

HUMAN SDR FAMILY VARIANTS

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|---------|--|----------------|
| SDR7C1 | -----MVELMFPLLLLLLPFLLYMAAPQIRKMLSSGVCTSTVQLPGKV | 1p.1 |
| SDR7C2 | -----MLVTLGLLTSFFSFLYMVAPSIKFFAGGVCRTNVQLPGKV | 1p.1 |
| SDR7C3 | -----MSRYLLPLSALGTVAGAAVLLKDYVTGGACPSKATIPGKTV | 1p.1 |
| SDR7C4 | -----MAVATAAAVLALGGALWLAARRFVGPRVQRLRRGGDPGLMHGKTV | |
| SDR7C5 | -----MEALLLGAGLLLGAYVLVYYNLVKAPPCGGMGNLRGRTA | |
| SDR40C1 | -----MSLYRSVVWFAKGLREYTKSGYESACKDFVPHDLEVQIPGRVF | 1p.1 |
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| SDR7C1 | VVTGANTGIGKETAKELAQRGARVYLACRDVEKGELVAKEIQTT-----TGN | 2p.2 |
| SDR7C2 | VITGANTGIGKETARELASRGARVYIACRDVLKGESAASEIRVD-----TKN | 2p.2 |
| SDR7C3 | IVTGANTGIGKQTALELARRGGNIIACRDMEKCEAAAKDIRGE-----TLN | 2p.2 |
| SDR7C4 | LITGANSGLGRATAAELLRLGARVIMGCRDRARAEAAAGQLRRELQAAECGPEPGVSGV | |
| SDR7C5 | VVTGANSIGIKMTALELARRGARVVLACRSQERGEAAAFDLRQE-----SGN | 1p.2 2p.0 |
| SDR40C1 | LVTGGNSGIGKATALEIAKRGGTVHLVCRDQAPAEARGEIIRE-----SGN | 2p.2 |
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| SDR7C1 | QQVLVRKLDLSDTKSIRAFAGFLAEKHLHVLINNAGVMMCPYSKTADGFEMHIGVNH | 3p.2 4p.2 |
| SDR7C2 | SQVLVRKLDLSDTKSIRAFAGFLAEKQLHILINNAGVMMCPYSKTADGFETHLGVNH | 3p.2 4p.2 |
| SDR7C3 | HHVNARHLDLASLKSIREFAAKIIEEERVDILINNAGVMRCPHWTTEDGFEMQFGVNH | 3p.2 4p.2 |
| SDR7C4 | GELIVRELDLASLRSVRAFQCEMLQEPRLDVLINNAGIFQCPYMKTEDGFEMQFGVNH | 1p.0 |
| SDR7C5 | NEVIFMALDLASLASVRAFATAFLSSEPRLDILIHNAAGISSCG--RTREAFNLLLRVNH | 3p.2 |
| SDR40C1 | QNIFLHVLDLSDPKQIWKFFVENFKQ-EHKLHVLINNAGCMVNKRELTEDGLEKNFAANT | 3p.0 4p.0 5p.2 |
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| SDR7C1 | GHFLLTHLLEKLKESAPSRIVNVSSLAHHLGRIHFHNLQG-EKFYNA-GLAYCHSKLAN | |
| SDR7C2 | GHFLLTYLLERLKVSAAPRVNVSSVAHHIGKIPFHDLQS-EKRYSR-GFAYCHSKLAN | |
| SDR7C3 | GHFLLTNLLLDKLKASAPSRIINLSSLAHVAGHIDFDDLNWQTRKYNT-KAAYCQSKLAI | |
| SDR7C4 | GHFLLTNLLGLLKSSAPSRIVVSSKLYKYGDINFDDLNS-EQSYNK-SFCYSRSKLAN | |
| SDR7C5 | GPFLTHLLLPCLKACAPSRVVVASAAHCRGRDLDFKRLDRPVVGWRQELRAYADTKLAN | |
| SDR40C1 | GVYILTGLIPVLEKEHDPVITVSSGGMLVQKLNNTDLQSQERTPFDG-TMVYAQNKRQQ | 6p.0 7p.0 |
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| SDR7C1 | ILFTQELARRLKGSGVTTYSVHPGTVQSELVRHSSFMRWM-----WWLFSFFIKTPQQG | 5p.2 |
| SDR7C2 | VLFTRELAKRLQGTGVTYAVHPGVVRSELVRHSSLLCLL-----WRLFSFVKTAREG | 5p.2 |
| SDR7C3 | VLFTKELSRRLQSGVTVNALHPGVARTELGRHTGIHGSTFSSTTLGPIFWLLVKSPELA | 5p.2 6p.2 |
| SDR7C4 | ILFTRELARRLEGNTVNVLHPGIVRTNLGRHIHPLLV--KPLFNLVSWAFFKTPVEG | |
| SDR7C5 | VLFARELANQLEATGVTCYAAHPGPVNSELF--RHVPGWL--RPLLRPLAWLVLRAPRG | 4p.2 |
| SDR40C1 | VVLTERWAQGHP--AIHFSSMHPGWADTPGVRQ-----AMPGFHARFGDRLRSEAQG | 8p.2 |
| | | *** |
| SDR7C1 | AQTSLHCALTEG-LEILSGNHFSCHVAWVS-AQARN---ETIARRLWDVSCDLLGLPID | 6p.1 |
| SDR7C2 | AQTSLHCALAEGLPLSGKYFSDCKRTWVS-PRARN---NKTAERLWNVSCCELLGIRWE | 6p.1 |
| SDR7C3 | AQPSTYLAVAAE-LADVSGKYFDGLKQKAPA-PEAD---EEVARRLWAESARLVGLEAP | |
| SDR7C4 | AQTSIYLASSE-VEGVSGRYFGDCKEELL-PKAMD---ESVARKLWDISEVMVGLLK- | |
| SDR7C5 | AQTPLYCALQEG-IEPLSGRYFANCHVEEVP-PAARD---DRAAHLWEASKRLAGLGPG | |
| SDR40C1 | ADTMLWLALSSAAAQPSGRFFQDRKPVSTHLPLATASSSPAEEKLEIEQLAQTFK- | 9p.2 |
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SDR7C1      -----
SDR7C2      -----
SDR7C3      SVREQPLPR-----
SDR7C4      -----
SDR7C5      EDAEPDEDPQSEDSEAPSSLSTPHPEEPTVSQPYPSQPSSPDLSKMTHRIQAKVEPEIQLS
SDR40C1      -----

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Figure S1. Alignment of the human SDR7C family and of SDR40C1 protein variants. × and + symbols mark the structure consensus and the catalysis consensus respectively; the couples of amino acid symbols in red lowercase mark the splicing-site positions. Splicing sites are progressively numbered and phase (p.) type is indicated after the splicing-site number. * symbol marks the position of identical amino acid residues of the aligned SDR protein sequences.

| | | |
|---|--|-----------|
| SDR9C1 | -----MLA-----TRLSRPLSRLP---GKTLSACDRENGA rr PL | 1p.1 |
| SDR9C2 | --MSTFFSDTAWICLAVPTVLCGTVFCKYKKSSGQLWSWMVCLAGLCAVCLLLILSPFWGL | |
| SDR9C3 | MERWPPWPSGGAWLLVAARALLQL--LRSDLRLGRPLLAALALLAALDWLCQRLLPFPAL | |
| SDR9C4 | -----MLFWVL- | |
| SDR9C5 | -----MWLPL | |
| SDR9C6 | -----MWLYL | |
| SDR9C7 | -----M | |
| SDR9C8 | -----MWLYL | |
| <div style="text-align: center;"> × × × </div> | | |
| SDR9C1 | LLGS-TSFIPIGRRTYASAAE PV GSKAVLVTGCDSGFGFSLAKHLHSGFLVFAGCLM KD | 2p.0 3p.0 |
| SDR9C2 | ILFSVSCFLMYTYLSGQ-ELLPVDQKAVLV TG GDGCLGHALCKYLDLGFTVFAGVLNEN | 1p.2 |
| SDR9C3 | AVLAAAGWIALSRLARP-QRLPVATRAVL ITG CDSGFGKETAKKLDSMGFTVLATVLELN | 1p.2 |
| SDR9C4 | --GLLLCGFLWTRKGKLIKIEDITDKYIFITGCDSGFGNLAARTFDKKGFHVIAACLTE- | |
| SDR9C5 | LLGA-LLWAVLWLLRDR-QSLPASNAFVFITGCDSGFGRLALQLDQGRFVLASCLTP- | |
| SDR9C6 | AAFGVGLYLLHWYRERQ-VVSHLQDKYVFITGCDSGFGNLLARQLDARGLRVLAACLTE- | |
| SDR9C7 | AALTDLSFMYRWFKNCN-LVGNLSEKYVFITGCDSGFGNLLAKQLVDRGMQVLAACFTE- | |
| SDR9C8 | AVFVGLYLLHWYRERQ-VLSHLRDKYVFITGCDSGFGKLLARQLDARGLRVLAACLTE- | |
| <div style="text-align: center;"> * * * * * * * * </div> | | |
| SDR9C1 | KGHDGVKELDSLNSDRLRTVQLNVCSSEEVEKVVVEIVRSSLKDPE KG MWGLVNNAGIST- | 4p.2 |
| SDR9C2 | --GPGAEELRRTCSPRLSVLQMDITKPVQIKDAYSKVAAML--QD RGL WAVINNAGVLGF | 2p.2 |
| SDR9C3 | --SPGAIELRTCCSPRLRLQLMDLTKPGDISRVLEFTKAHT--TS TGL WGLVNNAGHNEV | 2p.2 |
| SDR9C4 | ---SGSTALKAETSERLRTVLLDVTDPENVKRTAQWVKNQV--GE KGL WGLINNAGVPGV | 1p.2 |
| SDR9C5 | ---SGAEDLQRVASSRLHTTLLDITDPQSVQQAQWVEMHV--KE AGL FGLVNNAGVAGI | 1p.2 |
| SDR9C6 | ---KGAEQLRGQTSRLETVTLDTVKMESIAAATQWVKEHV--GD RGL WGLVNNAGILTP | 1p.2 |
| SDR9C7 | ---EGSQKLQRDTSYRLQTTLLDVTKSESIAAAQWVRDKV--GE QGL WALVNNAGVGLP | 1p.2 |
| SDR9C8 | ---KGAEQLRGQTSRLETVTLDTVKTESVAAAAQWVKECV--RD KGL WGLVNNAGISLP | 1p.2 |
| <div style="text-align: center;"> * * * * * * * * * * </div> | | |
| <div style="text-align: center;"> + </div> | | |
| SDR9C1 | FGEVEFTSLETYKQVAEVLNLTGTVRMTKSFLPLIRRA KGR VVNISMLGRMANPARSPYC | 5p.2 |
| SDR9C2 | PTDGEILLMTDYKQCMVNFVFGTVEVTKTFLPLLRKSKGRLVNVSSM GGG APMERLASYG | 3p.2 |
| SDR9C3 | VADAELSPVATFRSCMEVNFFGALELTGKLLPLLRSSRGRIVTVGSP AGD MPYPCLGAYG | 3p.2 |
| SDR9C4 | LAPTDLWTLEDYREPIEVNLFGLISVTLNMLPLVKKAQGRVINVSSVGGRLAIV-GGGYT | |
| SDR9C5 | IGPTPWLTRDDFQRLNVNTMGPIGVTLALLPLLQARGRVINITSVLGRLAAN-GGGYC | |
| SDR9C6 | ITLCEWLNTEDSMNMLKVNLIQVITLSMLPLVRRARGRIVNVSSILGRVAFF-VGGYC | |
| SDR9C7 | SGPNELWTKDDFVKVINVNVLGLIEVTLHMLPMVKRARGRVVNMSSSGGRVAVI-GGGYC | |
| SDR9C8 | TAPNELLTQDFVTILDVNLLGVIDVTLSSLPLVRRARGRVVNSSVMGRVSLF-GGGYC | |
| <div style="text-align: center;"> * * * * * * * * * * * </div> | | |
| <div style="text-align: center;"> + </div> | | |
| SDR9C1 | ITKFGVEAFSDCLRYEMYPLGVKVSVEPGNFIAATSLYSPESIQAIAKKMWEELPEVVR | |
| SDR9C2 | SSKAAVTMFSSVMRLELSKWGIKVASIQPGGF TN -IAGTSDKWEKLEKDILDHLP AEVQ | 4p.2 |
| SDR9C3 | TSKAAVALLMDTFSCCELLPWGVKVSIIQPGCFK TE -SVRNVGQWEKRQLLLNLPPQELL | 4p.2 |
| SDR9C4 | PSKYAVEGFNDSL RR DMKAFGVHVSCEIEPGLFKT--NLADPVKVIEKKLAIWEQLSPDIK | 2p.1 |
| SDR9C5 | VSKFGLAEFSDSL RR VAHFGIRVSVIEPGFFRT--PVTNLESLEKTLQACWARLPATQ | 2p.1 |
| SDR9C6 | VSKYGVAEFSDIL RR EIQHFGVKISIVIEPGYFRT--GMTNMTQSLERMQSWKEAPKHIK | 2p.1 |
| SDR9C7 | VSKFGEAFSDSI RR ELYFVGKVCIEPGNYRT--AILGKENLESRMKRLWERLPQETR | 2p.1 |
| SDR9C8 | ISKYGVAEFSDSL RR ELSYFGVKVAMIEPGYFKT--AVTSKERFLKSFLIWDRSSPEVK | 2p.1 |
| <div style="text-align: center;"> * * * * </div> | | |

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|--------|---|------|
| SDR9C1 | KDYGKKYFDEKIAKMET-YCSSGSTDTSFVIDAVTHALTATTPYTRYHPMDYYWWLRM-- | |
| SDR9C2 | EDYGQDYILAQRNFLLL-INSLASKDFSPLVRDIQHAILAKSPFAYYTPGKGAYLWIC-- | |
| SDR9C3 | QAYGKDYIEHLHGQFLH-SLRLAMSDLTPVVDAITDALLAARPRRRYYPQGGLGLMYF-- | |
| SDR9C4 | QQYGEGYIEKSLDKLKG-NKSYVNMDLSPVVECMDHALTSLFPKTHYAAGKDAKIFWI-- | 3p.2 |
| SDR9C5 | AHYGGAFLTKEYLKMQRIMNLICPDLTKVSRCLEHALTARHPRTRYSPGWDAKLLWL-- | 3p.2 |
| SDR9C6 | ETYGQQYFDALYNIMKE-GLLNCSTNLNLVTDCEHALTSVHPRTRYSGWDAKFFFI-- | 3p.2 |
| SDR9C7 | DSYGEDYFRIYTDKLN-IMQVAEPRVRDVINSMEHAIVSRSPRIRYNPGLDAKLLYI-- | 3p.2 |
| SDR9C8 | EAYGEKFVADYKKSAEQ-MEQKCTQDLSLVTNCMEHALIACHPRTRYSGAWDAKLLYL-- | 3p.2 |
| | <div style="display: flex; justify-content: space-around; width: 100%;"> ** * * * * </div> | |

Figure S2. Alignment of the human SDR9C family protein variants. For further details see Fig. S1.

* symbol marks the position of identical amino acid residues of the aligned SDR protein sequences.

| | | |
|---------|---|----------------|
| SDR10E1 | MVSIPEYYEGKNVLLTGATGFLGKVLEKLLRSCPKVNSVYVLVRQKAGQTPQERVEEVL | |
| SDR10E2 | MSTIAAFYGGKSILITGATGFLGKVLMEKLFRTSPDLKVIYIILVRPKAGQTLQQRVFQIL | |
| | * * * * * | |
| SDR10E1 | SGKLFDRLRDENPDFREKIIAINSELTQPKLALSEEDKEVIDSTNIIFHCAATVRFNEN | 1p.0 |
| SDR10E2 | DSKLFKFEKVKEVCPNVHEKIRAIYADLNQNDFAISKEDMQELLSCTNIIFHCAATVRFDDT | 1p.0 |
| | *** * * * * | |
| SDR10E1 | L RD AVQLNVIATRQLLILLAQQMKNLEVFMHVSTAYAYCNRKHIDEVVYPPVPDPKKLIDS | 2p.1 |
| SDR10E2 | L RH AVQLNVTATRQLLLMASQMPKLEAFIHISTAYSNCNLKHIDEVIYPCVPEPKKIIDS | 2p.1 |
| | ** * * * * * * * * * * | |
| | + + | |
| SDR10E1 | L EW MDDGLVNDITPKLIGDRPNTYIYTKALA EYVVQQEGAKLNVAIVRPSIVGASWKEPF | 3p.1 |
| SDR10E2 | L EW LDDAIIDEITPKLIRDWPNIYTYTKALGEMVVQQESRNLNIAIIRPSIVGATWQEPF | 3p.1 |
| | *** ** * * * * * | |
| SDR10E1 | PGWIDNFGPSGLFIAAGKGILRTIRASNNALADLVPDVVVNMSLAAAWYSGVNRPRNI | 4p.0 5p.0 6p.1 |
| SDR10E2 | PGWVDNNGPNGIIIIATGKGFLRAIKATPMAVADVIPVDTVNNLMLAVGWYTAVH RP KST | 4p.0 5p.0 6p.1 |
| | *** ** * * * * * | |
| SDR10E1 | MVYNCTTGSTNPFHWGE VE YHVISTFKRNPLEQAFRRPNVNLTSNHLLYHYWIAVSHKAP | 7p.2 |
| SDR10E2 | LVYHITSGNMNPCNWHK MG VQVLATFEKIPFERPFRRPANFTSNSFTSQYWNAVSHRAP | 7p.2 |
| | ** * * * * | |
| SDR10E1 | AFLYDIYLRMTGRSP RM MKTITRLHKAMVFLEYFTSNSWVWNTENVNMLMNQLNPEDK KT | 8p.1 9p.0 |
| SDR10E2 | AIIYDCYLRLTGRKP RM TKLMNRLLRTVSMLEYFINRSWEWSTYNTEMLMSELSPEDQ RV | 8p.1 9p.0 |
| | * * * * * | |
| SDR10E1 | FNIDVRQLHWA EYIENYCLGTTKKYVLNEEMSGLPAARKHLN KL RNIRYGFNTILVILIWR | 10p.1 |
| SDR10E2 | FNFDVRQLNWLEYIENYVLGVKKYLLKEDMAGIPKAKQRLK R LNIHYLFNTALFLIAWR | 10p.1 |
| | ** * * * * | |
| SDR10E1 | IFIARSQMARNIWFVVS L CYKFLSYFRASSTMR Y | |
| SDR10E2 | LLIARSQMARNVWFFIVSFCYKFLSYFRASSTLKV | |
| | ***** * * * | |

Figure S3. Alignment of the human SDR10E protein variants. For further details see Fig. S1.

* symbol marks the position of identical amino acid residues of the aligned SDR protein sequences.

| | | | |
|---------|--|-----------------------------------|-----------|
| | | x x x | |
| SDR11E1 | -----MTGWSCLVTGAGGFLGQRIIRLLV-KEKELKEIRVLDKAFGPPELREEF | SKLQNK | 1p.1 |
| SDR11E2 | -----MGWSCLVTGAGLLGQRIVRLLV-EEKELKEIRALDKAFRPPELREEF | SKLQNR | 1p.1 |
| SDR11E3 | MADSAQAQKLVLVTGGCGFLGEHVVRMLLQREPRLGELRVFDQHLGPWLEELK | TGP--- | 1p.1 |
| | **** * * * * * | | |
| SDR11E1 | TKLTVLEGDILDEPFLKRACQDVSVIHTACIIDVFGVTHRESIMNVNV | KGTQLLLEACV | 2p.1 |
| SDR11E2 | TKLTVLEGDILDEPFLKRACQDVSVIHTACIIDVFGVTHRESIMNVNV | KGTQLLLEACV | 2p.1 |
| SDR11E3 | VRVTAIQGDVTQAHEVAAAVAGAHVVIHTAGLVDVFGRASPKTIHEVNV | QGRNVIEACV | 2p.1 |
| | * * * * * * * * * * * * * * * * | | |
| | | + + | |
| SDR11E1 | QASVPVFIYTSSIEVAGPNSYKEIIQNGHEEEPLENTWPAPYPHSHKLAEKAVLAANGWN | | |
| SDR11E2 | QASVPVFIYTSSIEVAGPNSYKEIIQNGHEEEPLENTWPTPYPSKKLAEKAVLAANGWN | | |
| SDR11E3 | QTGTRFLVYTSSMEVVGPNKTHGHPFY | RGNEDTPYEAVHRHPYPCSKALAEWLVEANGRK | 3p.2 4p.0 |
| | * * * * * * * * * * * * * * * * * | | |
| SDR11E1 | LKNGGTLTYTCALRPMYIYGEGRFSLASINEALNNNGILS-SVGKFSTVNPVYVGNVAWA | | |
| SDR11E2 | LKNGDTLYTCALRPTYIYGEGRFPFLASINEALNNNGILS-SVGKFSTVNPVYVGNVAWA | | |
| SDR11E3 | VRGGLPLVTCALRPTGIYGEGRHQMIRDFYRQGLRLGGWLFRAIPASVEHGRVY | VGNVAMM | 5p.1 |
| | * * * * * * * * * * * * * * * * * | | |
| SDR11E1 | HILALRALQDPKKAPSIRGQFYIISDDTPHQSYDNLNYTSLKEFGLRLDSRW-SFPLSLM | | |
| SDR11E2 | HILALRALRDPKKAPSVRGQFYIISDDTPHQSYDNLNYILSKEFGLRLDSRW-SLPLTLM | | |
| SDR11E3 | HVLAARELEQ--RATLMGGQVYFCYDGPYRSYEDFNMEFLGPCGLRLVGARPLLPLYWLL | | |
| | * * * * * * * * * * * * * * * * * * | | |
| SDR11E1 | YWIGFLEIVSFLLRPIYTYRPPFNRHIVTSLNSVFTFSYKKAQRDLAYKPLYSWEEAKQ | | |
| SDR11E2 | YWIGFLEVVSFLLSPIYSYQPPFNRHTVTLSNSVFTFSYKKAQRDLAYKPLYSWEEAKQ | | |
| SDR11E3 | VFLAALNALLQWLLRPLVLYAPLLNPYTLAVANTTFTVSTDKAQRHFGYEPLFSWEDSRT | | |
| | * * * * * * * * * * * * * * | | |
| SDR11E1 | KTVEWVGSLVDRHKETLKSQTQ | | |
| SDR11E2 | KTVEWVGSLVDRHKETLKSQTQ | | |
| SDR11E3 | RTILWVQAATGSAQ----- | | |
| | * * * | | |

Figure S4. Alignment of the human SDR11E protein variants. For further details see Fig. S1.

* symbol marks the position of identical amino acid residues of the aligned SDR protein sequences.

| | | | |
|---------|---|------|---|
| | x | x | x |
| SDR21C1 | MSSGIHVALVTGGNKGIGLAIVRDLCRLFSGDVVLTARDVTRGQAAVQQQLQAEGLSPRFH | | |
| SDR21C2 | MSSCSRVALVTGANRGIGLAIARELCRFSGDVVLTARDVARGQAAVQQQLQAEGLSPRFH *** ***** * ***** * | | |
| | | | |
| SDR21C1 | QLDIDDLQSIRALRDFLRKEYGGDLVLNNAGIAFKVADPTPFHIQAEVTMKTNFFGTRD | 1p.1 | |
| SDR21C2 | QLDIDDLQSIRALRDFLRKEYGGNLVLNNAAVAFKSDDPMPFDIKAEMTLKTNFFATRNV ***** ***** ** ** ** * | 1p.1 | |
| | | | |
| SDR21C1 | VCTELLPLIKPQGRVVNVSSIMSVRALKSCSPELQQKFRRSETITEEELVGLMNKFVEDTK | 2p.1 | |
| SDR21C2 | MCNELLPIMKP HGRVVNISSLQCLRAFENCSEDLQERFHFSETLTEGDVLMDMKKFVEDTK * **** * * * | 2p.1 | |
| | | | |
| | | | |
| SDR21C1 | KGVHQKEGWPSAYGVTKIGVTVLSRIHARKLSEQRKDGDKILLNACCPGWVRTDMAGPKA | | |
| SDR21C2 | NEVHEREGWPNSPYGVSKLGVTVLSRILARRLDEKRKADRILVNACCPGPVKTDMDGKDS ** **** * * ***** ** * * ** * ***** * * | | |
| | | | |
| | | | |
| SDR21C1 | TKSPEGGAETPVYLALLPPDAEGPHGQFVSEKRVEQW | | |
| SDR21C2 | IRTVEEGAETPVYLALLPPDATEPQGQLVHDKVQNW ***** * * * * | | |

Figure S7. Alignment of the human SDR21C protein variants. For further details see Fig.S1.

* symbol marks the position of identical amino acid residues of the aligned SDR protein sequences.

| | | |
|-------------|---|-----------|
| SDR25C1Homo | MLSAVARGYQGWFHPCARLSVRMSSTGIDRKGVLANRVAVVTGSTSgiGFAIARRLARDG | 1p.1 |
| SDR25C2Homo | MHKAGLLGLCA----RAWNSVRMASSGMTRRDPLANKVALVTASTDgiGFAIARRLAQDG | 1p.1 |
| | * * * * * | |
| SDR25C1Homo | AHVVISSRKQQNVDRAMAKLQGEGLSVAGIVCHVGKAEDREQLVAKALEHCGGVDFLVCS | 2p.0 |
| SDR25C2Homo | AHVIVSSRKQQNVDAQAVATLQGEGLSVTGTVCHVGKAEDRERLVAtaVKLHGGIDILVSN | 2p.0 |
| | **** * | |
| SDR25C1Homo | AGVNPLVGSTLGTSEQIWDkiLSVNVKSPALLSQLLPYMEN-rrGAVILVSSIAAYNPV | 3p.0 4p.1 |
| SDR25C2Homo | AAVNPFFGSIMDVTEEVDktLDINVKAPALMTKAVVPEMEKRggGSVVIVSSIAAFSPS | 3p.0 4p.1 |
| | * * * * * | |
| | + + | |
| SDR25C1Homo | vaLGVYNVSKTALLGLTRTLALELAPKDIRVNCVVPGIKTDfSKvf-HGNESLWKNFKE | 5p.0 6p.0 |
| SDR25C2Homo | pgFSPYNVSKTALLGLTKTLAIELAPRNIRVNCLAPGLIKTSFSRml-WMDKEKEESMKE | 5p.0 6p.0 |
| | ***** * | |
| SDR25C1Homo | HHQLQriGESEDCAGIVSFLCSPDASYVNGENIAGYSTRL- | 7p.1 |
| SDR25C2Homo | TLRIRrlGEPEDCAGIVSFLCSEDASYITGETVVVGGGTPSRL | 7p.1 |
| | * * * * * | |

Figure S8. Alignment of the human SDR25C protein variants. For further details see Fig. S1 and Table S8.

* symbol marks the position of identical amino acid residues of the aligned SDR protein sequences.

| | | | |
|---------|--|-------|-------|
| SDR42E1 | ----- | | |
| SDR42E2 | MKSNPPRSSLEACKAAGQGEKSCPVCQACGEVSGPRSGSGSESRPAPKPGAIPGPGLGPK | | |
| SDR42E1 | ----- | | |
| SDR42E2 | AIPGPQAGSGTVPRPGAISGTGPGLGPGPGAGSVPGPGAGSVPLGARSVPGPAGSVPG | | |
| SDR42E1 | ----- | | |
| SDR42E2 | PGAGSVPGPGAGSVPGPGAGSGPGLGGGLGPGVGAGPGAGSVPGPGAGSVPGPGAGSVPG | | |
| SDR42E1 | -----MDPKRSQKESV | | |
| SDR42E2 | PGAGSVPGAGAGSTPEPELGPGLRQSGTGPRPSESTTTPTPAPQQKTQAKPTKAARQKV | | |
| | | * | * |
| | x x x | | |
| SDR42E1 | LITGGSGYFGFr1GCALNQNGVHVILFDISSPAQTIPEGIKFIQGDIRHLSDVEKAFQDA | 1p.1 | |
| SDR42E2 | LVTGGGGYLGFSLGSHLAKSGTSVILLDRRRPQWELSPETKFIqadVRDEEALYRAFE-- | 1p.2 | |
| | * * * * * | | |
| SDR42E1 | DVTCVFHIASYGMMSGREQLNRNLIKEVNVGRGTDNIIQVCQRRRVPRLVYTSTFNVIFGGQ | | |
| SDR42E2 | GVDCVFHVASYGMSGAEk1QKEQIESINVGGTKLVIDvCVRRRVPRLIYTSTVNVAFGGK | 3p.0 | 4p.2 |
| | * * * * * | | |
| | + + | | |
| SDR42E1 | VIRNGD-ESLPYLPLHLHPDHYSRTKSIAEQKVLEANATPLDRGDGVLRTCALRPAGIYG | | |
| SDR42E2 | PIEQGDEDSVPYFPLDehVDHYSRTKAIADQLTLMANGMPL-pgGGTLRTCVLRPPGIYG | 5p.0 | 6p.2 |
| | * * * * * | | |
| SDR42E1 | PGEQRHLPRIVSYIEKGLFKFVYGDPRSLVEFVHVDNLVQAHILASEALRADKGHIASGQ | | |
| SDR42E2 | PEEQRHLPRVagHIKKRLFMFRFGDHKARMNWVHVHNLVQAHVLAEEALTTAKGYVasGQ | 7p.0 | 8p.0 |
| | * * * * * | | |
| SDR42E1 | PYFISDGRPVNNFEFFRPLVEGLGYTFPSTRLPLTLVYCAFLTEMVHFILGRLYNFQPF | | |
| SDR42E2 | AYYINDGESVNLFEWMAPlfEKLGYSPWQIVPTSWWYItaAVMERLHLALRPICSLPPL | 9p.0 | 10p.2 |
| | * * * * * | | |
| SDR42E1 | LTRTEVYKTVGTHYFSLEKAKKELGYKAQPFDLQEAVEWFKAHGHRSSGSRDSECFVW- | | |
| SDR42E2 | LTRSevRSVAVTHTFQIAKARAQLGYAPDKFRFADAVELYVQSTTRRPRGSTARTLLRLL | 11p.0 | |
| | * * * * * | | |
| SDR42E1 | DGLLVFLLIIAVLM-WLPSSVILS----L | | |
| SDR42E2 | LRLLFLGLLALHFLGLQPLHAAVERL | | |
| | * * * * | | |

Figure S12. Alignment of the human SDR42E protein variants. For further details see Fig. S1.

* symbol marks the position of identical amino acid residues of the aligned SDR protein sequences.

| Family symbol and name | Enzyme symbol | Gene symbol | Gene ID | Chr | Exon number | Phase formula | aa n. | Structure consensus | Catalysis consensus |
|---|---------------|-------------|---------|-----|-------------|---------------|-------|---------------------|---------------------|
| SDR7C Retinol dehydrogenase | SDR7C1 | RDH11 | 51109 | 14 | 7 | 122221 | 318 | GANTGIG | YCHSK |
| | SDR7C2 | RDH12 | 145226 | | | | 316 | | |
| | SDR7C3 | RDH13 | 112724 | 19 | 7 | 122222 | 331 | | |
| | SDR7C4 | RDH14 | 57665 | 12 | 2 | 0 | 336 | GANSGLG | YSRSK |
| | SDR7C5 | DHRS13 | 147015 | 17 | 5 | 2022 | 377 | GANSGLG | YADTK |
| SDR40C Dehydrogenase/reductase SDR family | SDR40C1 | DHRS12 | 79758 | 13 | 10 | 120020022 | 317 | GGNSGIG | YAQNK |

Table S3a. Genetic and molecular data of the human SDR7C family and of the human SDR40C1 protein variants. Chr, chromosome; Phase formula contains phase type symbols aligned according to the sequence of their relative splicing sites; conserved amino acids of the consensus sequences are in red; aa n., number of the variant polypeptide amino acids.

| | % Identity | | | | |
|---------|------------|--------|--------|--------|--------|
| | SDR7C1 | SDR7C2 | SDR7C3 | SDR7C4 | SDR7C5 |
| SDR7C2 | 71.66 | | | | |
| SDR7C3 | 49.68 | 48.87 | | | |
| SDR7C4 | 46.15 | 46.47 | 48.88 | | |
| SDR7C5 | 45.78 | 46.41 | 42.32 | 44.48 | |
| SDR40C1 | 32.54 | 33.22 | 30.64 | 31.21 | 28.23 |

Table S3b. The relative percent identity of the human SDR7C family and of the human SDR40C1 protein variants.

| Family symbol and name | Enzyme symbol | Gene symbol | Gene ID | Chr | Exon s | Phase formula | aa n. | Structure consensus | Catalysis consensus |
|---|---------------|-------------|---------|-----|--------|---------------|-------|---------------------|---------------------|
| SDR11E 3beta-hydroxysteroid dehydrogenase | SDR11E1 | HSD3B1 | 3283 | 1 | 3 | 22 | 375 | GAGGFLG | YPHSK |
| | SDR11E2 | HSD3B2 | 3284 | | | | 372 | GAGLLG | YPYSK |
| | SDR11E3 | HSD3B7 | 80270 | 16 | 6 | 22201 | 369 | GGCGFLG | YPCSK |

Table S4a. Genetic and molecular data of the human SDR11E family protein variants. For further details see Table S3a.

| | % Identity | |
|---------|------------|---------|
| | SDR11E1 | SDR11E2 |
| SDR11E2 | 93.55 | |
| SDR11E3 | 38.61 | 39.00 |

Table S4b. Relative percent identity of the SDR11E family protein variants.

| Family symbol and name | Enzyme symbol | Gene symbol | Gene ID | Chr | Exons | Phase formula | % identity | aa | Structure consensus | Catalysis consensus |
|--|---------------|-------------|---------|-----|-------|---------------|------------|-----|---------------------|---------------------|
| SDR10E Fatty acyl-CoA dehydrogenase | SDR10E1 | FAR1 | 84188 | 11 | 11 | 0110012101 | 59.03% | 515 | GATGFLG | YIYTK |
| | SDR10E2 | FAR2 | 55711 | 12 | | | | | GATGFLG | YTYTK |

Table S5. Genetic and molecular data of the human SDR10E family protein variants. For further details see Table S3a.

| Family | Enzyme symbol | Gene Symbol | Gene ID | Chr | Exons n. | Phase formula | aa n. | Structure consensus | Catalysis consensus |
|--|---------------|-------------|---------|-----|----------|---------------|-------|---------------------|---------------------|
| SDR9C Steroid and retinol dehydrogenase | SDR9C1 | BDH1 | 622 | 3 | 6 | 10022 | 343 | GCDSGFG | YCITK |
| | SDR9C2 | HSD17B2 | 3294 | 16 | 5 | 2222 | 387 | GGDCGLG | YGSSK |
| | SDR9C3 | HSD11B2 | 3291 | | | | 405 | GCDSGFG | YGTSK |
| | SDR9C4 | DHRS9 | 10170 | 2 | 4 | 212 | 319 | GCDSGFG | YTPSK |
| | SDR9C5 | RDH5 | 5959 | 12 | | | 317 | | YCVSK |
| | SDR9C6 | HSD17B6 | 8630 | | | | 313 | | |
| | SDR9C7 | SDR9C7 | 121214 | | | | 317 | | |
| | SDR9C8 | RDH16 | 8608 | | | | | | |

Table S6a. Genetic and molecular data of the human SDR9C family protein variants. For further details see Table S3a.

| | % Identity | | | | | | |
|--------|------------|--------|--------|--------|--------|--------|--------|
| | SDR9C1 | SDR9C2 | SDR9C3 | SDR9C4 | SDR9C5 | SDR9C6 | SDR9C7 |
| SDR9C2 | 32.93 | | | | | | |
| SDR9C3 | 32.34 | 38.54 | | | | | |
| SDR9C4 | 35.53 | 28.80 | 29.25 | | | | |
| SDR9C5 | 34.87 | 30.06 | 32.81 | 43.63 | | | |
| SDR9C6 | 38.16 | 32.18 | 32.18 | 44.90 | 49.37 | | |
| SDR9C7 | 36.67 | 31.31 | 30.03 | 44.19 | 47.76 | 50.80 | |
| SDR9C8 | 37.17 | 32.81 | 33.12 | 46.18 | 51.58 | 66.25 | 51.76 |

Table S6b. Relative percent identity of the SDR9C family protein variants.

| Family symbol and name | Enzyme symbol | Gene symbol | Gene ID | Chr | Exons n. | Phase formula | aa n. | Structure consensus | Catalysis consensus |
|------------------------------------|---------------|-------------|---------|-----|----------|---------------|-------|---------------------|---------------------|
| 3beta-hydroxysteroid dehydrogenase | SDR12C1 | HSD17B12 | 51144 | 11 | 11 | 2022001000 | 312 | GSTDGIG | YSATK |
| | SDR12C2 | HSD17B3 | 3293 | 9 | | | 310 | GAGDGIG | YSASK |
| | SDR12C3 | HSDL1 | 83693 | 16 | 4 | 100 | 330 | GATDGIG | ESASK |

Table S7a. Genetic and molecular data of the human SDR12C family protein variants. Phenylalanine (F), diagnostic of the SDR12C3 catalysis consensus, is highlighted in turquoise. For further details see table S3a and Consensuses in Online Resources 1.

| | % Identity | |
|---------|------------|---------|
| | SDR12C1 | SDR12C2 |
| SDR12C2 | 41.67 | |
| SDR12C3 | 40.98 | 35.33 |

Table S7b. Relative percent identity of the SDR12C family protein variants.

| Family Symbol and name | Enzyme symbol | Gene symbol | Gene ID | Chr | Exons | Phase formula | aa n. | Structure consensus | Catalysis consensus |
|---|---------------|-------------|---------|-----|-------|---------------|-------|---------------------|---------------------|
| SDR16C Steroid and retinol dehydrogenase | SDR16C1 | DHRS3 | 9249 | 1 | 6 | 00011 | 302 | GGGRGIG | YCTSK |
| | SDR16C2 | HSD17B11 | 51170 | 4 | 7 | 000111 | 300 | GAGHGIG | YCSSK |
| | SDR16C3 | HSD17B13 | 345275 | | | | | | |
| | SDR16C4 | RDH10 | 157506 | 8 | 6 | 20011 | 341 | GAGSGLG | YCASK |
| | SDR16C5 | SDR16C5 | 195814 | 8 | 6 | 00211 | 309 | | |

Table S8a. Genetic and molecular data of the human SDR17C family protein variants. For further details see Table S3a.

| | % Identity | | | |
|---------|------------|---------|---------|---------|
| | SDR16C1 | SDR16C2 | SDR16C3 | SDR16C4 |
| SDR16C2 | 34.35 | | | |
| SDR16C3 | 32.31 | 63.33 | | |
| SDR16C4 | 36.45 | 40.33 | 39.33 | |
| SDR16C5 | 34.88 | 41.81 | 40.13 | 45.57 |

Table S8b. Relative percent identity of the SDR16C family protein variants.

| Family symbol and name | Enzyme symbol | Gene symbol | Gene ID | Gene name | Chr | Exons | Phase formula | % Identity | aa n. | Structure consensus | Catalysis consensus |
|------------------------------|---------------|-------------|---------|----------------------|-----|-------|---------------|------------|-------|---------------------|---------------------|
| SDR21C Carbonyl reductase | SDR21C1 | CBR1 | 873 | Carbonyl reductase 1 | 21 | 3 | 22 | 71.84% | 277 | GGNKGIG | YGVTK |
| | SDR21C2 | CBR3 | 874 | Carbonyl reductase 3 | | | | | | GANRGIG | YGVSK |

Table S9. Genetic and molecular data of the human SDR21C family protein variants. For further details see Table S3a.

| Family symbol and name | Enzyme symbol | Gene Symbol | Gene ID | Chr | Exons | Phase formula | % identity | aa n. | Structure consensus | Catalysis consensus |
|---|---------------|-------------|---------|-----|-------|---------------|------------|-------|---------------------|---------------------|
| SDR25C Dehydrogenase/reductase SDR family | SDR25C1 | DHRS2 | 10202 | 14 | 8 | 1001001 | 59.27 | 280 | GSTSGIG | YNVSK |
| | SDR25C2 | DHRS4 | 10901 | | | | | 278 | ASTDGIG | |

Table S10. Genetic and molecular data of the human SDR25C family protein variants. Alanine (A), diagnostic of the SDR25C2 structure consensus, is highlighted in turquoise. For further details see Table S3a and Consensuses in Online Resources 1.

| Family symbol and name | Enzyme symbol | Gene Symbol | Gene ID | Chr | Exons | Phase formula | % identity | aa n. | Structure consensus | Catalysis consensus |
|--|---------------|-------------|---------|-----|-------|---------------|------------|-------|---------------------|---------------------|
| SDR26C Corticosteroid 11beta-dehydrogenase | SDR26C1 | HSD11B1 | 3290 | 1 | 6 | 20222 | 41.22 | 292 | GASKGIG | YSASK |
| | SDR26C2 | HSD11B1L | 374875 | 19 | 7 | 202022 | | 315 | GANAGVG | YSAAK |

Table S11. Genetic and molecular data of the human SDR26C family protein variants. For further details see Table S3a.

| Family symbol and name | Enzyme symbol | Gene Symbol | Gene ID | Chr | Exons | Phase formula ¹ | % Id. | aa n. | Structure consensus | Catalysis consensus |
|--|---------------|-------------|---------|-----|-------|----------------------------|-------|-------|---------------------|---------------------|
| SDR28C 17beta-hydroxysteroid dehydrogenase | SDR28C1 | HSD17B1 | 3292 | 17 | 6 | 22210 | 44.12 | 328 | GCSSGIG | YCASK |
| | SDR28C2 | RDH8 | 50700 | 19 | | 22210 | | 331 | | YAASK |

Table S12. Genetic and molecular data of the human SDR28C family protein variants. For further details see Table S3a.

| Family symbol and name | Enzyme symbol | Gene | Gene ID | Chr | Exons | Phase formula | % identity | aa | Structure consensus | Catalysis consensus |
|--|---------------|--------|---------|-----|-------|---------------|------------|-----|---------------------|---------------------|
| SDR32C Dehydrogenase/ Reductase SDR Family | SDR32C1 | DHRS7B | 25979 | 17 | 6 | 110111 | 41.61 | 325 | GATSGLG | YAASK |
| | SDR32C2 | DHRS7C | 201140 | | 11 | 10111 | | 312 | DATSGLG | |

Table S13. Genetic and molecular data of the human SDR32C family protein variants. Asparagine (D), diagnostic of the SDR32C2 structure consensus, is highlighted in turquoise. For further details see Table s3a and Consensuses in Online Resources 1.

| Family symbol and name | Enzyme symbol | Gene symbol | Gene ID | Chr | Exons | Phase formula | aa n. | % identity | Structure consensus | Catalysis consensus |
|-----------------------------|---------------|-------------|-----------|-----|-------|---------------|-------|------------|---------------------|---------------------|
| SDR42E 3-beta-HSD family | SDR42E1 | SDR42E1 | 93517 | 16 | 2 | 1 | 393 | 47.18 | GGSGYFG | YSRTK |
| | SDR42E2 | SDR42E2 | 100288072 | | 12 | 20020200020 | 626 | | GGGGYLG | |

Table S14. Genetic and molecular data of the human SDR42E family protein variants. For further details see Table S3a.