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SUPPLEMENTARY MATERIAL TO

# Impaired local hydrophobicity, structural stability and conformational flexibility due to point mutations in SULT1 family of enzymes

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ProtScale tool[1] has been considered in order to obtain the hydrophobicity profiles of SULT1 enzymes. For this purpose, the Kyte&Doolitle hydrophobicity scale has been chosen as it is widely used for detecting hydrophobic regions in proteins.[2] This hydrophobicity scale contains values that define the hydrophobicity index, i.e., the relative hydrophobicity/hydrophilicity for every amino acid. The more positive the value, the more hydrophobic is the amino acid. In order to generate the hydrophobicity profile, the sequence of the analysed protein is scanned with a sliding window of a given size (the number of amino acids examined at a time to determine a point of hydrophobic character). For every position, the arithmetic mean value of the indexes of amino acids within the window is computed, and that value is attributed to the amino acid in the midpoint of the window. Window sizes of 5-9 amino acids are considered suitable for predicting surface-exposed or buried regions.[1]

TABLE S-I. Hydrophobicity profiles of the SULT1A1 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| Window of 5 amino acids | | | Window f 9 amino acids | | |
|---|---|---|---|---|---|
| | SUlT1A1 WT | SULT1A1*4 (R37Q),<br>SULT1A1*2 (R213H),<br>SULT1A1*3 (M223V) | | SUlT1A WT | SULT1A1*4 (R37Q),<br>SULT1A1*2 (R213H),<br>SULT1A1*3 (M223V) |
| 33 | -0.440 | -0.440 | 33 | -0.767 | -0.656 |
| 34 | -0.840 | -0.840 | 34 | -0.900 | -0.789 |
| 35 | -1.040 | -0.840 | 35 | -1.111 | -1.000 |
| 36 | -1.200 | -1.000 | 36 | -1.922 | -1.811 |

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| | | | | | |
|---|---|---|---|---|---|
| 37 | -2.460 | -2.260 | 37 | -1.111 | -1.000 |
| 38 | -2.260 | -2.060 | 38 | -0.600 | -0.489 |
| 39 | -1.860 | -1.660 | 39 | -0.411 | -0.300 |
| 40 | -0.200 | -0.200 | 40 | 0.000 | 0.111 |
| 41 | 1.020 | 1.020 | 41 | -0.278 | -0.167 |
| | | | | | |
| 209 | 2.360 | 2.360 | 209 | -0.056 | 0.089 |
| 210 | 1.380 | 1.380 | 210 | 0.244 | 0.389 |
| 211 | -0.280 | -0.020 | 211 | 1.100 | 1.244 |
| 212 | 0.260 | 0.520 | 212 | 0.422 | 0.567 |
| 213 | 0.460 | 0.720 | 213 | -0.389 | -0.244 |
| 214 | -0.700 | -0.440 | 214 | -0.389 | -0.244 |
| 215 | -1.320 | -1.060 | 215 | -0.778 | -0.633 |
| 216 | -1.120 | -1.120 | 216 | -0.778 | -0.633 |
| 217 | -1.100 | -1.100 | 217 | -1.122 | -0.978 |
| | | | | | |
| 219 | -1.400 | -1.400 | 219 | -0.011 | 0.244 |
| 220 | -0.140 | -0.140 | 220 | 0.033 | 0.289 |
| 221 | 0.940 | 1.400 | 221 | -0.178 | 0.078 |
| 222 | 1.920 | 2.380 | 222 | -0.144 | 0.111 |
| 223 | 0.380 | 0.840 | 223 | 0.167 | 0.422 |
| 224 | 0.440 | 0.900 | 224 | 0.156 | 0.411 |
| 225 | -0.260 | 0.200 | 225 | 0.000 | 0.256 |
| 226 | -0.800 | -0.800 | 226 | -0.044 | 0.211 |
| 227 | -1.080 | -1.080 | 227 | -0.744 | -0.489 |

TABLE S-II. Hydrophobicity profiles of the SULT1A2 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| Window of 5 amino acids | | | Window f 9 amino acids | | |
|---|---|---|---|---|---|
| | SUlT1A2 WT | SULT1A2*2 (I7T, N235T), SULT1A2*3 (P19L) | | SUlT1A2 WT | SULT1A2*2 (I7T, N235T), SULT1A2*3 (P19L) |
| 5 | 1.160 | 0.120 | 5 | -0.122 | -0.700 |
| 6 | 0.240 | -0.800 | 6 | -0.511 | -1.089 |
| 7 | -1.560 | -2.600 | 7 | -0.300 | -0.878 |
| 8 | -1.180 | -2.220 | 8 | -0.300 | -0.878 |
| 9 | -0.800 | -1.840 | 9 | -1.189 | -1.767 |
| 10 | -0.940 | -0.940 | 10 | -0.944 | -1.522 |
| 11 | -1.480 | -1.480 | 11 | -0.089 | -0.667 |
| 12 | -0.840 | -0.840 | 12 | -1.022 | -1.022 |
| 13 | 0.320 | 0.320 | 13 | -0.978 | -0.978 |
| | | | | | |
| 15 | -0.980 | -0.980 | 15 | -0.011 | 0.589 |
| 16 | 0.560 | 0.560 | 16 | 0.589 | 1.189 |
| 17 | 0.500 | 1.580 | 17 | 0.667 | 1.267 |

| | | | | | |
|---|---|---|---|---|---|
| 18 | 0.420 | 1.500 | 18 | 0.622 | 1.222 |
| 19 | 2.100 | 3.180 | 19 | 0.622 | 1.222 |
| 20 | 1.400 | 2.480 | 20 | 0.467 | 1.067 |
| 21 | 0.300 | 1.380 | 21 | 1.100 | 1.700 |
| 22 | 1.180 | 1.180 | 22 | 0.756 | 1.356 |
| 23 | 0.780 | 0.780 | 23 | 0.489 | 1.089 |
| | | | | | |
| 231 | -1.320 | -1.320 | 231 | -1.722 | -1.411 |
| 232 | -2.660 | -2.660 | 232 | -1.822 | -1.511 |
| 233 | -2.580 | -2.020 | 233 | -1.522 | -1.211 |
| 234 | -2.200 | -1.640 | 234 | -1.911 | -1.600 |
| 235 | -2.200 | -1.640 | 235 | -1.867 | -1.556 |
| 236 | -1.560 | -1.000 | 236 | -1.622 | -1.311 |
| 237 | -1.480 | -0.920 | 237 | -1.911 | -1.600 |
| 238 | -1.040 | -1.040 | 238 | -1.556 | -1.244 |
| 239 | -0.860 | -0.860 | 239 | -0.656 | -0.344 |

TABLE S-III. Hydrophobicity profiles of the SULT1A3 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| | Window of 5 amino acids | | | | Window f 9 amino acids | | |
|---|---|---|---|---|---|---|---|
| | SUIT1A3 WT | SULT1A3*2 (K234N), SULT1A3*3 (P101L), SULT1A3*5 (R144C) | SULT1A3*4 (P101H) | | SUIT1A3 WT | SULT1A3*2 (K234N), SULT1A3*3 (P101L), SULT1A3*5 (R144C) | SULT1A3*4 (P101H) |
| 97 | -1.000 | -1.000 | -1.000 | 97 | -0.878 | -0.278 | -1.056 |
| 98 | -1.180 | -1.180 | -1.180 | 98 | -1.478 | -0.878 | -1.656 |
| 99 | -2.260 | -1.180 | -2.580 | 99 | -1.589 | -0.989 | -1.767 |
| 100 | -1.800 | -0.720 | -2.120 | 100 | -1.089 | -0.489 | -1.267 |
| 101 | -2.000 | -0.920 | -2.320 | 101 | -1.011 | -0.411 | -1.189 |
| 102 | -1.100 | -0.020 | -1.420 | 102 | -1.011 | -0.411 | -1.189 |
| 103 | 0.120 | 1.200 | -0.200 | 103 | -0.711 | -0.111 | -0.889 |
| 104 | -0.340 | -0.340 | -0.340 | 104 | -0.989 | -0.389 | -1.167 |
| 105 | -0.180 | -0.180 | -0.180 | 105 | -0.389 | 0.211 | -0.567 |
| | | | | | | | |
| 140 | -0.760 | -0.760 | | 140 | -0.611 | 0.167 | |
| 141 | -1.240 | -1.240 | | 141 | -0.600 | 0.178 | |
| 142 | -1.880 | -0.480 | | 142 | -1.456 | -0.678 | |
| 143 | -1.240 | 0.160 | | 143 | -1.800 | -1.022 | |
| 144 | -1.300 | 0.100 | | 144 | -1.456 | -0.678 | |
| 145 | -2.640 | -1.240 | | 145 | -1.667 | -0.889 | |
| 146 | -1.640 | -0.240 | | 146 | -1.489 | -0.711 | |
| 147 | -1.380 | -1.380 | | 147 | -2.189 | -1.411 | |
| 148 | -2.080 | -2.080 | | 148 | -2.011 | -1.233 | |

| | | | | | |
|---|---|---|---|---|---|
| 230 | -0.700 | -0.700 | 230 | -1.689 | -1.644 |
| 231 | -1.320 | -1.320 | 231 | -1.722 | -1.678 |
| 232 | -2.660 | -2.580 | 232 | -1.822 | -1.778 |
| 233 | -2.580 | -2.500 | 233 | -1.522 | -1.478 |
| 234 | -2.200 | -2.120 | 234 | -1.911 | -1.867 |
| 235 | -2.200 | -2.120 | 235 | -1.867 | -1.822 |
| 236 | -1.560 | -1.480 | 236 | -1.622 | -1.578 |
| 237 | -1.480 | -1.480 | 237 | -1.911 | -1.867 |
| 238 | -1.040 | -1.040 | 238 | -1.556 | -1.511 |

TABLE S-IV. Hydrophobicity profiles of the SULT1B1 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| Window of 5 amino acids | | | Window f 9 amino acids | | |
|---|---|---|---|---|---|
| | SUlT1B1 WT | SULT1B1 (L145V) | | SUlT1B1 WT | SULT1B1 (L145V) |
| 141 | -0.760 | -0.760 | 141 | -0.011 | 0.033 |
| 142 | -1.300 | -1.300 | 142 | 0.289 | 0.333 |
| 143 | -0.280 | -0.200 | 143 | -0.567 | -0.522 |
| 144 | 0.360 | 0.440 | 144 | -0.867 | -0.822 |
| 145 | 0.300 | 0.380 | 145 | -0.300 | -0.256 |
| 146 | -0.960 | -0.880 | 146 | -0.544 | -0.500 |
| 147 | 0.500 | 0.580 | 147 | -0.367 | -0.322 |
| 148 | -0.960 | -0.960 | 148 | -0.367 | -0.322 |
| 149 | -1.660 | -1.660 | 149 | -0.156 | -0.111 |

TABLE S-V. Hydrophobicity profiles of the SULT1C1 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| Window of 5 amino acids | | | Window f 9 amino acids | | |
|---|---|---|---|---|---|
| | SUlT1C1 WT | SULT1C1*2 (S255A), SULT1C1*3 (D60A), SULT1C1*4 (R73Q), SULT1C1*5 (S111F) | | SUlT1C1 WT | SULT1C1*2 (S255A), SULT1C1*3 (D60A), SULT1C1*4 (R73Q), SULT1C1*5 (S111F) |
| 56 | 0.220 | 0.220 | 56 | 0.044 | 0.633 |
| 57 | 1.240 | 1.240 | 57 | 0.333 | 0.922 |
| 58 | -0.360 | 0.700 | 58 | 0.911 | 1.500 |
| 59 | 0.720 | 1.780 | 59 | 0.622 | 1.211 |
| 60 | 2.320 | 3.380 | 60 | -0.267 | 0.322 |
| 61 | 0.720 | 1.780 | 61 | -0.267 | 0.322 |
| 62 | -0.820 | 0.240 | 62 | 0.078 | 0.667 |
| 63 | -0.820 | -0.820 | 63 | -0.811 | -0.222 |
| 64 | -1.280 | -1.280 | 64 | -0.811 | -0.222 |
| | | | | | |
| 69 | -0.840 | -0.840 | 69 | -1.789 | -1.678 |
| 70 | -0.840 | -0.840 | 70 | -1.200 | -1.089 |

| | | | | | |
|---|---|---|---|---|---|
| 71 | -2.580 | -2.380 | 71 | -0.656 | -0.544 |
| 72 | -1.520 | -1.320 | 72 | 0.233 | 0.344 |
| 73 | 0.160 | 0.360 | 73 | -0.622 | -0.511 |
| 74 | 0.560 | 0.760 | 74 | -0.589 | -0.478 |
| 75 | 0.560 | 0.760 | 75 | -0.656 | -0.544 |
| 76 | 0.820 | 0.820 | 76 | -1.289 | -1.178 |
| 77 | -0.440 | -0.440 | 77 | -1.078 | -0.967 |
| | | | | | |
| 107 | 0.100 | 0.100 | 107 | -0.289 | 0.111 |
| 108 | -0.040 | -0.040 | 108 | -0.189 | 0.211 |
| 109 | -0.960 | -0.240 | 109 | -0.078 | 0.322 |
| 110 | -0.320 | 0.400 | 110 | -0.156 | 0.244 |
| 111 | -0.880 | -0.160 | 111 | -0.156 | 0.244 |
| 112 | 0.520 | 1.240 | 112 | 0.100 | 0.500 |
| 113 | 0.520 | 1.240 | 113 | 0.000 | 0.400 |
| 114 | 0.360 | 0.360 | 114 | 0.267 | 0.667 |
| 115 | 0.180 | 0.180 | 115 | 0.156 | 0.556 |
| | | | | | |
| 251 | 0.100 | 0.100 | 251 | 0.289 | 0.578 |
| 252 | -0.820 | -0.820 | 252 | 0.689 | 0.978 |
| 253 | -0.280 | 0.240 | 253 | 0.400 | 0.689 |
| 254 | 0.980 | 1.500 | 254 | -0.522 | -0.233 |
| 255 | 1.520 | 2.040 | 255 | -0.567 | -0.278 |
| 256 | -0.280 | 0.240 | 256 | -0.222 | 0.067 |
| 257 | -0.900 | -0.380 | 257 | -0.211 | 0.078 |
| 258 | -0.820 | -0.820 | 258 | -0.244 | 0.044 |
| 259 | -1.520 | -1.520 | 259 | -0.200 | 0.089 |

TABLE S-VI. Hydrophobicity profiles of the SULT1E1 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| | Window of 5 amino acids | | | Window f 9 amino acids | |
|---|---|---|---|---|---|
| | SUlT1E1 WT | SULT1E1*2 (D22Y),<br>SULT1E1*3 (A32V),<br>SULT1E1*4 (P253H) | | SUlT1E1 WT | SULT1E1*2 (D22Y),<br>SULT1E1*3 (A32V),<br>SULT1E1*4 (P253H) |
| 18 | 1.700 | 1.700 | 18 | 0.233 | 0.478 |
| 19 | 1.000 | 1.000 | 19 | 0.078 | 0.322 |
| 20 | -0.600 | -0.160 | 20 | 0.900 | 1.144 |
| 21 | -0.800 | -0.360 | 21 | 0.511 | 0.756 |
| 22 | -0.340 | 0.100 | 22 | -0.133 | 0.111 |
| 23 | -0.860 | -0.420 | 23 | -0.656 | -0.411 |
| 24 | -0.340 | 0.100 | 24 | -1.256 | -1.011 |
| 25 | 0.180 | 0.180 | 25 | -1.500 | -1.256 |
| 26 | -1.080 | -1.080 | 26 | -0.600 | -0.356 |
| | | | | | |
| 28 | -1.000 | -1.000 | 28 | -0.711 | -0.444 |
| 29 | -1.440 | -1.440 | 29 | -0.867 | -0.600 |

| | | | | | |
|---|---|---|---|---|---|
| 30 | -0.900 | -0.420 | 30 | -0.822 | -0.556 |
| 31 | 0.360 | 0.840 | 31 | -0.478 | -0.211 |
| 32 | 0.360 | 0.840 | 32 | -0.878 | -0.611 |
| 33 | -0.120 | 0.360 | 33 | -0.667 | -0.400 |
| 34 | -0.320 | 0.160 | 34 | -0.667 | -0.400 |
| 35 | -1.000 | -1.000 | 35 | -1.522 | -1.256 |
| 36 | -2.260 | -2.260 | 36 | -0.711 | -0.444 |
| 249 | -1.040 | -1.040 | 249 | -0.733 | -0.911 |
| 250 | -1.580 | -1.580 | 250 | -0.033 | -0.211 |
| 251 | -1.200 | -1.520 | 251 | -0.322 | -0.500 |
| 252 | 0.060 | -0.260 | 252 | -1.033 | -1.211 |
| 253 | 1.220 | 0.900 | 253 | -1.078 | -1.256 |
| 254 | -0.440 | -0.760 | 254 | -0.733 | -0.911 |
| 255 | -1.060 | -1.380 | 255 | 0.200 | 0.022 |
| 256 | -0.820 | -0.820 | 256 | -0.300 | -0.478 |
| 257 | -0.480 | -0.480 | 257 | -0.256 | -0.433 |

ProtScale tool[1] has also been considered in order to obtain the flexibility profiles of SULT1 enzymes. In this case, the average flexibility scale has been chosen[3]. This scale contains values that define the flexibility index for every type of amino acid, i.e., the fluctuational displacement of each residue in a protein. The lowest value (0.300) corresponds to methionine, and the highest value (0.540) to glycine. To generate the flexibility profile, the sequence of the analyzed protein is also scanned with a sliding window of a given size. For every position, the mean value of the flexibility indexes of amino acids within the window is computed, which is attributed to the amino acid in the midpoint of the window. Window sizes of 5-9 amino acids are considered similar to those used to obtain the hydrophobicity profiles.

TABLE S-VII. Average flexibility profiles of the SULT1A1 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| Window of 5 amino acids | | | Window f 9 amino acids | | |
|---|---|---|---|---|---|
| | SUlT1A1 WT | SULT1A1*4 (R37Q),<br>SULT1A1*2 (R213H),<br>SULT1A1*3 (M223V) | | SUlT1A WT | SULT1A1*4 (R37Q),<br>SULT1A1*2 (R213H),<br>SULT1A1*3 (M223V) |
| 33 | 0.442 | 0.442 | 33 | 0.461 | 0.457 |
| 34 | 0.440 | 0.440 | 34 | 0.458 | 0.453 |
| 35 | 0.448 | 0.440 | 35 | 0.458 | 0.453 |
| 36 | 0.448 | 0.440 | 36 | 0.473 | 0.469 |
| 37 | 0.488 | 0.480 | 37 | 0.460 | 0.456 |
| 38 | 0.484 | 0.476 | 38 | 0.444 | 0.440 |
| 39 | 0.486 | 0.478 | 39 | 0.461 | 0.457 |
| 40 | 0.454 | 0.454 | 40 | 0.459 | 0.454 |

| | | | | | |
|---|---|---|---|---|---|
| 41 | 0.444 | 0.444 | 41 | 0.468 | 0.463 |
| | | | | | |
| 209 | 0.406 | 0.406 | 209 | 0.451 | 0.428 |
| 210 | 0.422 | 0.422 | 210 | 0.453 | 0.430 |
| 211 | 0.454 | 0.412 | 211 | 0.442 | 0.419 |
| 212 | 0.456 | 0.414 | 212 | 0.448 | 0.424 |
| 213 | 0.468 | 0.426 | 213 | 0.462 | 0.439 |
| 214 | 0.492 | 0.450 | 214 | 0.462 | 0.439 |
| 215 | 0.484 | 0.442 | 215 | 0.477 | 0.453 |
| 216 | 0.478 | 0.478 | 216 | 0.477 | 0.453 |
| 217 | 0.464 | 0.464 | 217 | 0.473 | 0.450 |
| | | | | | |
| 219 | 0.468 | 0.468 | 219 | 0.426 | 0.436 |
| 220 | 0.430 | 0.430 | 220 | 0.428 | 0.438 |
| 221 | 0.390 | 0.408 | 221 | 0.426 | 0.436 |
| 222 | 0.380 | 0.398 | 222 | 0.406 | 0.416 |
| 223 | 0.400 | 0.418 | 223 | 0.399 | 0.409 |
| 224 | 0.362 | 0.380 | 224 | 0.407 | 0.417 |
| 225 | 0.388 | 0.406 | 225 | 0.398 | 0.408 |
| 226 | 0.430 | 0.430 | 226 | 0.393 | 0.403 |
| 227 | 0.414 | 0.414 | 227 | 0.414 | 0.424 |

TABLE S-VIII. Average flexibility profiles of the SULT1A2 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| Window of 5 amino acids | | | Window f 9 amino acids | | |
|---|---|---|---|---|---|
| | SUlT1A2 WT | SULT1A2*2 (I7T, N235T), SULT1A2*3 (P19L) | | SUlT1A2 WT | SULT1A2*2 (I7T, N235T), SULT1A2*3 (P19L) |
| 5 | 0.458 | 0.454 | 5 | 0.459 | 0.457 |
| 6 | 0.486 | 0.482 | 6 | 0.482 | 0.480 |
| 7 | 0.500 | 0.496 | 7 | 0.483 | 0.481 |
| 8 | 0.504 | 0.500 | 8 | 0.483 | 0.481 |
| 9 | 0.504 | 0.500 | 9 | 0.488 | 0.486 |
| 10 | 0.486 | 0.486 | 10 | 0.480 | 0.478 |
| 11 | 0.484 | 0.484 | 11 | 0.467 | 0.464 |
| 12 | 0.462 | 0.462 | 12 | 0.468 | 0.468 |
| 13 | 0.438 | 0.438 | 13 | 0.471 | 0.471 |
| | | | | | |
| 15 | 0.464 | 0.464 | 15 | 0.456 | 0.440 |
| 16 | 0.442 | 0.442 | 16 | 0.440 | 0.424 |
| 17 | 0.460 | 0.432 | 17 | 0.450 | 0.434 |
| 18 | 0.456 | 0.428 | 18 | 0.447 | 0.431 |
| 19 | 0.454 | 0.426 | 19 | 0.447 | 0.431 |
| 20 | 0.440 | 0.412 | 20 | 0.438 | 0.422 |
| 21 | 0.446 | 0.418 | 21 | 0.426 | 0.410 |
| 22 | 0.406 | 0.406 | 22 | 0.421 | 0.406 |

| | | | | | |
|---|---|---|---|---|---|
| 23 | 0.404 | 0.404 | 23 | 0.418 | 0.402 |
| 231 | 0.410 | 0.410 | 231 | 0.437 | 0.434 |
| 232 | 0.442 | 0.442 | 232 | 0.444 | 0.442 |
| 233 | 0.440 | 0.436 | 233 | 0.421 | 0.419 |
| 234 | 0.442 | 0.438 | 234 | 0.436 | 0.433 |
| 235 | 0.442 | 0.438 | 235 | 0.434 | 0.432 |
| 236 | 0.436 | 0.432 | 236 | 0.426 | 0.423 |
| 237 | 0.434 | 0.430 | 237 | 0.441 | 0.439 |
| 238 | 0.426 | 0.426 | 238 | 0.438 | 0.436 |
| 239 | 0.412 | 0.412 | 239 | 0.429 | 0.427 |

TABLE S-XI. Average flexibility profiles of the SULT1A3 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| Window of 5 amino acids | | | | Window f 9 amino acids | | | |
|---|---|---|---|---|---|---|---|
| | SUlT1 A3 WT | SULT1A3*2 (K234N), SULT1A3*3 (P101L), SULT1A3*5 (R144C) | SULT1 A3*4 (P101H) | | SUlT 1A3 WT | SULT1A3*2 (K234N), SULT1A3*3 (P101L), SULT1A3*5 (R144C) | SULT1A3*4 (P101H) |
| 97 | 0.446 | 0.446 | 0.446 | 97 | 0.458 | 0.442 | 0.437 |
| 98 | 0.460 | 0.460 | 0.460 | 98 | 0.473 | 0.458 | 0.452 |
| 99 | 0.488 | 0.460 | 0.450 | 99 | 0.477 | 0.461 | 0.456 |
| 100 | 0.496 | 0.468 | 0.458 | 100 | 0.469 | 0.453 | 0.448 |
| 101 | 0.500 | 0.472 | 0.462 | 101 | 0.479 | 0.463 | 0.458 |
| 102 | 0.486 | 0.458 | 0.448 | 102 | 0.479 | 0.463 | 0.458 |
| 103 | 0.476 | 0.448 | 0.438 | 103 | 0.479 | 0.463 | 0.458 |
| 104 | 0.468 | 0.468 | 0.468 | 104 | 0.466 | 0.450 | 0.444 |
| 105 | 0.468 | 0.468 | 0.468 | 105 | 0.450 | 0.434 | 0.429 |
| 140 | 0.396 | 0.396 | | 140 | 0.398 | 0.378 | |
| 141 | 0.358 | 0.358 | | 141 | 0.391 | 0.371 | |
| 142 | 0.380 | 0.344 | | 142 | 0.403 | 0.383 | |
| 143 | 0.356 | 0.320 | | 143 | 0.399 | 0.379 | |
| 144 | 0.392 | 0.356 | | 144 | 0.392 | 0.372 | |
| 145 | 0.424 | 0.388 | | 145 | 0.381 | 0.361 | |
| 146 | 0.432 | 0.396 | | 146 | 0.402 | 0.382 | |
| 147 | 0.390 | 0.390 | | 147 | 0.423 | 0.403 | |
| 148 | 0.432 | 0.432 | | 148 | 0.444 | 0.424 | |
| 230 | 0.418 | 0.418 | | 230 | 0.420 | 0.421 | |
| 231 | 0.410 | 0.410 | | 231 | 0.436 | 0.437 | |
| 232 | 0.440 | 0.442 | | 232 | 0.443 | 0.444 | |
| 233 | 0.438 | 0.440 | | 233 | 0.420 | 0.421 | |
| 234 | 0.440 | 0.442 | | 234 | 0.434 | 0.436 | |

| | | | | | |
|---|---|---|---|---|---|
| 235 | 0.440 | 0.442 | 235 | 0.433 | 0.434 |
| 236 | 0.434 | 0.436 | 236 | 0.424 | 0.426 |
| 237 | 0.434 | 0.434 | 237 | 0.440 | 0.441 |
| 238 | 0.426 | 0.426 | 238 | 0.437 | 0.438 |

TABLE S-X. Average flexibility profiles of the SULT1B1 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| Window of 5 amino acids | | | Window f 9 amino acids | | |
|---|---|---|---|---|---|
| | SUlT1B1 WT | SULT1B1 (L145V) | | SUlT1B1 WT | SULT1B1 (L145V) |
| 141 | 0.396 | 0.396 | 141 | 0.418 | 0.420 |
| 142 | 0.396 | 0.396 | 142 | 0.394 | 0.397 |
| 143 | 0.386 | 0.390 | 143 | 0.402 | 0.404 |
| 144 | 0.362 | 0.366 | 144 | 0.397 | 0.399 |
| 145 | 0.390 | 0.394 | 145 | 0.391 | 0.393 |
| 146 | 0.420 | 0.424 | 146 | 0.399 | 0.401 |
| 147 | 0.392 | 0.396 | 147 | 0.420 | 0.422 |
| 148 | 0.416 | 0.416 | 148 | 0.420 | 0.422 |
| 149 | 0.458 | 0.458 | 149 | 0.420 | 0.422 |

TABLE S-XI. Average flexibility profiles of the SULT1C1 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| Window of 5 amino acids | | | Window f 9 amino acids | | |
|---|---|---|---|---|---|
| | SUlT1C1 WT | SULT1C1*2 (S255A),<br>SULT1C1*3 (D60A),<br>SULT1C1*4 (R73Q),<br>SULT1C1*5 (S111F) | | SUlT1C1 WT | SULT1C1*2 (S255A),<br>SULT1C1*3 (D60A),<br>SULT1C1*4 (R73Q),<br>SULT1C1*5 (S111F) |
| 56 | 0.444 | 0.444 | 56 | 0.444 | 0.428 |
| 57 | 0.460 | 0.460 | 57 | 0.429 | 0.412 |
| 58 | 0.470 | 0.440 | 58 | 0.431 | 0.414 |
| 59 | 0.432 | 0.402 | 59 | 0.452 | 0.436 |
| 60 | 0.424 | 0.394 | 60 | 0.456 | 0.439 |
| 61 | 0.432 | 0.402 | 61 | 0.452 | 0.436 |
| 62 | 0.452 | 0.422 | 62 | 0.457 | 0.440 |
| 63 | 0.442 | 0.442 | 63 | 0.462 | 0.446 |
| 64 | 0.490 | 0.490 | 64 | 0.462 | 0.446 |
| | | | | | |
| 69 | 0.444 | 0.444 | 69 | 0.471 | 0.467 |
| 70 | 0.440 | 0.440 | 70 | 0.460 | 0.456 |
| 71 | 0.468 | 0.460 | 71 | 0.451 | 0.447 |

| | | | | | |
|---|---|---|---|---|---|
| 72 | 0.440 | 0.432 | 72 | 0.446 | 0.441 |
| 73 | 0.438 | 0.430 | 73 | 0.457 | 0.452 |
| 74 | 0.460 | 0.452 | 74 | 0.437 | 0.432 |
| 75 | 0.460 | 0.452 | 75 | 0.443 | 0.439 |
| 76 | 0.418 | 0.418 | 76 | 0.440 | 0.436 |
| 77 | 0.452 | 0.452 | 77 | 0.442 | 0.438 |
| | | | | | |
| 107 | 0.412 | 0.412 | 107 | 0.442 | 0.420 |
| 108 | 0.394 | 0.394 | 108 | 0.434 | 0.412 |
| 109 | 0.422 | 0.382 | 109 | 0.430 | 0.408 |
| 110 | 0.416 | 0.376 | 110 | 0.420 | 0.398 |
| 111 | 0.426 | 0.386 | 111 | 0.420 | 0.398 |
| 112 | 0.436 | 0.396 | 112 | 0.424 | 0.402 |
| 113 | 0.436 | 0.396 | 113 | 0.432 | 0.410 |
| 114 | 0.436 | 0.436 | 114 | 0.453 | 0.431 |
| 115 | 0.450 | 0.450 | 115 | 0.447 | 0.424 |
| | | | | | |
| 251 | 0.468 | 0.468 | 251 | 0.481 | 0.464 |
| 252 | 0.496 | 0.496 | 252 | 0.459 | 0.442 |
| 253 | 0.496 | 0.466 | 253 | 0.441 | 0.424 |
| 254 | 0.460 | 0.430 | 254 | 0.459 | 0.442 |
| 255 | 0.418 | 0.388 | 255 | 0.454 | 0.438 |
| 256 | 0.432 | 0.402 | 256 | 0.460 | 0.443 |
| 257 | 0.424 | 0.394 | 257 | 0.452 | 0.436 |
| 258 | 0.430 | 0.430 | 258 | 0.444 | 0.428 |
| 259 | 0.456 | 0.456 | 259 | 0.448 | 0.431 |

TABLE S-XII. Average flexibility profiles of the SULT1E1 enzyme (WT) and its frequently identified allozymes obtained using the ProtScale tool for a window of 5 and 9 amino acids, respectively. Only the regions covered by the windows of 5 and respectively 9 amino acids are highlighted in grey.

| Window of 5 amino acids | | | Window f 9 amino acids | | |
|---|---|---|---|---|---|
| | SUlT1E1 WT | SULT1E1*2 (D22Y),<br>SULT1E1*3 (A32V),<br>SULT1E1*4 (P253H) | | SUlT1E1 WT | SULT1E1*2 (D22Y),<br>SULT1E1*3 (A32V),<br>SULT1E1*4 (P253H) |
| 18 | 0.418 | 0.418 | 18 | 0.420 | 0.410 |
| 19 | 0.404 | 0.404 | 19 | 0.411 | 0.401 |
| 20 | 0.414 | 0.396 | 20 | 0.419 | 0.409 |
| 21 | 0.402 | 0.384 | 21 | 0.411 | 0.401 |
| 22 | 0.420 | 0.402 | 22 | 0.407 | 0.397 |
| 23 | 0.430 | 0.412 | 23 | 0.400 | 0.390 |
| 24 | 0.420 | 0.402 | 24 | 0.423 | 0.413 |
| 25 | 0.380 | 0.380 | 25 | 0.428 | 0.418 |
| 26 | 0.420 | 0.420 | 26 | 0.419 | 0.409 |

| | | | | | |
|---|---|---|---|---|---|
| 28 | 0.418 | 0.418 | 28 | 0.423 | 0.427 |
| 29 | 0.434 | 0.434 | 29 | 0.414 | 0.418 |
| 30 | 0.444 | 0.450 | 30 | 0.417 | 0.420 |
| 31 | 0.404 | 0.410 | 31 | 0.410 | 0.413 |
| 32 | 0.410 | 0.416 | 32 | 0.434 | 0.438 |
| 33 | 0.404 | 0.410 | 33 | 0.434 | 0.438 |
| 34 | 0.410 | 0.416 | 34 | 0.440 | 0.443 |
| 35 | 0.440 | 0.440 | 35 | 0.453 | 0.457 |
| 36 | 0.480 | 0.480 | 36 | 0.439 | 0.442 |
| | | | | | |
| 249 | 0.418 | 0.418 | 249 | 0.452 | 0.431 |
| 250 | 0.460 | 0.460 | 250 | 0.431 | 0.410 |
| 251 | 0.470 | 0.432 | 251 | 0.413 | 0.392 |
| 252 | 0.434 | 0.396 | 252 | 0.439 | 0.418 |
| 253 | 0.400 | 0.362 | 253 | 0.440 | 0.419 |
| 254 | 0.432 | 0.394 | 254 | 0.446 | 0.424 |
| 255 | 0.424 | 0.386 | 255 | 0.444 | 0.423 |
| 256 | 0.430 | 0.430 | 256 | 0.452 | 0.431 |
| 257 | 0.460 | 0.460 | 257 | 0.456 | 0.434 |

TABLE S-XIII. The clusters identified by the PDBFlex computational tool for assessing the structural flexibility of the SULT1 enzymes that revealing frequently identified allozymes.

| Subfamily of SULT1 | PDBFlex cluster | Members of the cluster |
|---|---|---|
| SULT1A1 / SULT1A2 | 3U3M_A | 1LS6<br>2D06 chains A and B<br>3U3J chains A and B<br>3U3K chains A and B<br>3U3O<br>3U3R<br>1Z28<br>3QVU chains A and B<br>3QVV chains A and B<br>1Z29[a]<br>1Z28[b]<br>4GRA[c] chains A and B |
| SULT1A3 | 2A3R_A | 1CJM<br>2A3R |
| SULT1B1 | 3CKL_B | 2Z5F chains A and B<br>3CKL |
| | 4JVM_A | 1G3M chains A and B |

| Subfamily of SULT1 | PDBFlex cluster | Members of the cluster |
|---|---|---|
| SULT1E1 |  | 1HY3 chains A and B<br>4JVL chains A and B<br>4JVN chains A and B |

[a]SULT1A2, [b]SULT1A1*3, [c]SULT1A1*2

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