Opioid Addiction Susceptibility Testing Via Cytochrome P450 Pharmacogenetic And Personalized Brain Region Specific (VTA) Organoid Assays

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Our long term goal is to develop and identify efficacious biomarker assays for detection of opioid addiction susceptibility in persons with chronic pain. Reprogramming of human somatic cells to alter cellular fate and identity has enormous potential for neurological disease modeling, high-throughput drug screening, cell therapy, and personalized medicine for discovery of biomarkers for substance abuse disorders. However, several challenges remain before patient-specific cells produced by reprogramming can provide reliable insights into neurological disease mechanisms (e.g., Drug abuse/ addiction, other neurological disorders) or be efficiently applied to drug discovery and transplantation therapy. Using a patented technology to develop Artificial 3D Microenvironment Niche and screen for reprogramming small molecules (US Patent # 9045737), we have resolved many of these hurdles and are developing robust and inexpensive methodologies for generation of personalized human brain region specific Ventral Tegmental Area (VTA) organoides, within a typical screening platform (multi well plate assay for routine laboratory testing). VTA is the region of the brain with dopaminergic neurons, primarily responsible for substance abuse disorders.

In addition, we are developing rapid and inexpensive genetic testing of Cytochrome P450 isoenzymes CYP1A2, 2C8, 2C9, 2C19, 2D6, 2E1, and 3A4, whose presence and activity levels vary based on a variety of factors including race, ethnic background and tobacco abuse as well as interactions with other medication, and other receptors, such as the opioid receptors.
Automated combined and comprehensive analysis of these two assay systems, in correlation with opioid addiction in population studies, is performed using Artificial Intelligence (AI) algorithms. A progress report of these developments as well as future plans for testing of Opioid addiction patient cohorts will be presented.