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Organoids as New Platform to Study Substance Use Disorders

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Three-dimensional *ex vivo* organoid cultures have been shown to resemble and recapitulate the functionality of diverse tissues and organs, such as Gut and Brain. Oral administrated alcohol, caffeine, and cocaine produce addiction. While intense research has been done to understand the neuronal signaling networks and intracellular signaling cascades associated with substance abuse, the biological mechanisms of the transition from “use” to “disorder” has still not been elucidated. There is a missing link in addiction between Gut and Brain. My publications demonstrated that murine gut organoids demonstrated epigenetic changes when treated with nutrients and vitamins, and organoids from different microbiota environments showed the concentration-dependent responses to inflammatory stimulants. These publications formulated my ***hypothesis*** that substances produce epigenetic changes of Gut-Brain Axis (GBA) to cause addiction. The ***rationale is that, for the first time,*** we will gain an in-depth understanding of the keystone substance species responsible, elucidating their addictive effects quantitatively through the GBA. This project is built on my established research platform that combines a unique set of murine models. My ***overall objective*** is to determine how age, gender, and microbiota modulate the GBA neuropeptides to manipulate reward, and addiction processes, thus identifying high-risk loci that may be suitable for functional study. The ***contribution will be significant*** because the successful execution will establish a novel conceptual framework linking modifiable factors such as organoids, neuropeptides, gut microbiota, ENS, and CNS with SUD and lead to new therapeutics. Together, my study will generate critical mechanistic insights into the role of GBA in SUD.