**Table S4\_**Associations between rs1257220, rs3814022 and rs4953911 and the different clinical and therapeutic outcomes of UC patients. In grey the statistically significant associations are highlighted.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Family history** | | | | | **Need for colectomy** | | | | | | **Need for Biologics** | | | | | | | **Prognosis** | | | | | |
|  | **No** | **Yes** |  | | | **No** | **Yes** |  | | | **No** | | **Yes** |  | | | | **Good** | | **Bad** |  |  |  |
|  | **N (%)** | **N (%)** | **OR** | **[95% IC]** | ***p* value** | **N (%)** | **N (%)** | **OR** | **[95% IC]** | ***p* value** | **N (%)** | | **N (%)** | **OR** | **[95% IC]** | ***p* value** | **N (%)** | | | **N (%)** | **OR** | **[95% IC]** | ***p* value** |
| ***Discovery Cohort*** | | | | | | | | | | | | | | | | | | | | | | | | |
| **rs1257220** |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| Dominant |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| G/G | **205 (53.1)** | **3 (21.4)** | **1.00** |  | **0.022** | 202 (50.6) | 15 (60.0) | 1.00 |  | 0.390 | 181 (51.4) | | 38 (52.8) | 1.00 |  | 0.921 | 210 (52.4) | | | 9 (40.9) | 1.00 |  | 0.258 |
| A/G-A/A | **181 (46.9)** | **11 (78.6)** | **4.02** | **1.09-14.86** | 197 (49.4) | 10 (40.0) | 0.70 | 0.31-1.59 |  | 171 (48.6) | | 34 (47.2) | 0.97 | 0.58-1.64 | 191 (47.6) | | | 13 (59.1) | 1.66 | 0.68-4.03 |  |
| Recessive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| G/G-A/G | 355 (92.0) | 12 (85.7) | 1.00 |  | 0.534 | 366 (91.7) | 23 (92.0) | 1.00 |  | 0.984 | 325 (92.3) | | 65 (90.3) | 1.00 |  | 0.466 | 370 (92.3) | | | 19 (86.4) | 1.00 |  | 0.302 |
| A/A | 31 (8.0) | 2 (14.3) | 1.69 | 0.35-8.12 | 33 (8.3) | 2 (8.0) | 1.02 | 0.23-4.52 |  | 27 (7.7) | | 7 (9.7) | 1.41 | 0.57-3.47 | 31 (7.7) | | | 3 (13.6) | 2.08 | 0.57-7.64 |  |
| log-Additive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| G\*/A (0,1,2) | 386 (96.5) | 14 (3.5) | 2.16 | 1.00-4.67 | 0.053 | 399 (94.1) | 25 (5.9) | 0.80 | 0.41-1.56 | 0.499 | 352 (83.0) | | 72 (17.0) | 1.05 | 0.70-1.58 | 0.813 | 401 (94.8) | | | 22 (5.2) | 1.52 | 0.82-3.00 | 0.182 |
| **rs3814022** |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| Dominant |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| C/C | 186 (48.2) | 4 (28.6) | 1.00 |  | 0.156 | 194 (48.6) | 10 (40.0) | 1.00 |  | 0.364 | 175 (49.9) | | 30 (41.1) | 1.00 |  | 0.082 | 194 (48.4) | | | 10 (45.5) | 1.00 |  | 0.618 |
| C/G-G/G | 200 (51.8) | 10 (71.4) | 2.27 | 0.70-7.42 | 205 (51.4) | 15 (60.0) | 1.46 | 0.64-3.34 |  | 176 (50.1) | | 43 (58.9) | 1.59 | 0.94-2.70 | 207 (51.6) | | | 12 (54.5) | 1.25 | 0.52-3.03 |  |
| Recessive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| C/C-C/G | 345 (89.4) | 12 (85.7) | 1.00 |  | 0.663 | 357 (89.5) | 21 (84.0) | 1.00 |  | 0.408 | **318 (90.6)** | | **60 (82.2)** | **1.00** |  | **0.032** | 356 (88.8) | | | 21 (95.5) | 1.00 |  | 0.305 |
| G/G | 41 (10.6) | 2 (14.3) | 1.43 | 0.31-6.65 | 42 (10.5) | 4 (16.0) | 1.64 | 0.54-5.02 |  | **33 (9.4)** | | **13 (17.8)** | **2.27** | **1.11-4.67** | 45 (11.2) | | | 1 (4.5) | 0.39 | 0.05-3.02 |  |
| log-Additive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| C\*/G (0,1,2) | 386 (96.5) | 14 (3.5) | 1.62 | 0.76-3.48 | 0.221 | 399 (94.1) | 25 (5.9) | 1.37 | 0.77-2.44 | 0.290 | **351 (82.8)** | | **73 (17.2)** | **1.56** | **1.07-2.27** | **0.021** | 401 (94.8) | | | 22 (5.2) | 0.98 | 0.51-1.89 | 0.955 |
| **rs4953911** |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| Dominant |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| A/A | 157 (41.1) | 4 (28.6) | 1.00 |  | 0.352 | 166 (41.9) | 8 (33.3) | 1.00 |  | 0.484 | 147 (42.2) | | 27 (37.5) | 1.00 |  | 0.219 | 165 (41.6) | | | 9 (40.9) | 1.00 |  | 0.659 |
| T/A-T/T | 225 (58.9) | 10 (71.4) | 1.72 | 0.53-5.63 | 230 (58.1) | 16 (66.7) | 1.50 | 0.63-3.62 |  | 201 (57.8) | | 45 (62.5) | 1.40 | 0.81-2.41 | 232 (58.4) | | | 13 (59.1) | 1.22 | 0.50-3.01 |  |
| Recessive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| A/A-T/A | 334 (87.4) | 12 (85.7) | 1.00 |  | 0.818 | 346 (87.4) | 19 (79.2) | 1.00 |  | 0.270 | 307 (88.2) | | 58 (80.6) | 1.00 |  | 0.059 | 343 (86.4) | | | 21 (95.5) | 1.00 |  | 0.203 |
| T/T | 48 (12.6) | 2 (14.3) | 1.20 | 0.26-5.58 | 50 (12.6) | 5 (20.8) | 1.84 | 0.66-5.18 |  | 41 (11.8) | | 14 (19.4) | 1.99 | 1.00-3.97 | 54 (13.6) | | | 1 (4.5) | 0.33 | 0.04-2.49 |  |
| log-Additive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| A\*/T (0,1,2) | 382 (96.5) | 14 (3.5) | 1.36 | 0.63-2.98 | 0.438 | 396 (94.3) | 24 (5.7) | 1.45 | 0.81-2.60 | 0.220 | 348 (82.9) | | 72 (17.1) | 1.42 | 0.97-2.09 | 0.065 | 397 (94.7) | | | 22 (5.3) | 0.93 | 0.48-1.78 | 0.815 |
| ***Validation Cohort*** | | | | | | | | | | | | | | | | | | | | | | | | |
| **rs1257220** |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| Dominant |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| G/G | 250 (56.7) | 11 (45.8) | 1.00 |  | 0.284 | 163 (54.0) | 97 (60.2) | 1.00 |  | 0.175 | 176 (57.3) | | 85 (53.8) | 1.00 |  | 0.531 | 234 (55.7) | | | 20 (57.1) | 1.00 |  | 0.846 |
| A/G-A/A | 191 (43.3) | 13 (54.2) | 1.57 | 0.69-3.60 |  | 139 (46.0) | 64 (39.8) | 0.76 | 0.52-1.13 |  | 131 (42.7) | | 73 (46.2) | 1.13 | 0.77-1.67 |  | 186 (44.3) | | | 15 (42.9) | 0.93 | 0.46-1.87 |  |
| Recessive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| G/G-A/G | **402 (91.2)** | **18 (75.0)** | **1.00** |  | **0.021** | 269 (89.1) | 149 (92.5) | 1.00 |  | 0.237 | 281 (91.5) | | 139 (88.0) | 1.00 |  | 0.191 | 377 (89.8) | | | 33 (94.3) | 1.00 |  | 0.368 |
| A/A | **39 (8.8)** | **6 (25.0)** | **3.59** | **1.33-9.69** | 33 (10.9) | 12 (7.5) | 0.67 | 0.33-1.33 |  | 26 (8.5) | | 19 (12.0) | 1.53 | 0.81-2.88 |  | 43 (10.2) | | | 2 (5.7) | 0.54 | 0.12-2.33 |  |
| log-Additive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| G\*/A (0,1,2) | 441 (94.8) | 24 (5.2) | 1.76 | 1.00-3.10 | 0.056 | 302 (65.2) | 161 (34.8) | 0.79 | 0.59-1.07 | 0.124 | 307 (66.0) | | 158 (34.0) | 1.17 | 0.88-1.56 | 0.292 | 420 (92.3) | | | 35 (7.7) | 0.87 | 0.51-1.48 | 0.599 |
| **rs3814022** |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| Dominant |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| C/C | 242 (55.0) | 11 (47.8) | 1.00 |  | 0.605 | 167 (55.5) | 86 (53.8) | 1.00 |  | 0.731 | 176 (57.7) | | 77 (48.7) | 1.00 |  | 0.078 | **236 (56.5)** | | | **13 (37.1)** | **1.00** |  | **0.027** |
| C/G-G/G | 198 (45.0) | 12 (52.2) | 1.25 | 0.54-2.91 |  | 134 (44.5) | 74 (46.2) | 1.07 | 0.73-1.58 |  | 129 (42.3) | | 81 (51.3) | 1.42 | 0.96-2.10 |  | **182 (43.5)** | | | **22 (62.9)** | **2.21** | **1.08-4.52** |
| Recessive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| C/C-C/G | 408 (92.7) | 23 (100) | 1.00 |  | 0.061 | 279 (92.7) | 150 (93.8) | 1.00 |  | 0.700 | 286 (93.8) | | 145 (91.8) | 1.00 |  | 0.385 | 390 (93.3) | | | 32 (91.4) | 1.00 |  | 0.663 |
| G/G | 32 (7.3) | 0 (0) | 0.00 | 0.00 |  | 22 (7.3) | 10 (6.2) | 0.86 | 0.40-1.87 |  | 19 (6.2) | | 13 (8.2) | 1.39 | 0.66-2.92 |  | 28 (6.7) | | | 3 (8.6) | 1.33 | 0.38-4.63 |  |
| log-Additive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| C\*/G (0,1,2) | 440 (95.0) | 23 (5.0) | 0.95 | 0.48-1.88 | 0.880 | 301 (65.3) | 160 (34.7) | 1.02 | 0.75-1.39 | 0.906 | 305 (65.9) | | 158 (34.1) | 1.32 | 0.97-1.80 | 0.078 | 418 (92.3) | | | 35 (7.7) | 1.67 | 0.99-2.80 | 0.057 |
| **rs4953911** |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| Dominant |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| A/A | 227 (51.6) | 11 (47.8) | 1.00 |  | 0.834 | 162 (53.6) | 76 (47.5) | 1.00 |  | 0.210 | 166 (54.4) | | 72 (45.6) | 1.00 |  | 0.082 | **223 (53.3)** | | | **11 (31.4)** | **1.00** |  | **0.012** |
| T/A-T/T | 213 (48.4) | 12 (52.2) | 1.09 | 0.47-2.55 |  | 140 (46.4) | 84 (52.5) | 1.28 | 0.87-1.88 |  | 139 (45.6) | | 86 (54.4) | 1.41 | 0.96-2.08 | **195 (46.7)** | | | **24 (68.6)** | **2.51** | **1.20-5.27** |
| Recessive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| A/A-T/A | **404 (91.8)** | **23 (100)** | **1.00** |  | **0.048** | 278 (92.1) | 148 (92.5) | 1.00 |  | 0.924 | 284 (93.1) | | 143 (90.5) | 1.00 |  | 0.256 | 387 (92.6) | | | 31 (88.6) | 1.00 |  | 0.392 |
| T/T | **36 (8.2)** | **0 (0)** | **0.00** | **0.00** | 24 (7.9) | 12 (7.5) | 0.97 | 0.47-1.99 |  | 21 (6.9) | | 15 (9.5) | 1.51 | 0.75-3.04 |  | 31 (7.4) | | | 4 (11.4) | 1.66 | 0.55-5.04 |  |
| log-Additive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| A\*/T (0,1,2) | 440 (95.0) | 23 (5.0) | 0.85 | 0.43-1.70 | 0.650 | 302 (65.4) | 160 (34.6) | 1.16 | 0.86-1.57 | 0.3443 | 305 (65.9) | | 158 (34.1) | 1.33 | 0.98-1.81 | 0.064 | **418 (92.3)** | | | **35 (7.7)** | **1.84** | **1.10-3.07** | **0.022** |
| ***Combined Cohort*** | | | | | | | | | | | | | | | | | | | | | | | | |
| **rs1257220** |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| Dominant |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| G/G | **455 (55.0)** | **14 (36.8)** | **1.00** |  | **0.025** | **365 (52.1)** | **112 (60.2)** | **1.00** |  | **0.037** | 357 (54.2) | | 123 (53.5) | 1.00 |  | 0.915 | 444 (54.1) | | | 29 (50.9) | 1.00 |  | 0.675 |
| A/G-A/A | **372 (45.0)** | **24 (63.2)** | **2.13** | **1.09-4.19** | **336 (47.9)** | **74 (39.8)** | **0.71** | **0.51-0.98** |  | 302 (45.8) | | 107 (46.5) | 1.02 | 0.75-1.38 | 377 (45.9) | | | 28 (49.1) | 1.12 | 0.65-1.93 |  |
| Recessive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| G/G-A/G | **757 (91.5)** | **30 (78.9)** | **1.00** |  | **0.019** | 635 (90.6) | 172 (92.5) | 1.00 |  | 0.447 | 606 (92.0) | | 204 (88.7) | 1.00 |  | 0.102 | 747 (91.0) | | | 52 (91.2) | 1.00 |  | 0.996 |
| A/A | **70 (8.5)** | **8 (21.1)** | **2.92** | **1.29-6.63** | 66 (9.4) | 14 (7.5) | 0.80 | 0.43-1.45 |  | 53 (8.0) | | 26 (11.3) | 1.54 | 0.93-2.55 | 74 (9.0) | | | 5 (8.8) | 1.00 | 0.38-2.59 |  |
| log-Additive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| G\*/A (0,1,2) | **827 (95.6)** | **38 (4.4)** | **1.92** | **1.22-3.01** | **0.006** | 701 (79.0) | 186 (21.0) | 0.78 | 0.60-1.01 | 0.052 | 659 (74.1) | | 230 (25.9) | 1.10 | 0.87-1.39 | 0.419 | 821 (93.5) | | | 57 (6.5) | 1.07 | 0.71-1.61 | 0.751 |
| **rs3814022** |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| Dominant |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| C/C | 428 (51.8) | 15 (40.5) | 1.00 |  | 0.182 | 361 (51.6) | 96 (51.9) | 1.00 |  | 0.980 | **351 (53.6)** | | **107 (46.3)** | **1.00** |  | **0.046** | 430 (52.5) | | | 23 (40.4) | 1.00 |  | 0.063 |
| C/G-G/G | 398 (48.2) | 22 (59.5) | 1.57 | 0.80-3.07 | 339 (48.4) | 89 (48.1) | 1.00 | 0.72-1.38 |  | **305 (46.5)** | | **124 (53.7)** | **1.36** | **1.01-1.85** | 389 (47.5) | | | 34 (59.6) | 1.68 | 0.97-2.90 |  |
| Recessive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| C/C-C/G | 753 (91.2) | 35 (94.6) | 1.00 |  | 0.430 | 636 (90.9) | 171 (92.4) | 1.00 |  | 0.554 | 604 (92.1) | | 205 (88.7) | 1.00 |  | 0.090 | 746 (91.1) | | | 53 (93.0) | 1.00 |  | 0.674 |
| G/G | 73 (8.8) | 2 (5.4) | 0.58 | 0.14-2.48 | 64 (9.1) | 14 (7.6) | 0.84 | 0.46-1.53 |  | 52 (7.9) | | 26 (11.3) | 1.56 | 0.94-2.59 | 73 (8.9) | | | 4 (7.0) | 0.80 | 0.28-2.29 |  |
| log-Additive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| C\*/G (0,1,2) | 826 (95.7) | 37 (4.3) | 1.19 | 0.73-1.95 | 0.486 | 700 (79.1) | 185 (20.9) | 0.97 | 0.75-1.24 | 0.784 | **656 (74.0)** | | **231 (26.0)** | **1.31** | **1.04-1.65** | **0.022** | 819 (93.5) | | | 57 (6.5) | 1.29 | 0.87-1.93 | 0.215 |
| **rs4953911** |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| Dominant |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| A/A | 384 (46.7) | 15 (40.5) | 1.00 |  | 0.475 | 328 (47.0) | 84 (45.7) | 1.00 |  | 0.670 | 313 (47.9) | | 99 (43.0) | 1.00 |  | 0.141 | **388 (47.6)** | | | **20 (35.1)** | **1.00** |  | **0.047** |
| T/A-T/T | 438 (53.3) | 22 (59.5) | 1.28 | 0.65-2.50 | 370 (53.0) | 100 (54.3) | 1.07 | 0.77-1.49 |  | 340 (52.1) | | 131 (57.0) | 1.26 | 0.93-1.71 | **427 (52.4)** | | | **37 (64.9)** | **1.75** | **1.00-3.08** |
| Recessive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| A/A-T/A | 738 (89.8) | 35 (94.6) | 1.00 |  | 0.289 | 624 (89.4) | 167 (90.8) | 1.00 |  | 0.697 | 591 (90.5) | | 201 (87.4) | 1.00 |  | 0.106 | 730 (89.6) | | | 52 (91.2) | 1.00 |  | 0.793 |
| T/T | 84 (10.2) | 2 (5.4) | 0.49 | 0.12-2.09 | 74 (10.6) | 17 (9.2) | 0.90 | 0.51-1.56 |  | 62 (9.5) | | 29 (12.6) | 1.49 | 0.93-2.41 | 85 (10.4) | | | 5 (8.8) | 0.88 | 0.34-2.28 |  |
| log-Additive |  |  |  |  |  |  |  |  |  |  |  | |  |  |  |  |  | | |  |  |  |  |
| A\*/T (0,1,2) | 822 (95.7) | 37 (4.3) | 1.02 | 0.62-1.69 | 0.927 | 698 (79.1) | 184 (20.9) | 1.02 | 0.80-1.30 | 0.884 | 653 (74.0) | | 230 (26.0) | 1.24 | 0.99-1.57 | 0.063 | 815 (93.5) | | | 57 (6.5) | 1.32 | 0.89-1.97 | 0.173 |

***\*****Reference category;* ***OR*** *- odds ratio;* ***CI*** *- confidence interval*