DNA METHYLTRANSFERASE 3 EXPRESSION AND ITS REGULATION BY A MICRORNA ARE POTENTIAL FACTORS INVOLVED IN AGING OF THE HONEY BEE (APIS MELLIFERA L).

Cardoso-Júnior, CAM 1; Guidugli-Lazzarini, KR 1; Hartfelder, K 1.

1 Departamento de Biologia Celular, Molecular e Bioagentes Patogênicos, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.

Aging is a multifactorial process that culminates in physiological damage to cells over time. One of the molecular machineries associated with aging in mammals is DNA methylation (DM), an epigenetic chemical modification that regulates gene expression. Notwithstanding, the association of DM and aging are poorly elucidated, especially since two of the principal biological models of aging, Caenorhabditis elegans and Drosophila melanogaster are either lacking important elements of the DM machinery, or DM does not occur in CpG nucleotides. So as to understand the role of DM in aging we chose the honey bee Apis mellifera as a model system because its DM system is similar and more simplified to that of mammals and its genome can give rise to two very different phenotypes, short-lived workers and long-lived queens. We assayed DNA methyltransferase 3 (DnMT3) expression in heads, thorax and abdomens of workers and queens of different ages by RT-qPCR. DnMT3 activity was inhibited by pharmacological intervention and the bees’ longevity was analyzed. We also investigated the possible role of microRNAs in the regulation of DnMT3 expression by: (1) in silico prediction of microRNAs targeting DnMT3; (2) RT-qPCR analysis to verify co-expression; (3) a functional assay to validate microRNA-DnMT3 interaction. We could show that DnMT3 is down-regulated in worker and queen heads and up-regulated in their abdomens. The DnMT3 inhibition extended the workers’ lifespan. During aging, the expression of ame-mir-317 varied in a manner opposite to that of DnMT3 in heads of queens, whereas a positive relationship was seen in abdomens. Finally, downregulation of DnMT3 was observed in queen abdomens treated in vitro with an ame-mir-317 mimic, indicating that DnMT3 is a bona fide target for this microRNA. Taken together, these results suggest that DM is involved in the aging process of honey bees and is susceptible to miRNA regulation.

Key words: Aging, DNA methylation, microRNAs.

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