Title: Germline polymorphisms in the nuclear receptors PXR and VDR as novel prognostic markers in metastatic colorectal cancer patients treated with FOLFIRI

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**Supplementary Table S4**: *In silico* predicted functional effect of polymorphisms in the **A)** *NR1I2*-rs1054190 and **B)** *VDR*-rs7299460 haploblocks by HaploReg v.4.1 and RegulomeDB v1.1. Targeted marker is evidenced in red.

|  |  |  |
| --- | --- | --- |
| **General data**  | **HaploReg\*** | **RegulomeDB Score\*\*** |
| **dbSNP ID** | **Chromosome Location (GRCh38)** | **LD (r2)** | **SNP Location** | **Promoterhistone marks** | **Enhancerhistone marks** | **DNAse** | **Proteinsbound** | **Motifschanged** | **GRASP QTLhits** | **Selected****eQTLhits** |
| **A) *NR1I2*-rs1054190 haploblock** |
| [rs11929668](https://pubs.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs11929668) | chr3:119816948 | 0.8 | NR1I2 (intronic) |  | BRST, SKIN | SKIN,MUS |  | GATA,Pax-5,p53 |  | 2 hits | 5 |
| [rs10511395](https://pubs.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs10511395) | chr3:119817712 | 0.8 | NR1I2 (3'UTR) |  |  |  |  | AP-2,Nr2f2,Zfx |  | 2 hits | 5 |
| [**rs1054190**](https://pubs.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs1054190) | **chr3:119817871** | **1** | **NR1I2 (3'UTR)** |  |  |  |  |  | **1 hit** | **2 hits** | **5** |
| [rs1054191](https://pubs.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs1054191) | chr3:119818050 | 0.8 | NR1I2 (3'UTR) |  |   |   |  | Rad21 |   | 2 hits | 4 |
| **B) *VDR*-rs7299460 haploblock** |
| [rs7136534](https://pubs.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs7136534) | chr12:47900843 | 0.82 | VDR (intronic) | BRST, BLD, GI | 20 tissues | 19 tissues | 7 bound proteins | 4 altered motifs |  | 2 hits | 4 |
| [rs10083198](https://pubs.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs10083198) | chr12:47902182 | 1 | VDR (intronic) |  |  | GI,BLD |  | SRF |  | 1 hit | 5 |
| [**rs7299460**](https://pubs.broadinstitute.org/mammals/haploreg/detail_v4.1.php?query=&id=rs7299460) | **chr12:47902485** | **1** | **VDR (intronic)** | **6 tissues** | **12 tissues** | **GI** |  | **GATA,Pax-5,TAL1** |  | **2 hits** | **5** |

\*ENCODE-HaploReg v4.1 (<https://pubs.broadinstitute.org/mammals/haploreg/haploreg.php>) was employed to test the functional effect of a selected polymorphism and all the others included in the same haploblock at a stringency of r2=0.80 using the linkage disequilibrium (LD) data from 1000 Genomes Project (EUR). HaploReg includes chromatin state and protein binding annotation from the Roadmap Epigenomics and the Encyclopedia of DNA Elements (ENCODE) projects, sequence conservation across mammals, the effect of polymorphisms on regulatory motifs, and the effect of polymorphisms on expression from expression quantitative trait locus (eQTL) studies.

\*\*RegulomeDB v1.1 (<http://www.regulomedb.org/>) is a database that annotates polymorphisms in the intergenic regions of the human genome by integrating a big collection of regulatory information from several public dataset. This tool presents a score system with categories ranging from 1 to 6 with the lower score indicating the stronger evidence for a variant to be in a functional region; the score is assigned by integration annotation data on methylation profile, chromatin structure, protein motifs, binding to transcription factors and enhancer activity. Score: 4= TF binding + DNase peak (minimal binding evidence); 5=TF binding or DNase peak (minimal binding evidence).

Abbreviation: SNP, single nucleotide polymorphism; UTR, untranslated region.