PYCP significantly reduced the levels of phosphorylated p38 and JNK. Moreover, by inhibiting the degradation of inhibitor of kappaB-α, PYCP significantly suppressed the TNF-α-induced increased transcriptional activity and nuclear translocation of nuclear factor-kappaB (NF-κB). Furthermore, PYCP inhibited E3-ubiquitin ligases in TNF-α-treated C2C12 myotubes. In conclusion, PYCP ameliorated TNF-α-induced muscle atrophy by inhibiting the mitogen-activated protein kinase-mediated NF-κB pathway, indicating that it has therapeutic potential for related disorders.

Reproductive Endocrinology

SEX, GENDER, AND HORMONES

An Exploration of Novel Clinical Benchmarks for Assessing the Practice of Gonadectomy in Conditions Affecting Sex Development - on Behalf of the I-DSD Consortium

Angela K. Lucas-Herald, MBChB MRCPCH[1], Jillian Bryce, PhD[1], Martine Cools, MD,PHD[2], S Faisal Ahmed, MBChB,MD,FRCPCH[3].

[1]University of Glasgow, Glasgow, United Kingdom, 20232987862, Ghent, Belgium, [3]Royal Hospital for Children, Glasgow, Scotland, United Kingdom.

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Introduction: Although the practice of gonadectomy in the field of differences/disorders of sex development (DSD) has undergone intense scrutiny, objective knowledge regarding current practice of gonadectomy is lacking in conditions affecting sex development. **Methods:** The International DSD Registry (www.I-DSD.org) was examined for clinical information reported by the DSD specialist centre on age at presentation, year of birth, diagnosis, karyotype, sex of rearing and age at gonadectomy in all cases over the age of 16 years at the time of search and who had a disorder of androgen action or synthesis, gonadal dysgenesis or a non-specific DSD.**Results:** Of the 3,618 cases available in the registry, 757 (21%) met the inclusion criteria and data regarding gonadectomy status were available in 668 (88%) from 44 participating centres. Of these, 248 (37%) with a median age of 24 years (range 17, 75) were registered as male and 420 (63%) with a median age of 26 years (16, 86) were registered as female. Gonadectomy was reported from 36 centres in 351 of these 668 cases (53%) of whom 302 (86%) had a 46 XY karyotype. Females were more likely to undergo gonadectomy (n=311, p<0.0001) and the most common diagnoses were complete androgen insensitivity syndrome (n=161, 24%) and partial gonadal dysgenesis (n=94, 14%). Of the 351 cases, the primary indication for gonadectomy was reported in 268 (76%) cases and included mitigation of tumourigenesis risk in 172 (64%), conformity to sex assignment in 74 (28%) and another indication in 22 (8%). Gonadectomy was bilateral in 295 (84%), unilateral in 16 (5%) and unknown in 40 (11%). The median ratio for age at first presentation to age at gonadectomy in those who presented before the age of 5 years and those who presented after the age of 10 years was 0.1 (range) and 0.9 (range), respectively (p<0.0001). Of the 351 cases, 17 (5%) had undergone a gonadectomy before their first presentation to the specialist centre and these cases were distributed across 9 of the 36 centres. **Conclusions:** Not only does the rate of gonadectomy vary according to underlying diagnosis and sex of rearing, it also seems that there is a variable discrepancy between the age at presentation and age at gonadectomy. The use of this objective marker to identify trends in practice may improve our understanding of the causes of variation.

Genetics and Development (including Gene Regulation)

GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING I

CDH2 Gene Analysis in a Cohort of Patients with Congenital Hypopituitarism

Renata Kertsz, Master Student[1], Nathália Ferreira, Dr[2], João L.o.m Madeira, Dr[2], Anna Flavia Figueredo Benedetti, MD[3], Bruna Azevedo, Master Student[2], Débora Delmonte Bissegatto, Undergraduate[4], Sally Camper, PhD[5], Berenice Bilharinho Mendonca, MD[6], Alexander Jorge, PhD[3], Ivo J.p Arnhold, PhD[1], Luciani Renata Silveira Carvalho, MD,PHD[2].

[1]Hospital das Clinicas University of Sao Paulo Medical School, Sao Paulo, Brazil, [2]Hospital das Clinicas, Sao Paulo, Brazil, [3]Hospital das Clínicas, Sao Paulo, Brazil, [4]Hospital das Clinicas da Faculdade de Medicina da USP, So Caetano do Sul, Brazil, [5]University of Michigan, Ann Arbor, MI, USA, [6]Univ Sao Paulo Fac Med, Sao Paulo, Brazil.

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Introduction: Hypopituitarism is defined as a deficiency of one or more pituitary hormones. Pathogenic allelic variants in genes implicated in pituitary development were associated in 15% of the patients with congenital hypopituitarism (CH). To improve the molecular diagnosis we performed whole exome sequencing of ten patients born from consanguineous parents with CH. One patient with GH, TSH, ACTH and LH/FSH deficiencies presented an allelic variant c.865G>A, p.V289I in *CDH2* gene (exon 7) in homozygous state that was absent in populational databanks. *CDH2* produces an N-cadherin protein implicated in cellular adhesion and is responsible for epithelial-mesenchymal transition during pituitary development and differentiation. **Aim:** To analyze the *CDH2* gene in a cohort of unrelated patients with CH. **Methods:** We selected 143 patients with CH from a single Brazilian center. Genomic DNA, extracted by salting out technique, was submitted to PCR amplification of 15 coding regions, except CG rich exon 1, of the *CDH2* gene followed by the Sanger sequencing. Rare allelic variant frequency (MAF<1%) was searched in the populational data bank (ExAC, gnomAD, ABraom). Bioinformatic sites (Human Splicing Finder, Polyphen2, Mutation Taster and Mutation assessor) were used to look for deleterious effects. **Results:** Three allelic variants were found in this cohort. The allelic variant *CDH2* (c.865G>A, p.V289I) was found in heterozygous state in a male patient with short stature diagnosed with GH and TSH deficiencies at the age of 11 that evolved with LH/FSH and ACTH deficiencies. Family segregation showed 3 among 11 normal siblings heterozygous carriers. This variant is rare, in heterozygous state, in populational data bank and it was predicted as deleterious or possibly harmful. The allelic variant c.1202C>