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Use of Pig as an Animal Model for Assessing the Differential MicroRNA Profiling in Kidney after Aristolochic Acid Intoxication

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Abstract : Aristolochic acid (AA) is a carcinogenic, mutagenic, and nephrotoxic compound commonly found in the Aristolochiaceae family of plants. AA is frequently associated with urothelial carcinoma of the upper urinary tract in human and animals and is considered as being responsible for Balkan Endemic Nephropathy. The pig provides a good animal model because the porcine urological system is very similar to that of humans, both in aspects of physiology and anatomy. MicroRNA (miRNA) are small non-coding RNAs that have an impact on a wide range of biological processes by regulating gene expression at post-transcriptional level. The objective of this study was to analyze the miRNA profiling in the kidneys of AA intoxicated swine. For this purpose, ten TOPIGS-40 crossbred weaned piglets, 4-week-old, male and females with an initial average body weight of 9.83 ± 0.5 kg were studied for 28 days. They were given ad libitum access to water and feed and randomly allotted to one of the following groups: control group (C) or aristolochic acid group (AA). They were fed a maize-soybean-meal-based diet contaminated or not with 0.25mgAA/kg. To profile miRNA in the kidneys of pigs, microarrays and bioinformatics approaches were applied to analyze the miRNA in the kidney of control and AA intoxicated pigs. After normalization, our results have shown that a total of 5 known miRNAs and 4 novel miRNAs had different profiling in the kidney of intoxicated animals versus control ones. Expression of miR-32-5p, miR-497-5p, miR-423-3p, miR-218-5p, miR-128-3p were up-regulated by 0.25mgAA/kg feed, while the expression of miR-9793-5p, miR-9835-3p, miR-9840-3p, miR-4334-5p was down-regulated. The microRNA profiling in kidney of intoxicated animals was associated with modified expression of target genes as: RICTOR, LASP1, SFRP2, DKK2, BMI1, RAF1, IGF1R, MAP2K1, WEE1, HDGF, BCL2, EIF4E etc, involved in cell division cycle, apoptosis, cell differentiation and cell migration, cell signaling, cancer etc. In conclusion, this study provides new data concerning the microRNA profiling in kidney after aristolochic acid intoxications with important implications for human and animal health.

Keywords : aristolochic acid, kidney, microRNA, swine
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