn1 impacts mitochondrial membrane dynamics 'from deep inside'.

Recent years have seen a sudden boom in the discovery of new mitochondrial dynamin superfamily proteins. A dynamin related protein named MidX (mitochondria DRP of unknown function) can also remodel mitochondria from within the matrix, albeit via a peripheral interaction with the inner membrane[5] (Figure 1A). But unlike MfnL,

MidX's true biological role remains unknown because it occurs in sporadic eukaryotic lineages and giant viruses from the phylum *Nucleocytoviricota*, all lacking experimental models for functional characterization. Perhaps the mitochondrial repertoire of dynamin superfamily proteins will continue to be remodelled in the coming years with the discovery of new dynamin superfamily proteins and a deeper understanding of newcomers like MfnL to clarify the evolution and origin of mitochondrial membrane dynamics.

DECLARATION OF INTERESTS

The author declares no competing interests.

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Animal camouflage: Sculpting with light

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The three-dimensional nanostructure of butterfly and moth wing scales produces directional reflections that are impossible with an artist's brush. Here, we compare the visual effects used by a moth that masquerades as a dead leaf with those of computer graphics.

From the pioneering three dimensionality of portraits like the Mona Lisa, to Turner's hazy landscapes, depicting the interplay of light and material has been essential to the art of painting since the Renaissance[1]. Thus, the Victorian art critic John Ruskin instructed would-be artists[2] that "everything that you can see,