Supplementary table 8. Differences in *FKBP5* methylation according to therapy quality assessed by glucocorticoid replacement score

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Under-replacement**  **(n=5)** | **Appropriate replacement**  **(n=97)** | **Over-replacement**  **(n=12)** | **p** |
| **Sex** |  |  |  |  |
| Male, n (%) | 1 (3) | 22 (76) | 6 (21) | 0.11 |
| Female, n (%) | 4 (5) | 75 (88) | 6 (7) |
| **AI etiology** |  |  |  |  |
| Primary, n (%) | 4 (6) | 53 (80) | 9 (14) | 0.23 |
| Secondary, (%) | 1 (2) | 44 (92) | 3 (6) |
| **Hydrocortisone replacement dose** |  |  |  |  |
| mg/day | 22 ± 6 | 23 ± 6 | 25 ± 8 | 0.7 |
| mg/BSA/day | 13 ± 3 | 12 ± 4 | 12 ± 5 | 0.9 |
| **FKBP5 methylation, %,**  **mean ± SD** |  |  |  |  |
| Intron1A1 CpG185 | 20 ± 2 | 18 ± 7 | 15 ± 9 | 0.55 |
| Intron1A1 CpG189 | 38 ± 5 | 34 ± 9 | 32 ± 12 | 0.64 |
| Intron1A2 CpG49 | 97 ± 2 | 96 ± 2 | 96 ± 1 | 0.51 |
| Intron1A2 CpG126 | 94 ± 2 | 94 ± 1 | 94 ± 1 | 0.85 |
| Intron1A2 CpG143 | 98 ± 0.8 | 97 ± 1 | 97 ± 1 | 0.70 |
| Intron1A2 CpG190 | 98 ± 0.9 | 97 ± 1 | 97 ± 1 | 0.34 |
| Intron2A1 CpG62 | 93 ± 2 | 92 ± 2 | 92 ± 2 | 0.52 |
| Intron2A1 CpG115 | 95 ± 2 | 94 ± 2 | 95 ± 2 | 0.54 |
| Intron2A1 CpG180 | 97 ± 0.9 | 96 ± 1 | 96 ± 1 | 0.51 |
| Intron2A1 CpG228 | 92 ± 2 | 92 ± 2 | 92 ± 3 | 0.79 |
| Intron5A1 CpG97 | 2 ± 0.7 | 1.7 ± 1 | 1.7 ± 1 | 0.78 |
| Intron5A1 CpG123 | 1.1 ± 0.4 | 1 ± 0.6 | 0.8 ± 0.5 | 0.45 |
| Intron5A1 CpG242 | 2 ± 1 | 2 ± 1 | 1.3 ± 0.8 | 0.29 |
| Intron5A1 CpG262 | 2 ± 0.9 | 1.9 ± 1 | 1 ± 0.8 | 0.25 |
| Intron5A1 CpG268 | 2.2 ± 1 | 2 ± 1 | 1.4 ± 0.8 | 0.24 |
| Intron5A2 CpG66 | 92 ± 3 | 91 ± 3 | 92 ± 2 | 0.30 |
| Intron5A2 CpG127 | 98 ± 0.5 | 97 ± 1 | 97 ± 2 | 0.25 |
| Intron5A2 CpG218 | 97 ± 2 | 96 ± 2 | 96 ± 2 | 0.41 |
| Intron5A3 CpG133 | 8 ± 4 | 9 ± 4 | 7 ± 4 | 0.47 |
| Intron7A1 CpG127 | 62 ± 4 | 59 ± 6 | 58 ± 8 | 0.67 |
| Intron7A1 CpG138 | 58 ± 4 | 55 ± 6 | 52 ± 7 | 0.25 |
| Intron7A1 CpG282 | 79 ± 4 | 79 ± 5 | 76 ± 6 | 0.30 |
| Intron7A2 CpG41 | 84 ± 3 | 81 ± 4 | 78 ± 6 | 0.26 |
| Intron7A2 CpG94 | 98 ± 0.7 | 96 ± 1 | 96 ± 1 | 0.33 |
| Intron7A2 CpG119 | 98 ± 2 | 97 ± 1 | 96 ± 1 | 0.46 |
| Intron7A2 CpG169 | 76 ± 4 | 72 ± 9 | 68 ± 11 | 0.36 |
| Intron7A2 CpG221 | 86 ± 2 | 83 ± 6 | 81 ± 6 | 0.39 |
| PromoterA1 CpG112 | 9 ± 12 | 11 ± 9 | 10 ± 7 | 0.80 |
| PromoterA1 CpG128 | 29 ± 4 | 24 ± 5 | 21 ± 5 | 0.32 |
| PromoterA1 CpG175 | 31 ± 3 | 30 ± 5 | 26 ± 5 | 0.29 |
| PromoterA1 CpG199 | 9 ± 2 | 8 ± 2 | 7 ± 2 | 0.30 |
| PromoterA2 CpG48 | 87 ± 2 | 86 ± 2 | 85 ± 3 | 0.23 |
| PromoterA2 CpG89 | 97 ± 2 | 97 ± 1 | 96 ± 2 | 0.46 |
| PromoterA2 CpG101 | 98 ± 0.9 | 97 ± 1 | 96 ± 2 | 0.24 |
| PromoterA2 CpG168 | 95 ± 2 | 95 ± 2 | 94 ± 2 | 0.78 |
| PromoterA2 CpG215 | 73 ± 3 | 70 ± 5 | 66 ± 5 | 0.26 |
| PromoterA2 CpG253 | 98 ± 1 | 96 ± 1 | 96 ± 1 | 0.34 |
| PromoterA2 CpG288 | 90 ± 3 | 89 ± 2 | 87 ± 2 | 0.43 |
| Proximal EnhancerA1CpG83 | 16 ± 6 | 13 ± 5 | 10 ± 4 | 0.23 |
| Proximal EnhancerA1CpG91 | 15 ± 6 | 13 ± 5 | 10 ± 4 | 0.28 |
| Proximal EnhancerA1CpG134 | 4 ± 2 | 3 ± 1 | 2 ± 1 | 0.29 |
| Proximal EnhancerA1CpG207 | 27 ± 8 | 22 ± 8 | 17 ± 7 | 0.26 |
| Proximal EnhancerA1CpG216 | 26 ± 9 | 22 ± 8 | 16 ± 7 | 0.31 |
| Proximal EnhancerA1CpG226 | 21 ± 8 | 19 ± 7 | 14 ± 6 | 0.24 |
| Proximal EnhancerA1CpG265 | 29 ± 10 | 26 ± 10 | 19 ± 6 | 0.22 |
| Proximal EnhancerA2 CpG84 | 9 ± 11 | 12 ± 9 | 11 ± 7 | 0.78 |
| Proximal EnhancerA2 CpG100 | 28 ± 4 | 25 ± 6 | 22 ± 6 | 0.29 |
| Proximal EnhancerA2 CpG147 | 30 ± 4 | 29 ± 5 | 26 ± 5 | 0.24 |
| Proximal EnhancerA2 CpG171 | 9 ± 2 | 8 ± 2 | 7 ± 2 | 0.28 |
| Proximal EnhancerA2 CpG244 | 21 ± 5 | 19 ± 4 | 17 ± 5 | 0.29 |
| Proximal EnhancerA3 CpG148 | 9 ± 15 | 13 ± 11 | 11 ± 8 | 0.80 |
| Proximal EnhancerA3 CpG199 | 62 ± 7 | 57 ± 7 | 52 ± 11 | 0.36 |
| Proximal EnhancerA4 CpG191 | 24 ± 2 | 26 ± 6 | 26 ± 7 | 0.80 |
| Proximal EnhancerA4 CpG232 | 42 ± 4 | 38 ± 9 | 37 ± 10 | 0.68 |

AI adrenal insufficiency, BSA body surface area