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## **Extracellular Vesicle miRNA Screening On-Chip: Technology, Progress and Potential Application in Opioid Abuse Screening**

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Opioid abuse represents a significant public health crisis, with prescriptions and overdose related deaths increasing over fourfold since 2010. One cause is prescribed opioid misuse, but there are few tools to indicate which patients are at risk of opioid dependence. Development of monitoring tools to assess development of dependence in patients undergoing opioid therapy would facilitate timely opioid discontinuation. Liquid biopsy, the collection and analysis of biomarkers from patient fluid samples, may allow for better monitoring of patients. Recent work has demonstrated differences in miRNA composition of extracellular vesicles (EVs) between controls and opioid dependents. Liquid biopsy platforms for EV miRNA analysis in opioid disorders could help manage this public health crisis. Our group has developed a microchip for separating EVs, and microfluidics-enabled strategy for rational design of functional immunomagnetic nanomaterials to screen biomarkers from patient blood for downstream analysis in cancer. We have demonstrated a high retention rate (>50%) of captured mock EVs on-chip, and importantly, the physicochemical properties of functional nanomaterials can significantly improve screening efficiency of biomarkers. By modifying this microchip to quantify EV miRNAs in opioid users and non-using controls, we could gain information about biomarkers relevant to opioid abuse. We also demonstrated rational design of functional nanoproboscopes which could be used to separate EVs on the microchip, and determine miRNA expression using sequencing and RT-PCR. Through this consortium, we will team up with collaborations to collect the data set determining differential EV miRNA cargo expression among opioid users.