

Regulation of Luteinizing Hormone Receptor mRNA Expression in the Ovary:  
Involvement of a Cytosolic RNA Binding Protein.

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During the ovarian cycle, the expression of LH/hCG receptor (LHR) is up-regulated by FSH and estradiol during follicle maturation and down-regulated in response to the preovulatory LH surge. Available evidence suggests that LH/hCG –mediated down-regulation occurs post-transcriptionally. In several eukaryotic systems, it is now recognized that mRNA levels can be modulated post-transcriptionally by the interaction of cytosolic proteins with either the coding region or the untranslated 5' or 3' regions of the messenger RNA. In the rat ovary, we have identified a cytoplasmic LHR mRNA binding protein (LRBP) as a *trans*-factor in regulating LHR mRNA levels. LRBP binds to a 40 bp, polypyrimidine-rich bipartite sequence (LBS), in the coding region of LHR mRNA. We have shown that LRBP causes accelerated decay of LHR mRNA in an in vitro system. The expression of LRBP shows inverse relationship to the steady state levels of LHR mRNA during the ovarian cycle. LRBP was purified to homogeneity and N-terminal sequencing and MS-MALDI analysis established the identity of LRBP as being mevalonate kinase (MVK), an enzyme involved in cholesterol biosynthesis and belonging to GHMP family of kinases containing a potential RNA binding domain. The identity was further confirmed by demonstrating the ability of the recombinant mevalonate kinase to interact with LHR mRNA in a sequence specific manner. The expression of MVK mRNA was induced in response to hCG treatment and this occurred prior to down regulation of LHR mRNA expression. In a rabbit reticulocyte lysate system, gel purified LRBP decreased the in vitro translation of capped, full length LHR mRNA. The inhibition was reversed by LBS in a concentration dependent manner, but not mutated LBS. Mevalonate, the substrate for mevalonate kinase was also able to reverse the inhibition of LHR translation by purified LRBP. It is postulated that the resulting untranslatable LHR-RNP complex with LRBP may be targeted for degradation by components associated with the ovarian ribosome. These processes might be responsible for the down regulation of LHR mRNA expression in the ovary. [Supported by NIH Grant HD R37 06656]