**Supplementary Table 1. Clinical characteristics of the *AIP* positive prospectively diagnosed patients**

|  |  |
| --- | --- |
| Clinical characteristic | N=19 |
| Familial, n (%) | 19 (100%) |
| Gender, n (% male) | 12 (63.2%) |
| Diagnosis, n (%)  GH excess  NFPA | 9 (47.4%)  10 (52.6%) |
| Age at diagnosis (years) | 30 [19-37] |
| Maximum diameter (mm)\* | 6 [4.9-10] |
| Macroadenoma, n (%) | 6 (31.6 %) |
| Extrasellar extension, n (%) | 2 (11.8%) |
| Pituitary apoplexy, n (%) | 0 (0%) |
| Number of treatments\* | 0 [0-2] |

NFPA: non-functioning pituitary adenoma

\*Median and interquartile range

**Supplementary Table 2. List of *AI****P* **mutations in our cohort divided into truncating and non-truncating**

|  |  |
| --- | --- |
| Truncating mutations | Non-truncating mutations † |
| g.4856\_4857CG>AA[1–3] | c.140\_163del (p.G47\_R54del)[4] |
| c.1-?\_993+?del- (whole gene deletion)[1] | c.469-2A>G (p.E158\_Q184del)[5–7] |
| c.100-1025\_279+357del (p.A34\_K93del) (exon 2 deletion)[8] | c.562C>T(p.R188W)[9] |
| c.240\_241delinsTG (p.M80\_R81delinsIG) | **c.605A>G (p.Y202C)** |
| c.241C>T (p.R81\*)[2,3,10–12] | c.713G>A (p.C238Y)[3,13] |
| c.249G>T (p.G83Afs\*15)[1] | c.760T>C (p.C254R)[9] |
| c.333delC (p.K112Rfs\*44) | c.762C>G (p.C254W)[9] |
| c.338\_341dupACCC (p.L115Pfs\*16)[14,15] | c.805\_825dup (p.F269\_H275dup)[2,3,6] |
| c.376\_377delCA (p.Q126Dfs\*3) | c.807C>T (p.(=))[1,3,8,16–18] |
| c.3G>A (p.?)[19] | c.811C>T p.R271W[1,4,17,20] |
| c.40C>T (p.Q14\*)[14,21–23] | c.815G>G (p.G272D)[19,24] |
| c.427C>T (p.Q143\*)[14] | c.872\_877delTGCTGG (p.V291\_L292del)[25] |
| c.490C>T (p.Q164\*)[1] | **c.991T>C(p.331Rext91)** |
| c.570C>G (p.Y190\*)[14] |  |
| c.645+1G>C (p.?) |  |
| c.662dupC (p.E222\*)[1] |  |
| c.70G>T (p.E24\*)[3,13] |  |
| c.74\_81delins7 (p.L25Pfs\*130)[1,26] |  |
| c.783C>G (p.Y261\*)[6,14,27] |  |
| c.787+9C>T[14] |  |
| c.804C>A (p.Y268\*)[10,14,28] |  |
| c.816delC (p.K273Rfs\*30)[14] |  |
| c.868A>T (p.K290\*)[14] |  |
| c.910C>T (p.R304\*)[3–6,17,21,27,29] |  |
| c.967delC (p.R323Gfs\*39)[14] |  |
| c.976\_977insC (p.G326Afs\*?)[14] |  |
| c.978dupG (p.I327Dfs\*?)[14] |  |

Mutations in bold are novel mutations not previously described. These patients’ clinical characteristics are shown in Table 1.

† Patients with the c.911G>A (p.R304Q) and c.100-18C>T variants were excluded from this study, as recent data suggest that these might represent variants of unknown significance.

**Supplemental Figure 1. Observed versus model-derived *AIP* mutation risk model with low (<5%), moderate (5-19%) and high risk (≥20%) categories.**

C:\Users\Francesca Caimari\Documents\AIP database\Journal of Medical Genetics\Fig 3.tif

The similar probabilities for estimated and observed risk indicates a good calibration of the model.

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