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**Nicotine exposure caused significant transgenerational impact on microRNA expression and related disorder in *C. elegans***

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Early developmental stages are highly sensitive to stress and it has been reported that pre-conditioning with tobacco smoking during adolescence predisposes those youngsters to become smokers as adults. However, the molecular mechanisms of nicotine-induced transgenerational consequences are unknown. In this study, we genome-widely investigated the impact of nicotine exposure on small regulatory microRNAs (miRNAs) and its implication on health disorders at a transgenerational aspect. Our results demonstrate that nicotine exposure, even at the low dose, affected the global expression profiles of miRNAs not only in the treated worms (F0 parent generation) but also in two subsequent generations (F1 and F2, children and grandchildren). Some miRNAs were commonly affected by nicotine across two or more generations while others were specific to one. The general miRNA patterns followed a "two-hit" model as a function of nicotine exposure and abstinence. Target prediction and pathway enrichment analyses showed *daf-4*, *daf-1*, *fos-1*, *cmk-1*, and *unc-30* to be potential effectors of nicotine addiction. These genes are involved in physiological states and phenotypes that paralleled previously published nicotine induced behavior. Our study offered new insights and further awareness on the transgenerational effects of nicotine exposed during the vulnerable post-embryonic stages, and identified new biomarkers for nicotine addiction