Developing an Opioid Painkiller Alternative Using the Epigenetic Correlation Between the Nav1 VGSC Family and miRNAs 30b & 182

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The opioid crisis has taken a huge toll on our country. Noting that in 2018, nearly 22% of opioid related deaths in the U.S. were due to prescription painkiller overdose, this research aims to develop a safer, more precise epigenetic pain treatment. The NaV1 VGSC family plays a crucial role in affecting nociception (pain sensitivity), since NaV1 channels are significantly expressed in nociceptors. Furthermore, miR-30b and miR-182 overexpression has been proven to decrease nociception in mice. This research aims to decrease pain sensitivity by downregulating genes that are both directly correlated to nociception and targets of the two miRNAs. Data from the National Center for Biotechnology Information was used to determine differentially expressed genes (p-value <.05) between wild type and NaV1.7 knockout mice. Using R, these genes were cross-compared with target genes of miR-30b and miR-182 to find commonalities. 5 genes of interest, USP46, VANGL1, TRUB1, UCK2, and UNC13A, were underexpressed in knockout mice and also targets of miR-30b and miR-182. Because their expression is directly correlated to NaV1 channel presence, downregulating these genes should lead to decreased nociception (confirmed by current literature for USP46 and UNC13A, more experimental support required for VANGL1, TRUB1, and UCK2). siRNA probes were then created to downregulate expression of the 5 target genes, and thus decrease sensitivity to pain. When delivered to cells post-transcriptionally, these probes offer much promise in the realm of novel pain treatments and can combat opioid addiction by providing a possible painkiller alternative.