LETTER TO THE EDITOR

Inactivating mutations of the LH receptor gene: more than two different phenotypes

Response to *European Journal of Endocrinology* 1998 **139** 145-147: Mutations of the G protein-coupled receptors of the hypothalamo-pituitary-gonadal axis. Where do we stand?

I read with interest the invited commentary of Dr M Simoni on the 'Mutations of the G protein-coupled receptors of the hypothalamic-pituitary-gonadal axis. Where do we stand?' (1). Dr Simoni discusses lucidly the relationship between phenotype and genotype in this group of endocrine diseases. Regarding the inactivating mutations involving the luteinizing hormone (LH) receptor gene, it was stated that these mutations lead to two different phenotypes, primary amenorrhea in female and male pseudohermaphroditism (MPH) as previously reported (2, 3).

There is an additional phenotype that is represented by familial cases of male hypergonadotrophic hypogonadism associated with micropenis, without MPH, in which hypoplasia of Leydig cells was found (4). Mutation in the LH receptor gene in these cases was first suspected to be present (4). Recently, a mutation in the LH receptor gene was documented in these patients, affecting its seventh transmembrane domain (5). We consider that for clinical purposes Leydig cell hypoplasia may be classified as type I (with MPH) and type II (without MPH) (4).

These data reinforce that this is a third phenotype resulting from inactivating mutations occurring in the

LH receptor gene and may be added to the two noted by Dr Simoni.

References

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- 3 Toledo SPA, Brunner HG, Kraaij R, Post M, Dahia PLM, Hayashida CY, Kremer H & Themmen APN. An inactivating mutation of the luteinizing hormone receptor gene causes amenorrhea in a 46,XX female. *Journal of Clinical Endocrinology and Metabolism* 1996 **11** 3850-3854.
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S P A Toledo, Endocrine Genetics Unit, Endocrinology, Department of Medicine, University of São Paulo School of Medicine, Av. Dr Arnaldo 455, 5th - 01246-903, São Paulo, Brazil

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