Supplementary table 7. Differences in *FKBP5* methylation between patients with cortisol producing adenoma (CPA) and patients with adrenal insufficiency (AI) from PROSAI split by frequency of dose adjustments over 6 months

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **AI** | | |  |  |
|  | **Frequency of dose adjustments over previous 6 months** | | | **CPA** | **p** |
| **Methylation, %, mean ± SD** | **1x**  **(n=13)** | **2-3x**  **(n=15)** | **>3**  **(n=40)** | **(n=64)** |  |
| Intron1A1 CpG185 | 23 ± 12 | 20 ± 6 | 18 ± 7 | 20 ± 5 | 0.43 |
| Intron1A1 CpG189 | 35 ± 14 | 38 ± 9 | 35 ± 8 | 37 ± 8 | 0.79 |
| Intron1A2 CpG49 | 97 ± 1 | 96 ± 2\* | 96 ± 2\* | 98 ± 0.5 | <0.01 |
| Intron1A2 CpG126 | 94 ± 1 | 93 ± 1\* | 94 ± 1 | 94 ± 0.9 | <0.01 |
| Intron1A2 CpG143 | 98 ± 0.7 | 97 ± 1 | 97± 0.9\* | 98 ± 0.4 | <0.01 |
| Intron1A2 CpG190 | 98 ± 0.9 | 97 ± 1\* | 97 ± 1\* | 98 ± 0.5 | <0.01 |
| Intron2A1 CpG62 | 94 ± 2 | 91 ± 2\* | 91 ± 2\* | 94 ± 1 | <0.01 |
| Intron2A1 CpG115 | 95 ± 2 | 94 ± 2\* | 94 ± 3\* | 96 ± 1 | 0.01 |
| Intron2A1 CpG180 | 97 ± 1 | 96 ± 0.7\* | 96 ± 1\* | 97 ± 0.6 | <0.01 |
| Intron2A1 CpG228 | 93 ± 2 | 91 ± 2 | 92 ± 2\* | 93 ± 1 | 0.01 |
| Intron5A1 CpG97 | 2.3 ± 2 | 1.8 ± 1 | 1.5 ± 0.7\* | 2.9 ± 1 | <0.01 |
| Intron5A1 CpG123 | 0.9 ± 0.4 | 0.9 ± 0.6\* | 1 ± 0.5\* | 1.3 ± 0.5 | <0.01 |
| Intron5A1 CpG242 | 1.9 ± 0.8 | 1.6 ± 1 | 1.7 ± 0.9\* | 2.4 ± 1 | 0.01 |
| Intron5A1 CpG262 | 1.6 ± 0.8 | 1.5 ± 1 | 1.8 ± 0.9 | 2.3 ± 1 | 0.03 |
| Intron5A1 CpG268 | 2 ± 0.9 | 1.6 ± 0.9\* | 1.9 ± 0.9 | 2.4 ± 1 | 0.01 |
| Intron5A2 CpG66 | 93 ± 2 | 91 ± 2\* | 91 ± 2\* | 93 ± 2 | <0.01 |
| Intron5A2 CpG127 | 98 ± 0.8 | 97 ± 1\* | 97 ± 1\* | 98 ± 0.5 | <0.01 |
| Intron5A2 CpG218 | 97 ± 1 | 96 ± 2\* | 96 ± 2\* | 98 ± 0.5 | <0.01 |
| Intron5A3 CpG133 | 7.4 ± 4 | 7.7 ± 2 | 8 ± 3 | 7 ± 3 | 0.43 |
| Intron7A1 CpG127 | 58 ± 7 | 57 ± 7 | 58 ± 6 | 59 ± 5 | 0.68 |
| Intron7A1 CpG138 | 53 ± 7 | 52 ± 6 | 54 ± 6 | 55 ± 5 | 0.35 |
| Intron7A1 CpG282 | 77 ± 7 | 77 ± 5 | 78 ± 5 | 79 ± 4 | 0.45 |
| Intron7A2 CpG41 | 80 ± 5 | 79 ± 5 | 80 ± 5 | 82 ± 4 | 0.19 |
| Intron7A2 CpG94 | 97 ± 1 | 96 ± 1\* | 96 ± 1\* | 97 ± 0.4 | <0.01 |
| Intron7A2 CpG119 | 97 ± 2 | 96 ± 1\* | 97 ± 1\* | 98 ± 0.4 | <0.01 |
| Intron7A2 CpG169 | 69 ± 9 | 71 ± 11 | 72 ± 9 | 71 ± 10 | 0.89 |
| Intron7A2 CpG221 | 83 ± 6 | 82 ± 6 | 82 ± 8 | 83 ± 6 | 0.99 |
| PromoterA1 CpG112 | 8 ± 8 | 12 ± 9 | 11 ± 9 | 11 ± 8 | 0.85 |
| PromoterA1 CpG128 | 25 ± 5 | 23 ± 6 | 24 ± 5 | 24 ± 4 | 0.89 |
| PromoterA1 CpG175 | 29 ± 4 | 29 ± 5 | 29 ± 5 | 29 ± 4 | 0.98 |
| PromoterA1 CpG199 | 8.3 ± 2 | 8.2 ± 2 | 7.8 ± 2 | 8 ± 1 | 0.80 |
| PromoterA2 CpG48 | 86 ± 1 | 84 ± 2\* | 86 ± 2 | 86 ± 2 | 0.02 |
| PromoterA2 CpG89 | 97 ± 0.8 | 97 ± 2 | 97 ± 0.9\* | 97 ± 0.4 | 0.01 |
| PromoterA2 CpG101 | 97 ± 1 | 97 ± 2 | 97 ± 1\* | 97 ± 0.4 | 0.01 |
| PromoterA2 CpG168 | 96 ± 1 | 94 ± 2\* | 94 ± 2\* | 96 ± 0.5 | <0.01 |
| PromoterA2 CpG215 | 69 ± 3 | 68 ± 5 | 70 ± 4 | 68 ± 5 | 0.15 |
| PromoterA2 CpG253 | 97 ± 1 | 96 ± 1 | 96 ± 1 | 97 ± 0.4 | 0.02 |
| PromoterA2 CpG288 | 88 ± 3 | 88 ± 3 | 88 ± 3 | 88 ± 2 | 0.89 |
| Proximal EnhancerA1 CpG83 | 11 ± 4 | 12 ± 5 | 12 ± 5 | 11 ± 5 | 0.79 |
| Proximal EnhancerA1 CpG91 | 11 ± 4 | 12 ± 5 | 12 ± 5 | 11 ± 5 | 0.90 |
| Proximal EnhancerA1 CpG134 | 2.7 ± 1 | 2.9 ± 1 | 2.9 ± 1 | 3 ± 1 | 0.90 |
| Proximal EnhancerA1 CpG207 | 18 ± 7 | 20 ± 8 | 20 ± 8 | 18 ± 7 | 0.68 |
| Proximal EnhancerA1 CpG216 | 18 ± 7 | 20 ± 8 | 20 ± 8 | 18 ± 7 | 0.71 |
| Proximal EnhancerA1 CpG226 | 15 ± 6 | 17 ± 7 | 17 ± 7 | 15 ± 6 | 0.70 |
| Proximal EnhancerA1 CpG265 | 20 ± 7 | 23 ± 8 | 24 ± 10 | 20 ± 8 | 0.35 |
| Proximal EnhancerA2 CpG84 | 9 ± 9 | 12 ± 8 | 12 ± 9 | 12 ± 8 | 0.89 |
| Proximal EnhancerA2 CpG100 | 26 ± 6 | 24 ± 6 | 24 ± 6 | 25 ± 4 | 0.86 |
| Proximal EnhancerA2 CpG147 | 29 ± 5 | 28 ± 5 | 29 ± 4 | 30 ± 4 | 0.44 |
| Proximal EnhancerA2 CpG171 | 9 ± 2 | 8 ± 2 | 8 ± 2\* | 9 ± 2 | <0.01 |
| Proximal EnhancerA2 CpG244 | 21 ± 6 | 19 ± 5 | 19 ± 4 | 19 ± 5 | 0.77 |
| Proximal EnhancerA3 CpG148 | 6 ± 7 | 12 ± 10 | 12 ± 11 | 10 ± 9 | 0.35 |
| Proximal EnhancerA3 CpG199 | 60 ± 11 | 54 ± 10 | 57 ± 7 | 56 ± 9 | 0.42 |
| Proximal EnhancerA4 CpG191 | 26 ± 10 | 26 ± 7 | 27 ± 4 | 26 ± 5 | 0.98 |
| Proximal EnhancerA4 CpG232 | 41 ± 11 | 41 ± 7 | 41 ± 7 | 39 ± 7 | 0.45 |

\* p<0.05 post-hoc AI vs CPA