**Supplementary Table 1.** A total of 16 reported and novel variants identified in two isoforms of *PGAP2*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **PGAP2 Variants** | | **Zygosity** | **Ethnicity** | **Detailed Phenotype** | **Reference** |
| **Isoform 8**  [**NM\_001256240.2**](https://www.ncbi.nlm.nih.gov/nucleotide/NM_001256240.2)  [**NP\_001243169.1**](https://www.ncbi.nlm.nih.gov/protein/NP_001243169.1) | **Isoform 1**  **NM\_014489.4**  [**NP\_055304.1**](https://mutalyzer.nl/normalizer/NM_014489.4(NP_055304.1):p.(Arg238Pro)) |
| c.2T>G, p.M1?  c.221G>A, p.R74H | c.2T>G, p.M1?  c.404G>A, [p.R135H](https://mutalyzer.nl/normalizer/NM_014489.4(NP_055304.1):p.(Arg135His)) | compound heterozygous | Polish | flat occiput and pectus excavatum, epilepsy, no speech, hyporeflexia, hypotonia, hyperthermia, progressive  neurological deterioration, hyperphosphatasemia. | (Jezela-Stanek et al., 2016) |
| psychomotor retardation, generalized weakness, seizures, sustained hyperphosphatasaemia | (Pronicka et al., 2016) |
| c.46C>T, p.R16W  c.479C>T, p.T160I | c.46C>T, p.R16W  c.662C>T, [p.T221I](https://mutalyzer.nl/normalizer/NM_014489.4(NP_055304.1):p.(Thr221Ile)) | compound heterozygous | Finnish | febrile seizure, epilepsy, subtle facial dysmorphism, mild ID, tapering fingers, hyperphosphatasia | (Krawitz et al., 2013) |
| c.380T>C, p.L127S | c.563T>C, [p.L188S](https://mutalyzer.nl/normalizer/NM_014489.4(NP_055304.1):p.(Leu188Ser)) | homozygous | Turkish | median cleft palate, atrial septal  defect, hypoplasia of the corpus callosum, marked ID, microcephaly, facial dysmorphism, [brachytelephalangy, tapering fingers, hearing impairment, hyperphosphatasia](https://en.wiktionary.org/wiki/brachytelephalangy) |
| c.103del, p.L35Sfs\*90,  c.134A>G, p.H45R | c.103del, p.L35Sfs\*90,  c.134A>G, p.H45R | compound heterozygous | Afro-Caribbean | global developmental delay, speech delay, precocious puberty, esotropia and myopic astigmatism, and hyperphosphatasia | (Messina et al., 2023) |
| c.165+5954C>T | c.191C>T, p.A64V | homozygous | Saudi Arabian | developmental delay, ID, epilepsy, poor hearing, microcephaly, hyperphosphatasia | (Naseer et al., 2016) |
| c.220C>T, p.R74C | c.403C>T, [p.R135C](https://mutalyzer.nl/normalizer/NM_014489.4(NP_055304.1):p.(Arg135Cys)) | homozygous | Jordanian | nystagmus, global developmental delay, aganglionic megacolon, hyperphosphatasia | (Froukh et al., 2020) |
| c.284A>G, p.Y95C | c.467A>G, p.Y156C | homozygous | Guatemalan (personal communication with Miles Thompson) | hyperphosphatasia and neurologic  deficit with additional homozygous *PGAP3* VUS | (Thompson et al., 2023) |
| c.296A>G, p.Y99C | c.479A>G, [p.Y160C](https://mutalyzer.nl/normalizer/NM_014489.4(NP_055304.1):p.(Tyr160Cys)) | homozygous | Syrian | fetal hypokinesia, development delay, severe ID, hyperphosphatasia, hypotonia, strabismus, sleep disturbance, absence  seizures, cerebral atrophy and increased gyration, Dandy‐Walker malformation, short stature | (Hansen et al., 2013; Reuter et al., 2017) |
| c.347A>G, p.N116S  c.463G>A, p.G155R | c.530A>G, p.N177S  c.646G>A, p.G216R | compound heterozygous | German | prominent forehead, facial dysmorphism, epilepsy, tapering fingers, brachydactyly, camptodactyly, and syndactyly, hyperphosphatasia | This study |
| c.530G>C, p.R177P | c.713G>C, [p.R238P](https://mutalyzer.nl/normalizer/NM_014489.4(NP_055304.1):p.(Arg238Pro)) | homozygous | Pakistani | Severe ID, macrocephaly, hearing loss, facial dysmorphism, tapering fingers, brachydactyly, camptodactyly, and syndactyly, hyperphosphatasia | This study |
| Pakistani | severe ID,  hyperphosphatasia, absence  seizures | (Hansen et al., 2013) |
| Pakistani  (personal communication with JB Vincent) | Non-syndromic ID | (Harripaul et al., 2018) |
| c.554G>A, p.R185Q | c.737G>A, [p.R246](https://mutalyzer.nl/normalizer/NM_014489.4(NP_055304.1):p.(Arg246Gln))Q | heterozygous  (carriers) | Bedouin | learning disability without ID and mild hyperphosphatasia | (Perez et al., 2017) |
| homozygous | ID, speech delay, behavioral problems, seizures, depression, enuresis, hyperphosphatasia. |
| c.698C>T, p.T233M | c.881C>T, [p.T294M](https://mutalyzer.nl/normalizer/NM_014489.4(NP_055304.1):p.(Thr294Met)) | homozygous | American | Mabry syndrome, hyperphosphatasia with  neurologic deficit ((HPMRS), developmental disability, seizures, brachytelephalangy | (Thompson et al., 2020) |

ID: intellectual disability

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