

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

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Potential competing interests: No potential competing interests to declare.

In this paper, Wada & Ito showed in Saccharomyces cerevisiae that luc-reporters with consecutive CGA codons increase their associated protein level when Arg-tRNA(ACG) genes are added. This result suggests that the deficiency in tRNA(ACG) supply is the reason for reduced protein level and the inefficient decoding of this codon. Further, by using different expression levels of adenosine deamination enzymes, authors also showed that the ratio of the Arg-tRNA(ICG) and its precursor Arg-tRNA(ACG) changes. This result suggests that this ratio responds to the Tad2/Tad3 complex concentration. Thus, authors provide valuable evidence about CGA codon decoding in S. cerevisiae and the role of Tad2/Tad3 complex activity in tRNA A->I modification. These findings are important but something expected in part. However, I would like to see the impact of different Tad2/Tad3 complex activities on the resulting expression of lucreporters (mixing the experiments shown in Fig.1C and Fig.4C). This, together a stoichiometric and quantitative analysis, could provide an strong evidence about CGA codon decoding by Arg-tRNA(ICG) and/or Arg-tRNA(ACG) and the role Tad2/Tad3 complex in the decoding and contribute to the establishment of the anticodonome concept.

The paper is poorly written and it is difficult to follow in some parts. I think the text must be improved.

I also suggest two papers about translational efficiency and consecutive codon pairs in Saccharomyces cerevisiae that authors can find of their interest.

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