

	SNP-ID	Gene	Primer sequences	Concentration [μ M]
Multiplex 1				
1	rs11894252	<i>EPAS1</i>	CATTGTGCTGTGTGTCTACCC CCCTAACCAGAGGCAGTCAG	0.25 0.25
2	rs7579899	<i>EPAS1</i>	TCTGTAGGGCATGACACAGC GCTGCTCTACCCAGGTGACT	0.125 0.125
3	rs3118523	<i>RXRA</i>	GGCAGTGGGGTTGATTACTG TCTGTCCTCACCTTCCCTGA	0.125 0.125
4	rs833061	<i>VEGFA</i>	TTCGAGAGTGAGGACGTGTG AGGGAGCAGGAAAAGTGAGGT	0.1875 0.1875
5	rs748964	<i>RXRA</i>	CTTCCGTGGTCTGGAAAAGG CTCACTCTCACCCCAAGGAC	0.25 0.25
6	rs4765623	<i>SCARB1</i>	GCTCAGGGACATCACACGTA GATGCGTTCAGCAGTTCAGA	0.125 0.125
7	rs7105934	<i>11q13.3</i>	TCAGCTGAGGAATGATGAACA TTCCTGCCCTACAGTCTTG	0.25 0.25
Multiplex 2				
1	rs132770	<i>XRCC6</i>	TAGAAGCTGGTTGGGGAGTG CTAGCTGGCGAACAACACAA	0.25 0.25
2	rs9904341	<i>BIRC5</i>	GCCATTAACCGCCAGATTTG GCAACGTCGGGGCACCCAT	0.125 0.125
3	rs9679290	<i>EPAS1</i>	TGTCCCTGAACTGAGGCTCT AAAGACCTTGCTTTGCCAGA	0.125 0.125
4	rs7121	<i>GNAS1</i>	CTGACCGCTTTGCTAAATCA CACAAGTCGGGGTGTAGCTT	0.125 0.125
5	rs4953346	<i>EPAS1</i>	AGGCATGGTTCTCTGCATAC AACCTCAGCGTCTATGAGTG	0.25 0.25
6	rs1049380	<i>ITPR2</i>	AAAAGGGTTTTGTTCCCTCTG CAAGCATTTTCTCATCTAAAAGTGT	0.25 0.25
Multiplex 3				
1	rs17849897	<i>ZC3H12A</i>	CCCTTACACGGGCTACAGTC GGGAAACACACCACACAGC	0.25 0.25
2	rs113322875	<i>ZC3H12A</i>	GCTGGGCTAGGAGCTAGGTT CAGGAAGTTTGAGGCTGGAA	0.125 0.125
3	rs34796867	<i>ZC3H12A</i>	AGCTGGTGAAACACGGGACA GGGACTAGAGGGAGCTGAG	0.0625 0.0625
4	rs113655247	<i>ZC3H12A</i>	CCCTTACACGGGCTACAGTC GGGAAACACACCACACAGC	0.0625 0.0625
5	rs34031609	<i>ZC3H12A</i>	TCATCCCAGTCCAGCTCTCT CTGATGGGGCATAGGTCTGT	0.125 0.125
6	rs12105918	<i>ZEB2</i>	CCACTGGAATTAGTACAACAAACAA AGGCAGGAGAATTGCTTGAA	0.25 0.25

Supplementary Table 1. PCR primer sequences for three multiplex reactions.

	SNP-ID	Neutral 5'→3'	Target 5'→3'	Size	Concentration [μM]
Multiplex 1					
1	rs11894252	----	AAAAAATACACACATTTCACT	21	1.20
2	rs7579899	----	GAACAGCTTGGTCGCAGTGCT	21	0.40
3	rs3118523	(ct) ₃	CAAGCGGTCCAGTCAGGAGCC	27	0.70
4	rs833061	----	TGAGTGAGTGTGTGCGTGTGGGGTTGAGGG	30	0.60
5	rs748964	t(ct) ₁₆	CAGCACTCAGCCATGTGCGCA	54	1.00
6	rs4765623	(ct) ₉	CTCAGTAGATTTTGCCAGTGGCTCTCC	46	0.20
7	rs7105934	(ct) ₁₀	GCAGACTTTGAGTCGGCTTCTTAGCA	46	1.40
Multiplex 2					
1	rs132770	----	GCACATGCGTGATGACGTAG	20	0.40
2	rs9904341	t(ct) ₂	ATTAACCGCCAGATTTGAATCGC	28	0.80
3	rs9679290	(ct) ₅	CAGTGGCCTTGAGGTTTGTGTCAGAA	34	0.30
4	rs7121	(ct) ₁₀	GAACCAGTTCAGAGTGGACTACAT	44	0.40
5	rs4953346	(ct) ₁₃	CAGAGCCTCTGTGAGGAATAAATA	50	1.00
6	rs1049380	(ct) ₁₃	TTATTTTAACTCAGAAAACATACT	50	1.00
Multiplex 3					
1	rs17849897	CAA	GCCTGCTCCTTGCCAGGCTG	24	1.4
2	rs113322875	CTGACAA	CCCCGAGGTGGGTGCGT	24	0.15
3	rs34796867	AGTCTGACA A	GTGAGGTCTGGCGCTCCCGCT	31	0.5
4	rs113655247	GTCGTGAAA GTCTGACAA	GGCCAGCACCCATGGCCC	36	0.3
5	rs34031609	GTGAAAGTC TGACAA	AGCTTCTTCCCATCCAGGCTGCACT	40	0.1
6	rs12105918	----	CGTGAAAGTCTGACAATGCTATAAGTAACA TGCAGTTGTAAGCC	44	0.8

Supplementary Table 2. Extension primer sequences for three multiplex reactions.

Nr	Haplotype	Frequency [%]
Chromosome 2, EPASI gene: rs11894252, rs7579899		
1	CC	64.20
2	CT	0.08
3	TC	0.17
4	TT	35.55
Chromosome 2, EPASI gene: rs9679290, rs4953346		
1	GC	0.16
2	GA	54.49
3	CC	45.35
Chromosome 2, EPASI gene: rs11894252, rs7579899, rs9679290, rs4953346		
1	CCGA	44.95
2	CCCC	19.21
3	CTGA	0.27
4	TCCC	0.14
5	TTGC	0.14
6	TTGA	9.54
7	TTCC	25.75
Chromosome 9, RXRA gene: rs748964, rs3118523		
1	GG	14.30
2	GA	0.14
3	CG	5.86
4	CA	79.70
Chromosome 12, VDR gene, block 1: rs739837, rs731236, rs7975232, rs1544410		
1	CAGC	51.63
2	CAGT	0.68
3	CGGC	0.27
4	CGTT	0.27
5	AAGC	0.41
6	AATC	11.04
7	AATT	0.82
8	AGGT	0.14
9	AGTC	0.54
10	AGTT	34.20
Chromosome 12, VDR gene, block 3: rs2238136, rs4516035, rs7139166, rs11568820		
1	GTCC	10.35
2	GTCT	11.58
3	GTGC	0.41
4	GTGT	0.41
5	GCCC	0.54
6	GCCT	0.27
7	GCGC	39.92

8	ATCC	30.93
9	ATCT	0.54
10	ACCC	0.41
11	ACGC	4.64

Supplementary Table 3. Frequency of the haplotypes reconstructed with PHASE v2.1.

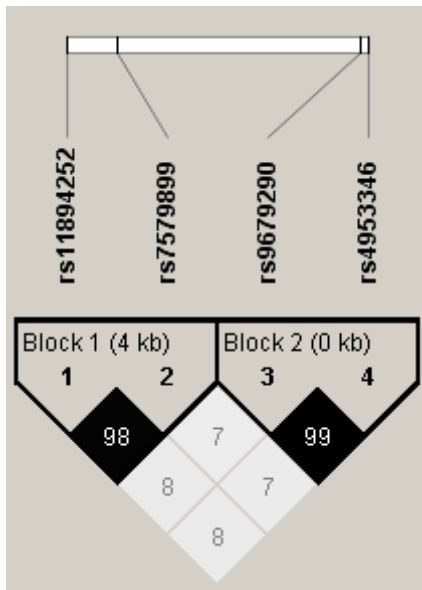
Nr	Locus	Gene	Minor Allele	OR (95% CI)*	P value
1	rs34796867	ZC3H12A	T	monomorphic	-
2	rs113322875	ZC3H12A	A	monomorphic	-
3	rs34031609	ZC3H12A	A	monomorphic	-
4	rs113655247	ZC3H12A	C	monomorphic	-
5	rs17849897	ZC3H12A	T	0.793 (0.220-2.860)	0.724
6	rs12105918	ZEB2	G	1.198 (0.638-2.262)	0.579
7	rs11894252	EPAS1	T	1.142 (0.836-1.560)	0.405
8	rs7579899	EPAS1	T	1.185 (0.869-1.617)	0.284
9	rs9679290	EPAS1	C	1.259 (0.939-1.687)	0.124
10	rs4953346	EPAS1	C	1.247 (0.930-1.672)	0.140
11	rs3834129	CASP8	del	1.086 (0.974-1.445)	0.576
12	rs833061	VEGFA	C	1.056 (0.789-1.414)	0.714
13	rs748964	RXRA	G	0.907 (0.603-1.366)	0.643
14	rs3118523	RXRA	G	0.953 (0.660-1.380)	0.800
15	rs7105934	11q13.3	T	0.513 (0.227-1.158)	0.108
16	rs1049380	ITPR2	G	1.076 (0.806-1.434)	0.617
17	rs739837	VDR	A	0.929 (0.697-1.238)	0.614
18	rs731236	VDR	G	1.064 (0.791-1.431)	0.684
19	rs7975232	VDR	T	0.967 (0.724-1.291)	0.821
20	rs1544410	VDR	T	1.153 (0.861-1.544)	0.340
21	rs2228570	VDR	A	1.195 (0.884-1.617)	0.246
22	rs2238136	VDR	A	1.086 (0.786-1.501)	0.615
23	rs4516035	VDR	C	1.003 (0.741-1.355)	0.987
24	rs7139166	VDR	G	0.987 (0.731-1.335)	0.935
25	rs11568820	VDR	T	0.833 (0.539-1.286)	0.409
26	rs4765623	SCARB1	A	1.321 (0.971-1.798) 1.688 (1.104-2.582)***	0.076 0.016***
27	N29insA	MC1R	A	monomorphic	-
28	rs1805005	MC1R	T	1.079 (0.639-1.822)	0.776
29	rs1805006	MC1R	A	cs**	0.209
30	rs2228479	MC1R	A	1.062 (0.664-1.699)	0.801
31	rs11547464	MC1R	A	0.796 (0.131-4.821)	0.804
32	rs1805007	MC1R	T	0.973 (0.466-2.030)	0.941
33	Y152OCH	MC1R	A	monomorphic	-
34	rs1110400	MC1R	C	1.352 (0.536-3.409)	0.523
35	rs1805008	MC1R	T	1.318 (0.744-2.337)	0.344
36	rs885479	MC1R	T	1.434 (0.644-3.191)	0.378
37	rs1805009	MC1R	C	cs**	0.209
38	MC1R "R"	MC1R	"R"	1.227 (0.782-1.927)	0.373
39	MC1R "r"	MC1R	"r"	1.182 (0.843-1.657)	0.332
40	rs9904341	BIRC5	C	0.984 (0.727-1.332)	0.918
41	rs7121	GNAS1	T	1.244 (0.928-1.668)	0.144
42	rs132770	XRCC6	A	0.913 (0.599-1.392)	0.674

Supplementary Table 4. Results of association logistic regression analysis between ccRCC status and single polymorphisms. Significant results marked with bold.

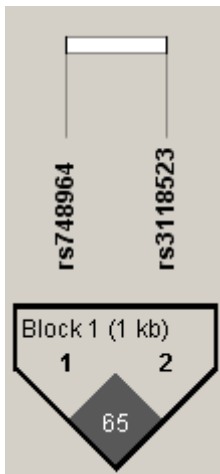
* OR – the allelic odds ratio for the minor allele; CI - confidence interval

** cs – complete separation of the genotypes

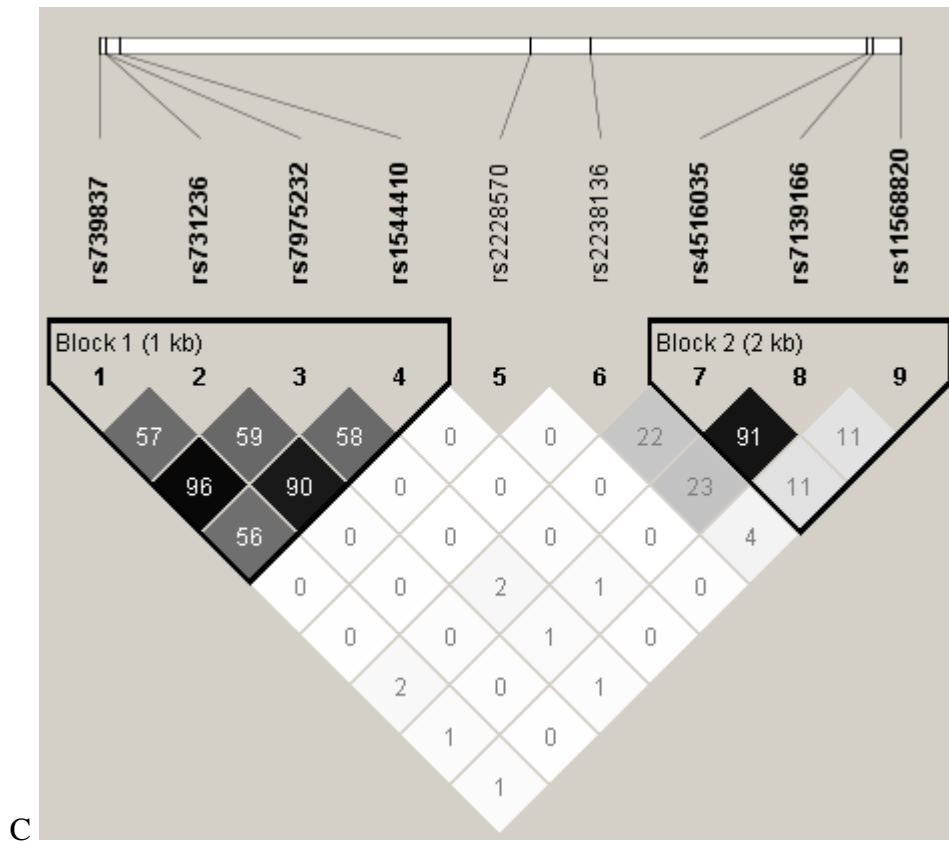
*** dominant model



A



B



Supplementary Figure 1. LD schemes generated with Haploview program for SNPs in *EPASI* (A), *RXRA* (B) and *VDR* (C) genes. Values of r^2 parameter are presented with white colour indicating $r^2=0$, shades of grey representing values of r^2 between 0-1 and black colour indicating complete LD with $r^2=1$. Values of r^2 are given in percentages.