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Functional expression of TcoAT1 reveals it to be a P1-type nucleoside transporter with no capacity for diminazene uptake.

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It has long been established that the *Trypanosoma brucei* TbAT1/P2 aminopurine transporter is involved in the uptake of diamidine and arsenical drugs including pentamidine, diminazene aceturate and melarsoprol. Accordingly, it was proposed that the closest *Trypanosoma congolense* paralogue, TcoAT1, might perform the same function in this parasite, and an apparent correlation between a Single Nucleotide Polymorphism (SNP) in that gene and diminazene tolerance was reported for the strains examined. Here, we report the functional cloning and expression of TcoAT1 and show that in fact it is the syntenic homologue of another *T. brucei* gene of the same Equilibrative Nucleoside Transporter (ENT) family: TbNT10. The *T. congolense* genome does not seem to contain a syntenic equivalent to TbAT1. Two TcoAT1 alleles, differentiated by three independent SNPs, were expressed in the *T. brucei* clone B48, a TbAT1-null strain that further lacks the High Affinity Pentamidine Transporter (HAPT1); TbAT1 was also expressed as a control. The TbAT1 and TcoAT1 transporters were functional and increased sensitivity to cytotoxic nucleoside analogues. However, only TbAT1 increased sensitivity to diamidines and to cymelarsan. Uptake of [3H]-diminazene was detectable only in the B48 cells expressing TbAT1 but not TcoAT1, whereas uptake of [3H]-inosine was increased by both TcoAT1 alleles but not by TbAT1. Uptake of [3H]-adenosine was increased by all three ENT genes. We conclude that TcoAT1 is a P1-type purine nucleoside transporter and the syntenic equivalent to the previously characterised TbNT10; it does not mediate diminazene uptake and is therefore unlikely to play a role in diminazene resistance in *T. congolense*.

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