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Non-coding RNAs as markers of opioid use and pathological pain

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Background: Opioid misuse and pathological pain are seen clinically both independently and concomitantly. Identifying mechanisms responsible for susceptibility to pathological pain and opioid use disorder could yield improved therapeutic strategies. These mechanisms could be controlled through noncoding (nc) RNA. Paclitaxel cancer treatment can produce peripheral neuropathy. We characterized ncRNAs from mice that developed paclitaxel-induced pain, with or without morphine treatment, and compared to another model of neuropathic pain: sciatic nerve chronic constriction injury (CCI).

METHODS: Male and female C57BL6/J mice received 4 paclitaxel doses (8 mg/kg/dose IP) or vehicle. Allodynia was assessed using the von Frey assay. After paclitaxel, morphine (or vehicle) was administered. Mice underwent behavioral testing and were sacrificed for collection of blood and spinal cord. A separate cohort of C57BL6/J mice underwent CCI or sham surgery. Allodynia was assessed, and tissues were collected. cDNA was synthesized to 627 miRNAs, and qPCR was performed on total RNA from spinal cord and sciatic nerve.

RESULTS: Of the 627 miRNAs examined, 414 and 376 were detectable (CT ≤ 35) in the spinal column and sciatic nerve, respectively. CCI mice displayed allodynia, and 11 and 126 miRNAs were differentially expressed in spinal cord and sciatic nerve. Three members of the miR-183 cluster were reduced in sciatic nerve. When administered by themselves, paclitaxel and morphine both induced allodynia.

Conclusions: MiRNAs are differentially expressed in preclinical pain models, which supports that miRNAs may be used as biomarkers to identify and treat subpopulations of patients with pathological pain, and those with an opioid-use history.