

# Review of: "The CGA Codon Decoding through Arg-tRNA<sup>ICG</sup> Supply Governed by Tad2/Tad3 in *Saccharomyces cerevisiae*"

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Potential competing interests: No potential competing interests to declare.

First of all, this paper is very poorly written and difficult to understand. The writing in the manuscript must be significantly improved. Obtain the help of a native English speaker/writer with an interest in the subject to help.

A tad2 or tad3 mutation would be expected to abolish all inosine-containing tRNAs blocking many amino acid additions. Is wobble A tolerated in these mutant strains? Please explain.

Are tad2 and tad3 essential genes in yeast?

Why were tad2 and tad3 degon strains not used?

I assume that tad2 and tad3 are essential genes in yeast? Is this so? This must be stated clearly to understand the paper.

Could the reverse transcription system be extended to the other inosine-containing tRNAs? There is a ribo-endonuclease that cleaves tRNAs at inosine modifications. Could this be used as a tool?

I think this paper lacks sufficient dimensions. The authors must strive for a more complete and compelling story.

The data are reasonable but incomplete.

## Questions

Why is unmodified A not often utilized in the wobble position? In Archaea, wobble A is never utilized. Why? This is fundamental to genetic code evolution and degeneracy of coding. This issue must be addressed for someone to understand and benefit from reading this paper.

Does the inosine modification stimulate accurate tRNA charging?

What is wrong with unmodified A in the wobble position? What would it read? Are there any instances in which unmodified wobble A is utilized? What is its specificity or lack thereof? It appears from the paper that unmodified Arg(ACG) is always present with Arg(ICG). Is unmodified Arg(ACG) utilized in translation?

Does A go to I wobble modification cause changes in codon bias, generally, or just in some species?

The CGA codon is rare in *Saccharomyces cerevisiae* and is decoded by tRNA<sup>Arg</sup>(ICG). Why does mcm5UCG (present in yeast) not decode CGA?

A modified to I decodes wobble A, C, U.

Does the failure to modify wobble A to wobble I affect other tRNA modifications necessary to make the tRNA functional?

Does the failure to modify A to I block tRNA charging?

Arg anticodons:

**ICG utilizes codon** (CGA), CGU, CGC

**U\*CG utilizes codon (CGA), CGG** \*mcm5U

CCG utilizes codon CGG

I think this can be a much better paper with some improvements, clarifications and additions.