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


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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Received 18 November 1998
Accepted 23 November 1998