The tandem zinc-fingers of RNA helicase-associated KH2F1 differentially impact the editing of distinct mitochondrial transcripts in *Trypanosoma brucei.*

Joshua Meehan[1], Tyler Rodshagen[2], Jorge Cruz-Reyes[1], Suzanne M McDermott[2,3]

[1] Department of Biochemistry and Biophysics, Texas A&M University, College Station, TX, 77843, USA.

[2] Center for Global Infectious Disease Research, Seattle Children's Research Institute, Seattle, WA, 98109, USA.

[3] Department of Pediatrics, University of Washington School of Medicine, Seattle, WA, USA.

Abstract

The generation of functional mRNAs encoding respiratory complex components in trypanosome mitochondria involves U-insertion/deletion (U-indel) RNA editing. Editing is developmentally regulated between mammalian bloodstream form and insect procyclic form *T. brucei*, correlating with the differential utilization of glycolysis and oxidative phosphorylation between the forms. However, the mechanisms underlying this regulation are only just beginning to be understood. The editing process requires the coordinated actions of several multiprotein complexes. One such complex is the RNA Editing Helicase 2 Complex (REH2C) that contains the DEAH-box RNA Editing Helicase 2 (KREH2), and its partner proteins, KREH2-associated zinc-finger protein (KH2F1), and KH2F2. Of these, KREH2 and KH2F1, are essential for growth and are required to achieve full and accurate editing in procyclic form *T. brucei*, and KREH2 is essential for growth and editing in bloodstream form. Here we report the generation of bloodstream form *T. brucei* cells that are conditionally null for KH2F1 and show for the first time that KH2F1 is also essential for bloodstream form growth and editing. KH2F1 contains eight tandem zinc-fingers, and we assessed the importance of each of the zinc fingers via mutagenesis. Surprisingly, we show that the individual zinc fingers have different effects on bloodstream form growth, and on the abundances of edited transcripts whose editing is developmentally regulated. Together these data suggest that the KH2F1 zinc fingers may direct specific substrates to KREH2, including those whose editing differs between mammalian bloodstream form and insect procyclic form *T. brucei*, thereby playing a key role in the developmental regulation of editing across the parasite life cycle.