# *Alpha-Tubulin Acetylation in Trypanosoma cruzi: A Dynamic Instability of Microtubules Is Required for Replication and Cell Cycle Progression*


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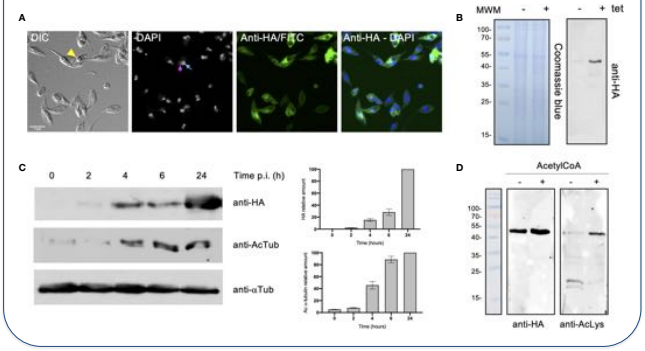
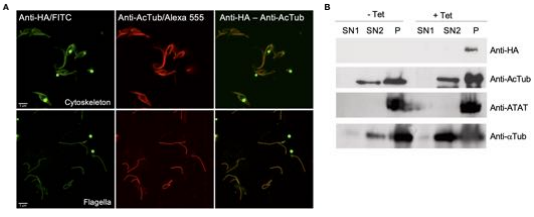
Trypanosomatids have a cytoskeleton arrangement that is simpler than what is found in most eukaryotic cells. However, it is precisely organized and constituted by stable microtubules. Such microtubules compose the mitotic spindle during mitosis, the basal body, the flagellar axoneme and the subpellicular microtubules, which are connected to each other and also to the plasma membrane forming a helical arrangement along the central axis of the parasite cell body. Subpellicular, mitotic and axonemal microtubules are extensively acetylated in *Trypanosoma cruzi*. Acetylation on lysine (K) 40 of alpha-tubulin is conserved from lower eukaryotes to mammals and is associated with microtubule stability. It is also known that K40 acetylation occurs significantly on flagella, centrioles, cilia, basal body and the mitotic spindle in eukaryotes. Several tubulin posttranslational modifications, including acetylation of K40, have been catalogued in trypanosomatids, but the functional importance of these modifications for microtubule dynamics and parasite biology remains largely undefined. The primary tubulin acetyltransferase was recently identified in several eukaryotes as Mec-17/ATAT, a Gcn5-related N-acetyltransferase. We have expressed *Tc*ATAT with an HA tag using the inducible vector p*Tc*INDEX-GW in *T. cruzi* and analyse the morphological alterations induced by over-expression.

Over-expression of *Tc*ATAT causes increased levels of the alpha-tubulin acetylated species, induces morphological and ultrastructural defects, especially in the mitochondrion, and causes a halt in the cell cycle progression of epimastigotes, which is related to an impairment of the kinetoplast division.

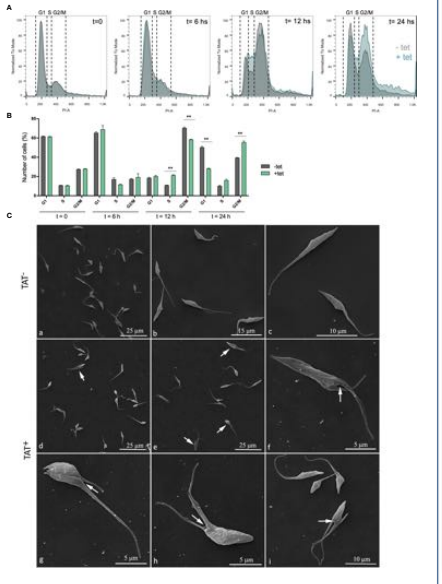
## *T. cruzi* ATAT acetylates alpha-tubulin *in vivo* and is capable of auto-acetylation *in vitro*



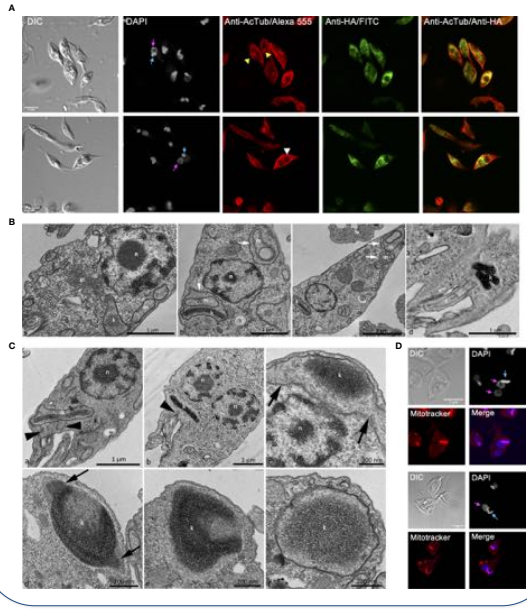

## TcATAT is located in the cytoskeleton and flagella of epimastigotes



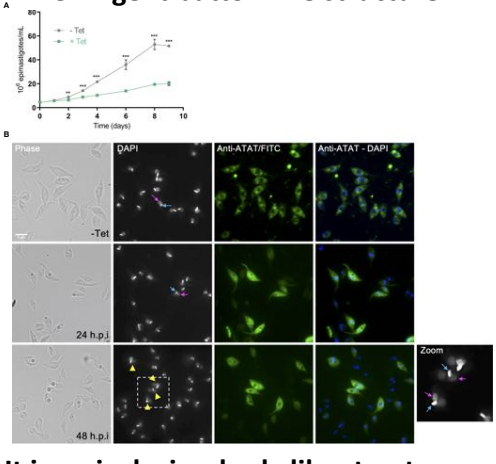

## Hyperacetylation alters the cell cycle progression of epimastigotes



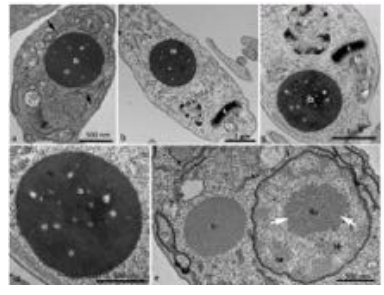

## Over-expression TcATAT-HA causes phenotypic alterations in acetylated a-tubulin distribution and on mitochondrion ultrastructures.




## One of the most evident morphological defect observed in over-expressing epimastigotes is the formation of a refringent button-like structure.




## It is an inclusion-body like structure.



These results supports the idea that tubulin acetylation is crucial for replication and differentiation and that *Tc*αTAT is responsible for this posttranslational modification in *Trypanosoma cruzi* microtubules.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