# Trabalhos Científicos

**Título:** Otx2 Gene Mutations Are Rare In Patients With Combined Pituitary Hormone Deficiency (cphd) And/or Midline Cerebral Defects (mcd)

**Autores:** NOVARETTI N (FACULDADE DE MEDICINA DE RIBEIRÃO PRETO - UNIVERSIDADE DE SÃO PAULO); PAULO S (FACULDADE DE MEDICINA DE RIBEIRÃO PRETO - UNIVERSIDADE DE SÃO PAULO); SANTOS A (FACULDADE DE MEDICINA DE RIBEIRÃO PRETO - UNIVERSIDADE DE SÃO PAULO); MOREIRA A (FACULDADE DE MEDICINA DE RIBEIRÃO PRETO - UNIVERSIDADE DE SÃO PAULO); MARTINELLI JUNIOR CE (FACULDADE DE MEDICINA DE RIBEIRÃO PRETO - UNIVERSIDADE DE SÃO PAULO); IGARASHI M (NATIONAL RESEARCH INSTITUTE FOR CHILD HEALTH AND DEVELOPMENT, JAPAN ); OGATA T (NATIONAL RESEARCH INSTITUTE FOR CHILD HEALTH AND DEVELOPMENT, JAPAN ); FUKAMI M (NATIONAL RESEARCH INSTITUTE FOR CHILD HEALTH AND DEVELOPMENT, JAPAN ); CASTRO M (FACULDADE DE MEDICINA DE RIBEIRÃO PRETO - UNIVERSIDADE DE SÃO PAULO); ANTONINI S (FACULDADE DE MEDICINA DE RIBEIRÃO PRETO - UNIVERSIDADE DE SÃO PAULO)

**Resumo:** Objective: To investigate the presence of OTX2 mutations in patients with CPHD with different MCD degrees. Patients and Methods: We evaluated 117 patients with CPHD and/or MCD (61 with CPHD without MCD, 32 with septo-optic dysplasia (SOD), 15 with holoprosencephaly (HPE) and 9 with isolated anomaly of corpus callosum - ACC). OTX2 coding/boundary regions were sequenced. Transactivating activity of mutant OTX2 was examined in vitro by luciferase assays using reporter vectors containing promoter sequences of IRBP, HESX1, POU1F and GNRH1. Results: Mean age 5.8 years (0.7-4.4) in SOD patients, 9 (6.5-11.7) in patients ACC and 10.7 (1.2-27) in CPHD without MCD patients. Endocrine deficiencies (CPHD with or without ADH deficiency or isolated GH deficiency-GHD) were found in 69%, 67%, and 53% in SOD, ACC, and HPE patients, respectively. A OTX2 variant c.757G>A (p.A253T) was identified in a CPHD patient. In vitro analysis showed no differences between the wild-type OTX2 and Ala253Thr OTX2. OTX2 variant c.444G>C (p.P148) was identified in a SOD patient and the intronic variant c.*19T>A was identified in a SOD and in a CPHD patients. These variants were not found in 120 Brazilian controls neither in the 1000genomes project. In silico analysis showed that none of these OTX2 variants are likely to impair splicing. Conclusions: OTX2 variants were identified in patients with CPHD and/or MCD but in vitro and in silico analysis revealed that these variants are likely to be non functional. Mutations in OTX2 gene appear to be a rare cause of CPHD and/or MCD.