

Cytochrome P450 3A5 Plays a Prominent Role in the Oxidative Metabolism of the Anti-HIV Drug Maraviroc

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Drug Metabolism and Disposition

Supplementary Table 1

Sequence of oligonucleotides used for site-directed mutagenesis for CYP3A4 and CYP3A5^a.

Mutation	Oligonucleotide Sequence
<i>CYP3A5</i>	
L57F	5'-aaatgtttgtcctatcgtcagggttctggaaattgacac-3' 5'-gtgtcaaattccagaaacctgacgataggacaaaacattt-3'
S107P	5'-cttcacaaatcgaaggccttaggccagtgagg-3' 5'-cccactgggcctaaaggccttcgatttgaag-3'
L108F	5'-cttcacaaatcgaaggcttccggccagtgagg-3' 5'-cccactgggcctaaaggaccttcgatttgaag-3'
L120I	5'-ttatgaaaagtccatctctatagctgaggatgaagaatgg-3' 5'-ccattctcatcctcagctatagatggcactttcataa-3'
F146V	5'-gaaaactcaaggagatggccccatcattgccag-3' 5'-ctgggcaatgatggggaccatctccttgagtttc-3'
K166T	5'-acttgaggcgggaagcagagacggggcaagcctgt-3' 5'-acaggcttcccgtctctgctcccgcctcaagt-3'
G186S	5'-cctacagcatggatgtgattactagcacatcatttga-3' 5'-tccaaatgatgtgctagtaatacatccatgctgtagg-3'
S206N	5'-caagaccctttgtggagaactaagaagtccataaaa-3' 5'-tttaggaacttcttagtctccacaaaggggtctg-3'
F210L	5'-tttgtggagagcactaagaagttactaaaatttggttcttagatcc-3' 5'-ggatctaagaaccaaatttagtaacttctagtctccacaaa-3'
K212R	5'-ggagagcactaagaagttcctaaagatttggttcttagatccattat-3' 5'-ataatggatctaagaaccaaatttaggaacttcttagtctctcc-3'
G214D	5'-gcactaagaagttcctaaaattgatttcttagatccattatttctctc-3' 5'-gagagaataatggatctaagaatacaatttaggaacttcttagtgc-3'
L219F	5'-cctaaaatttggttcttagatccattcttctcaataatactcttccatt-3' 5'-aatggaaagagtattattgagagaaagaatggatctaagaaccaaatttagg-3'
I224T	5'-cttagatccattatttctctcaataacgctcttccattcctaccag-3' 5'-actggggtaaggaatggaaagagcgttattgagagaaataatggatctaag-3'
V238I	5'-tcctaccccagttttgaagcattaaatctctctgttccaa-3' 5'-ttggaacagagagatattaatgctcaaaaactggggtaagga-3'
S239C	5'-cccagttttgaagcattaaatgtctgtctgttccaaaag-3' 5'-cttttggaaacagacagacatttaagcttcaaaaactgggg-3'

L240V	5'-ccccagttttgaaacattaatgtctct <u>gt</u> gtttccaaaagata-3' 5'-tatcttttgaaacacagagacatttaatgcttcaaaaactgggg-3'
K243R	5'-tttgaagcattaatgtctctgtttcca <u>ag</u> gataaccataaatttttaagtaa-3' 5'-atttacttaaaaaatttatggtatctcttggaaacagagagacatttaatgcttcaaa-3'
A296V	5'-gtctgatctggagctc <u>gt</u> agcccagtcataatct-3' 5'-agattattgactgggctacgagctccagatcagac-3'
V369I	5'-gaaacactcagattattccca <u>att</u> gctattagacttgagagga-3' 5'-tcctctcaagtctaataagcaattgggaataatctgagtgttc-3'
I371M	5'-cactcagattattccagttgctat <u>g</u> agacttgagagga-3' 5'-tcctctcaagtctcatagcaactgggaataatctgagtg-3'
T376V	5'-ccagttgctattagacttgagagg <u>gt</u> ttgcaagaaagatggtgaaatcaa-3' 5'-ttgattcaacatctttctgcaaacctctcaagtctaatagcaactgg-3'
S392V	5'-gggtattcattcccaaagg <u>gt</u> aatggtggtgattccaactt-3' 5'-aagtggaatcaccaccattaccctttgggaatgaataccc-3'
R415L	5'-agcctgaggagtcc <u>cc</u> ctgaaagggtcag-3' 5'-ctgaacctttcagggaggaactcctcaggct-3'
D477S	5'-tgtaaagaacacagatccccttgaaatta <u>ag</u> cacgcaaggacttctt-3' 5'-aagaagtccttgctgcttaattcaaggggatctgtttctttaca-3'
T478L	5'-aacacagatcccctgaaattagac <u>ct</u> acaaggacttctcaaccagaaaaac-3' 5'-gttttctggttgaagaagtccttgtaggtctaattcaaggggatctgtgtt-3'
Q479G	5'-ccccttgaaattagacac <u>gg</u> aggacttctcaaccagaa-3' 5'-ttctggttgaagaagtcctcccgtgcttaattcaagggg-3'
<i>CYP3A4</i>	
F57L	5'-tattttgcctaccataagggctt <u>at</u> gtatgttgacatggaatg-3' 5'-cattcatgtcaaacatacataagcccttatgtaggacaaaata-3'
P107S	5'-gtcttcacaaaccggagg <u>ag</u> ttttggtccagtgggatt-3' 5'-aatcccactggacaaaactcctccggtttgtgaagac-3'
F108L	5'-caaaccggaggccttt <u>ag</u> gtccagtggg-3' 5'-cccactggacctaaaggcctccggtttg-3'
D214G	5'-caccaagaagcctttaaagattt <u>gg</u> tttttggatccattctttctt-3' 5'-agagaaagaatggatccaaaaacaaatcttaaaagcttcttgggtg-3'
Δ423N ^b	5'-cctgaaagattcagcaagaag---aaggacaacatagatccttac-3' 5'-gtaaggatctatgttgcctt---cttcttgcctgaatctttcagg-3'
L479T	5'-cagatccccctgaaattaagc <u>ac</u> gggaggacttctcaaccagaa-3' 5'-ttctggttgaagaagtcctcccgtgcttaattcaggggatctg-3'

^a The underlined nucleotide(s) in bold represent the introduced mutations that were used to make the desired residue changes. ^b Three nucleotides were omitted in the primer sequence in order to delete residue N423 of CYP3A4.