# A polymorphism in the *OPRM1* 3' untranslated region is associated with methadone efficacy in treating opioid dependence

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**Abstract:**

The mu-opioid receptor (MOR) is the primary target of methadone and buprenorphine. The primary neuronal transcript of the *OPRM1* gene, MOR-1, contains a large 3' untranslated region with five common haplotypes in European-Americans. We analyzed the effects of these haplotypes on the percentage of opioid positive urine tests in European-Americans (n = 582) during a 24-week, randomized, open-label trial of methadone or buprenorphine/naloxone (Suboxone) for the treatment of opioid dependence. A single haplotype, tagged by rs10485058, was significantly associated with patient urinalysis data in the methadone treatment group. Methadone patients with

the A/A genotype at rs10485058 were less likely to have opioid-positive urine drug screens than those in the combined A/G and G/G genotypes group (Relative Risk = 0.68, 95% confidence intervals = 0.64-0.73, p = 0.0013). Genotype at rs10485058 also predicted self-reported relapse rates in an independent population of Australian patients of European descent (n = 1215) who were receiving opioid substitution therapy (p = 0.003). *In silico* analysis predicted that miR-95-3p would interact with the G, but not the A allele of rs10485058. Luciferase assays indicated miR-95-3p decreased reporter activity of constructs containing the G, but not the A allele of rs10485058, suggesting a potential mechanism for the observed pharmacogenetic effect. These findings suggest that selection of a medication for opioid dependence based on rs10485058 genotype might improve outcomes in this ethnic group.