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ηF (ETA factor) is involved in translation pace regulation in kinetoplastids

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Kinetoplastids are a group of flagellated unicellular eukaryotes, which includes species infectious to mammals such as *Trypanosoma cruzi*, *Trypanosoma brucei* and *Leishmania* spp, the causative agents of Chagas disease, Sleeping sickness and Leishmaniasis, respectively. Current treatments against these parasites are in its majority based on non-specific drugs with aggressive side effects in addition to increasing drug resistance issues. The ribosome is a choice target for a wide range of therapeutic molecules (antibiotic). When compared to mammals, the kinetoplastids ribosome presents numerous structural differences that suggest a level of variability in the regulation of their mRNA translation process.
Among these structural differences, figures an interesting functionally uncharacterized protein that we have termed η (ETA) factor. ηF is a kinetoplastid-specific factor that was first observed by our team on the intersubunit side of the 40S platform from T. cruzi in late-log phase of cells growth. Its specific interactions extend to the ribosomal P and E -site where its main core binds near the platform region on the 40S subunit. Our cryo-EM structure shows that its binding clashes with the association of the 40S subunit, but also with the recruitment of eIF2-ternary complex and mRNA attachment to the 43S pre-initiation complex (PIC), acting possibly as a regulatory factor related to downregulate the formation of the PIC on the 40S and the formation of the 80S. Finally, in order to study its possible role, we have setup in vitro translation assays from Leishmania tarentolae cell extracts, where we use ηF (expressed and purified from E.coli) in increasing concentrations to show its impact on translation, but also on the formation of the PIC and the association of both ribosomal subunits.
Keywords: translation, kinetoplastids, cryo-EM

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