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Research Interests

The major interest of our research is to understand the reproductive consequences of premature and chronic activation of the luteinizing hormone receptor. The luteinizing hormone receptor (LHR), a seven transmembrane G protein-coupled receptor is critical in male and female reproduction. The gonadotropins, luteinizing hormone (LH) and chorionic gonadotropin, bind LHR and activate the cAMP signal transduction pathway. Several naturally occurring mutations in LHR have been identified that render the receptor constitutively active. These mutations are primarily found in boys presenting with precocious puberty and in boys with testicular adenoma. The current focus of our research is the characterization of a transgenic mouse model expressing a genetically engineered, constitutively active yoked hormone receptor complex (YHR) in which hCG is covalently linked to the N-terminus of LHR. The initial studies suggest that premature and constitutive activation of LHR will lead to precocious puberty and premature ovarian failure due to a combination of increased follicle recruitment and atresia in female mice and alter testicular development in male mice. These transgenic mice will be utilized as a novel tool to study signaling pathways leading to accelerated ovarian senescence and abnormalities in ovarian and testicular development. To understand the molecular basis for the hormonal and histological changes, alterations in gonadotropin and steroid hormone levels will be examined and the expression of key molecules in the LHR signaling pathway analyzed. A major thrust of these studies will be the analysis of alterations in gene expression in the ovaries and testis of YHR mice. A combination of *in situ* hybridization and real time RT-PCR to detect RNA levels and immunohistochemistry to analyze protein levels will be utilized. The developmental changes in testicular and ovarian morphology will also be analyzed by quantitative morphometric methods. Additional studies include the generation and characterization of transgenic mice expressing LHR containing a naturally occurring mutation resulting in constitutively activity to compare the effects of ligand-independent activation with that of the engineered ligand-receptor complex.

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