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TbUNC119 and its binding protein complex are a potential drug target for African trypanosomiasis

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African trypanosomes (e.g., Trypanosoma brucei and related subspecies) are uniflagellated protozoan parasites that cause African trypanosomiasis in humans and nagana disease in wild and domestic animals. T. brucei is transmitted to the bloodstream of mammalian hosts through the bite of an infected tsetse fly. Flagellum-mediated motility of Trypanosoma brucei is considered to be essential for the parasite to complete stage development in the tsetse fly vector, while the mechanism by which flagellum-mediated motility is controlled are not fully understood. T. brucei whole gene products (amino acid sequence) were thus compared with Caenorhabditis elegans UNC (uncoordinated) proteins, in order to find uncharacterized motility-related T. brucei genes. Through in silico analysis, 88 gene products which were highly similar to C. elegans UNC proteins were found and categorized as TbCEUN (T. brucei gene products which have high similarity to C. elegans UNC proteins). Approximately two thirds of the 88 TbCEUN gene products were kinesin-related molecules. A gene product highly similar to C. elegans UNC119 protein was designated as TbUNC119. Knock-down analysis of both TbUNC119 and its binding protein (TbUNC119BP) which was found by yeast two-hybrid analysis showed characteristic phenotypes, including reduced motility, morphological change (extended cell shape), and cellular apoptosis. TbUNC119 expression was found to be localized on flagellum of the parasite. Based on the findings, possible molecular functions of TbUNC119 and its binding complex will be discussed.

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