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Gene x Cannabis Interactions in Neuropsychiatric disorders

Each person's distinct genetics and environment predispose them to some phenotypes and confers resilience to others. We seek to understand the genetic regulation of phenotype, and how it is impacted by developmental, cellular, and environmental contexts. Our functional genomics approach integrates human induced pluripotent stem cell (hiPSC) models with high-throughput genome screening technologies to characterize the impact of trait-associated variants and uncover modifiers that alter it. We study how genotype-phenotype relationships vary across people and dynamic conditions, across contexts including stress, inflammation, and sex hormones. Here, given the increased cannabis use and potency in society, and in light of increasing evidence that prenatal exposure to cannabis is associated with negative childhood and adult outcomes on behavior, cognition, and lifetime neuropsychiatric disorder risk, we discuss application of hiPSCs to model the impacts of prenatal and adolescent cannabis exposure on the developing brain. Although the direction of causality between cannabis exposure and neuropsychiatric disorder risk remains unclear, our unifying and testable hypothesis is that THC exposure modifies genetic regulation of (a subset of) NPD risk variants in a cell-type-specific manner. Our goal is to decipher the frameworks that buffer genetic risk, in order to confer biological resilience and promote healthy development. Understanding the basic biology governing the complex interplay between genetic variants and the environment will springboard the development of novel, personalized approaches to improve health and prevent disease.

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