Review of: "The CGA Codon Decoding through Arg-tRNA^ICG Supply Governed by Tad2/Tad3 in Saccharomyces cerevisiae"

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Potential competing interests: No potential competing interests to declare.

In this manuscript, Wada and Ito test the decoding properties of the CGA codon in Saccharomyces cerevisiae. It is an interesting history that started a while ago with uncovering of an adenosine deaminase that converts the ACG anti-codon in ICG. The CGA codon in yeast is rare and inefficiently decoded, as detailed by the authors. The manuscript aims to demonstrate the CGA decoding by ICG-tRNA, and its dependence on adenosine deaminase heterodimer complex Tad2/Tad3. It is worth noting the inexistence of the CGA codon in the yeast mitochondrial genome. The proposed need for the cytosolic Tad2/Tad3 complex for proper CGA decoding, for instance, restrains allotopic expression of nuclear genes into the mtDNA, more importantly, provides regulatory steps for distribution of ACGtRNA and ICGtRNA pool and, therefore, translation control. The authors investigate the ratio of ACG-tRNA and ICG-tRNA by modulating the expression of Tad2 and Tad3 using promoters with different strengths, while GPD is well known to be the strongest among the tested promoters. At any rate, they should show the GPD-TAD3 product in figure 3D. Moreover, TAD2 overexpression was sufficient to complement the tad3 ts mutant, which raised the question of whether Tad2 excess can complement the tad3 null mutant and vice-versa. The authors could answer that, as well as explore the growth properties and fitness of the strains containing an excess of Tad2 or Tad3, or both. Indeed, a strain overexpressing TAD2 and TAD3 should also be constructed, and the levels of the mentioned tRNAs evaluated. Minor improvements in the figures, such as western blot band analyses, and densitometric measurements should be included.