

Table 1. Mutations of the NR3C1 gene causing Chrousos syndrome

| Author (Reference) | Mutation Position | | Molecular Mechanisms | Genotype | Phenotype |
|---|-----------------------------------|--------------|---|--------------|---|
| | cDNA | Amino acid | | | |
| Chrousos et al ⁷¹ Hurley et al ⁷⁷ Charmandari et al ⁸⁴ | 1922 (A→T) | 641 (D→V) | Transactivation ↓ Affinity for ligand ↓ (×3) Nuclear translocation: 22 min Abnormal interaction with GRIP1 | Homozygous | Hypertension Hypokalemic alkalosis |
| Karl et al ⁷⁸ | 4 bp deletion in exon-intron 6 | | hGRα number: 50% of control Inactivation of the affected allele | Heterozygous | Hirsutism Male-pattern hair-loss Menstrual irregularities |
| Malchoff et al ⁷⁹ Charmandari et al ⁸⁴ | 2185 (G→A) | 729 (V→I) | Transactivation ↓ Affinity for ligand ↓ (×2) Nuclear translocation: 120 min Abnormal interaction with GRIP1 | Homozygous | Precocious puberty Hyperandrogenism |
| Karl et al ⁷⁶ Kino et al ⁸⁰ Charmandari et al ⁸⁴ | 1676 (T→A) | 559 (I→N) | Transactivation ↓ Decrease in hGR binding sites Transdominance (+) Nuclear translocation: 180 Abnormal interaction with GRIP1 | Heterozygous | Hypertension Oligospermia Infertility |
| Ruiz et al ⁸¹ Charmandari et al ⁸⁶ | 1430 (G→A) | 477 (R→H) | Transactivation ↓ No DNA binding Nuclear translocation: 20 min | Heterozygous | Hirsutism Fatigue Hypertension |
| Ruiz et al ⁸¹ Charmandari et al ⁸⁶ | 2035 (G→A) | 679 (G→S) | Transactivation ↓ Affinity for ligand ↓ (×2) Nuclear translocation: 30 min Abnormal interaction with GRIP1 | Heterozygous | Hirsutism Fatigue Hypertension |

Table 1. (continued) Mutations of the NR3C1 gene causing Chrousos syndrome

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| | cDNA | Amino acid | | | |
| Mendonca et al ⁸² Charmandari et al ⁸⁴ | 1712 (T→C) | 571 (V→A) | Transactivation ↓ Affinity for ligand ↓ (×6) Nuclear translocation: 25 min Abnormal interaction with GRIP1 | Homozygous | Ambiguous genitalia Hypertension Hypokalemia Hyperandrogenism |
| Vottero et al ⁸³ Charmandari et al ⁸⁴ | 2241 (T→G) | 747 (I→M) | Transactivation ↓ Transdominance (+) Affinity for ligand ↓ (×2) Nuclear translocation ↓ Abnormal interaction with GRIP1 | Heterozygous | Cystic acne Hirsutism Oligo-amenorrhea |
| Charmandari et al ⁸⁵ | 2318 (T→C) | 773 (L→P) | Transactivation ↓ Transdominance (+) Affinity for ligand ↓ (×2.6) Nuclear translocation: 30 min Abnormal interaction with GRIP1 | Heterozygous | Fatigue Anxiety Acne Hirsutism Hypertension |
| Charmandari et al ⁸⁷ | 2209 (T→C) | 737 (F→L) | Transactivation ↓ Transdominance (+) Affinity for ligand ↓ (×1.5) Nuclear translocation: 180 min | Heterozygous | Hypertension Hypokalemia |
| McMahon et al ⁷⁴ | 2 bp deletion at nt 2318-9 | 773 | Transactivation ↓ Affinity for ligand: absent No suppression of IL-6 | Homozygous | Hypoglycemia Fatigability with feeding Hypertension |
| Nader et al ⁷³ | 2141 (G→A) | 714 (R→Q) | Transactivation ↓ Transdominance (+) Affinity for ligand ↓ (×2) Nuclear translocation ↓ Abnormal interaction with GRIP1 | Heterozygous | Hypoglycemia Hypokalemia Hypertension Mild clitoromegaly Advanced bone age Precocious pubarche |
| Bouligand et al ⁸⁸ | 1405 (C→T) | 469 (R→X) | Transactivation ↓ Ligand-binding sites ↓ No DNA binding No nuclear translocation | Heterozygous | Adrenal hyperplasia Hypertension Hypokalemia |
| Zhu Hui-juan et al ⁸⁹ Nicolaidis et al ⁹³ | 1667 (G→T) | 556 (T→I) | Transactivation ↓ Transrepression Affinity for ligand ↓ Nuclear translocation ↓ Abnormal interaction with GRIP1 | Heterozygous | Adrenal incidentaloma |

Table 1. (continued) Mutations of the NR3C1 gene causing Chrousos syndrome

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|--------------------------------|-------------------|----------------|--|--------------|--|
| | cDNA | Amino acid | | | |
| Roberts et al ⁹⁰ | 1268 (T→C) | 423 (V→A) | Transactivation ↓ Affinity for ligand: N No DNA binding Nuclear translocation: 35 min Interaction with GRIP1: N | Heterozygous | Fatigue Anxiety Hypertension |
| Nicolaides et al ⁹¹ | 1724 (T→G) | 575 (V→G) | Transactivation ↓ Transrepression Affinity for ligand ↓ (×2) Nuclear translocation ↓ Abnormal interaction with GRIP1 | Heterozygous | Melanoma Asymptomatic daughters |
| Nicolaides et al ⁹² | 2177 (A→G) | 726 (H→R) | Transactivation ↓ Transrepression ↓ Affinity for ligand ↓ (×2) Nuclear translocation ↓ Abnormal interaction with GRIP1 | Heterozygous | Hirsutism, Acne, Alopecia, Anxiety, Fatigue Irregular menstrual cycles |
| Velayos et al ⁹⁴ | 1429 (C→T) | 477 (R→C) | Not studied yet | Heterozygous | Mild hirsutism Asymptomatic mother |
| Velayos et al ⁹⁴ | 1762_1763insTTAC | 588 (H→L*5) | Not studied yet | Heterozygous | Hirsutism, Anxiety Chronic fatigue |
| Vitellius et al ⁹⁵ | 1429 (C→A) | 477 (R→S) | No Transactivation Affinity for ligand: N No DNA binding Nuclear translocation ↓ | Heterozygous | Adrenal incidentaloma |
| Vitellius et al ⁹⁵ | 1433 (A→G) | 478 (Y→C) | Transactivation ↓ Affinity for ligand: N DNA binding ↓ Nuclear translocation ↓ | Heterozygous | Adrenal incidentaloma |
| Vitellius et al ⁹⁵ | 2015 (T→C) | 672 (L→P) | No Transactivation No Affinity for ligand No DNA binding No Nuclear translocation | Heterozygous | Adrenal incidentaloma |