

Characterization of the *Aedes aegypti* tRNA Methyltransferase Dnmt2

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INTRODUCTION: *Aedes aegypti* is an important vector for Dengue and other viruses. Dengue replication has been previously shown to be influenced by the tRNA methyltransferase AaDnmt2 and it was suggested that Dnmt2-dependent DNA methylation could be involved in this effect. However, the DNA modification status of the *Aedes aegypti* genome has so far only been investigated by indirect detection methods. Furthermore, it has been shown that Dnmt2 is not a DNA methyltransferase in other organisms, including *Drosophila*. As such, the molecular activity of Dnmt2 in *Aedes* remained to be established.

OBJECTIVES: Evaluate the methylation status of *Aedes aegypti* DNA and/or tRNA by Dnmt2, and correlate this methylation to Dengue virus replication.

MATERIAL AND METHODS: Expression analysis by qPCR of Dnmt2, Mettl4 and Tet in whole adults, specific tissues and various developmental stages. Masspec analysis of methylation; Bisulfite genome sequencing; Western blot analysis; RNAi analysis

DISCUSSION AND RESULTS: Whole-genome bisulfite sequencing methylation showed that *Aedes aegypti* genome lacks cytosine methylation. Alternatively, we showed that *Aedes* Dnmt2 have strong RNA binding, and tRNA methylation activities. *A. aegypti* cells silenced for AaDnmt2 showed a decrease in Dengue virus titers. Dnmt2, Mettl4 and Tet are expressed in adults, embryos and tissues of *A. aegypti*.

CONCLUSION: The *Aedes aegypti* genome lacks DNA methylation, but presents tRNA methylation by Dnmt2. Dnmt2 seems to play a role in Dengue virus replication.

Key words: *Aedes aegypti*, Dnmt2, tRNA methylation, Dengue virus replication

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