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Identifying Genetic Risk Factors for Opioid Use Disorder in Chronic Pain Patients using the AllOfUs Research Dataset

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The opioid epidemic remains a pressing public health crisis, claiming over 100,000 lives in 2021. Chronic pain patients are at heightened risk of opioid dependence, with up to 50% of those on chronic opioid therapy meeting criteria for opioid use disorder (OUD) diagnoses. Therefore, it is essential to risk stratify which chronic pain patients are at highest risk for OUD. Ample evidence suggests that both OUD and chronic pain exhibit heritable risk, yet their genetic overlap is poorly understood. We aim to identify novel genetic loci associated with OUD across a diverse set of individuals with chronic pain using the AllofUs Research dataset. Using HAIL, we performed a cross-ancestry genome-wide association study on participants of European, African, East Asian, South Asian, Middle Eastern, and admixed American ancestries (N=51,639; 1,157 OUD cases). Six potential risk loci were identified (rs9383796, rs12186751, rs80343897, rs112770742, ss1388049152, rs10157494). Functional annotation via FUMA linked these loci to genes, including fibroblast growth factor 1 (FGF1), implicated in dopamine and GABA neuron regulation. These neurotransmitter systems play critical roles in reward processing and addiction pathways, suggesting FGF1 may contribute to OUD development in chronic pain patients. While none of our variants reached genome-wide significance (5×10^{-8}) due to limited sample size, our findings using a suggestive significance of 5×10^{-6} highlight promising associations warranting further investigation. In the future, we plan to conduct a meta-analysis to further improve the power of our study along with validating our findings with external datasets.