Two Defective Heterozygous Luteinizing Hormone Receptors Can Rescue Hormone Action*

Received for publication, December 11, 2001, and in revised form, February 20, 2002
Published, JBC Papers in Press, February 21, 2002, DOI 10.1074/jbc.M111818200

ChangWoo Lee‡, Inhae Ji‡, KiSung Ryu‡, YongSang Song‡, P. Michael Conn§, and Tae H. Ji†

From the ‡Department of Chemistry, University of Kentucky, Lexington, Kentucky 40506-0055 and the §Oregon Regional Primate Research Center and Department of Physiology and Pharmacology, Oregon Health Sciences University, Portland, Oregon 97201

Luteinizing hormone receptor is a G protein-coupled receptor and consists of two halves: the N-terminal extracellular half (exodomain) and C-terminal membrane-associated half (endodomain). Hormone binds to the exodomain, and the resulting hormone-exodomain complex modulates the endodomain to generate signals. There are mutations that impair either hormone binding or signal generation. We report that the coexpression of a binding defective mutant and a signal-defective mutant rescues signal generation to produce cAMP. This rescue requires both types of mutant receptors and is dependent on the human chorionic gonadotropin dose, the surface concentration of mutant receptors, and the amino acid position of mutations. Furthermore, random collisions among mutant receptors are not involved in the rescue. Our observations provide new insights into the mechanisms of the functional and structural relationship of the exo- and endodomain, signal transduction, and receptor genetics, in particular for defective heterozygotes.

The luteinizing hormone receptor (LHR)1 plays a crucial role in the development of the gonads in both sexes and ovulation in females. Defective mutations of the receptor often cause infertility (1). Gain of function mutations are generally dominant, whereas loss of function mutations are recessive. The genetic prediction of mutations is not straightforward, because the effects of some mutations are partial and some patients are defective heterozygotes. For example, there are patients with two defective heterozygous LHR mutations (2, 3) and the precise relationship of two mutant receptors in a patient is unclear. This is particularly relevant for LHR, which has two distinct domains, one for hormone binding and the other for signal generation (4–6). We raise the question of whether the exodomain of an LHR can modulate the endodomain of another LHR. As a first step toward understanding this novel and intriguing question, we have investigated the relationship of two different LHR mutants, one with defective hormone binding and the other with normal hormone binding but defective signal generation.

LHR belongs to the structurally unique glycoprotein hormone receptor subfamily of the G protein-coupled receptor family (5). Unlike other receptor subfamilies, they comprise two equal halves, an extracellular N-terminal half (exodomain) and a membrane-associated C-terminal half (endodomain) (7–11). The exodomain is ~350 amino acids long, and it alone is capable of high affinty hormone binding (12–15) with hormone selectivity (16–18) but without hormone action (14, 19, 20). Hormone signal is generated in the ~350-amino acid-long endodomain (4), which is structurally equivalent to the entire molecule of many other G protein-coupled receptors such as rhodopsin and adrenergic receptors (5). Growing evidence suggests that glycoprotein hormones initially bind to the exodomain (5) and that the resulting hormone-exodomain complex undergoes a conformational change (21) and modulates the endodomain. This secondary interaction is thought to generate a signal in the endodomain (4–6, 22). These findings are consistent with the observations that signal generation is generally impacted by endodomain mutants (23), whereas mutations in the endodomain tend to affect hormone binding (24–26).

Considering the existence of heterozygous mutant LHRs in a patient (2, 3), we wondered about the relationship between the two alleles as to whether they would be dependent on or independent of each other. Particularly, there is the intriguing possibility that two heterozygous mutants, one defective in hormone binding and the other with normal hormone binding but defective signal generation, might interact with each other to rescue hormone action. Obviously, this would require the novel intermolecular interaction of the exodomain of one LHR with the endodomain of another LHR. Although it has never been described, it would have significant impact on the interpretation of receptor genetics and provide new insights into clinical treatments. To test the hypothesis, we co-expressed various pairs of heterozygous defective LHRs and tested for their functional rescue.

EXPERIMENTAL PROCEDURES

Mutagenesis and Functional Expression of Receptors—Mutant rat LHR and FSHR cDNAs were prepared in a pSELECT vector using the non-polymerase chain reaction-based Altered Sites Mutagenesis System (Promega), sequenced, and subcloned into pcDNAs (Invitrogen) as described previously (27). After subcloning pcDNAs, the mutant cDNAs were sequenced again. Varying concentrations of plasmids were transfected into human embryonic kidney (HEK) 293 cells by the calcium phosphate method (28). Transiently transfected cells were assayed 60–72 h after transfection. Stable cell lines were established in minimum essential medium containing 8% horse serum and 500 μg/ml G-418. All assays were carried out in duplicate and repeated three to four times. Means and standard deviations were calculated.

125I-hCG Binding and Intracellular cAMP Assay—hCG and human follicle-stimulating hormone, provided by the National Hormone and Pituitary Program, were radioiodinated as described previously (29). Cells were assayed for 125I-hormone (150,000 cpm) binding in the presence of increasing concentrations of nonradioactive hormone. Kd values

* This work was supported by Grants HD-18702 and DK-51469 from the National Institutes of Health. The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

† To whom correspondence should be addressed: Dept. of Chemistry, University of Kentucky, Lexington, KY 40506-0055. Tel.: 859-257-3163; Fax: 859-257-3229; E-mail: tj@uky.edu.

‡ The abbreviations used are: LHR, LH receptor; LH, luteinizing hormone; hCG, human chorionic gonadotropin; HEK, human embryonic kidney; FSHR, follicle-stimulating hormone receptor; wt, wild type.

This paper is available on line at http://www.jbc.org

Vol. 277, No. 18, Issue of May 3, pp. 15795–15800, 2002
Printed in U.S.A.
were determined by Scatchard plots. For intracellular cAMP assay, cells were washed twice with minimum essential medium and incubated in the medium containing isobutylmethylxanthine (0.1 mg/ml) for 15 min. Increasing concentrations of hCG were then added, and the incubation was continued for 45 min at 37 °C. After the medium was removed, the cells were rinsed once with fresh medium without isobutylmethylxanthine, lysed in 70% ethanol, freeze-thawed in liquid nitrogen, and scraped. After pelleting cell debris at 16,000 × g for 10 min at 4 °C, the supernatant was collected, dried under vacuum, and resuspended in 10 μl of the cAMP assay buffer provided by the manufacturer. cAMP concentrations were determined with a 125I-cAMP assay kit (Amersham Biosciences) following the manufacturer’s instructions and validated for use in our laboratory.

Radioimmunoassay for Flag-LHR—Flag-LHR was prepared by inserting the Flag epitope, Asp-Tyr-Lys-Asp-Asp-Asp-Asp-Lys (5-GAC), between the C terminus of the vector, or the vector with the wild type LHR and various mutants. The cells were assayed for 125I-hCG binding in the presence of increasing concentrations of unlabeled hCG (A). The results were converted to Scatchard plots (B). In addition, the cells were treated with increasing concentrations of unlabeled hCG, and intracellular cAMP was measured (C) as described under “Experimental Procedures.” The experiments were performed in duplicate and repeated several times. The means and standard deviations are presented in the table (below panels A–C). NS, not significant.

Co-expression of Two Mutant LHGs and Successful Rescue of cAMP Production—Next, cells were cotransfected with a pair of LHRC22A and LHRK583R plasmids, for example, K583R and L20A mutants or K583R and C22A mutants. The cells that were cotransfected with either LHRK583R and LHRP479G, LHRK583R and LHRP479G, or LHRK583R and LHRP479G did not show hCG binding or cAMP induction, consistent with previous reports (31, 32). If cells transfected with the blank plasmid, pcDNA3, failed to bind hCG and produce cAMP, indicating that the vector itself was not involved in hCG binding.

Specificity for the Rescue of cAMP Induction—It is unclear whether cAMP was induced by accidental collisions between the endodomains of two different mutant receptors. To test this possibility, several pairs of two different LHRC22A mutants were co-expressed. As shown in Fig. 4, none of the co-expressed pairs (LHRC22A and LHRP479GA, LHRP479GA and LHRP479GA, LHRP479GA and LHRP479GA, and LHRP479GA and LHRP479GA) was capable of inducing cAMP or binding hCG. These results show that one of the mutant pairs has to be capable of binding hCG to rescue cAMP induction.

To test the dependence of the rescue on hCG binding, cells were co-transfected with varying concentrations (6, 12, and 18 μg) of the LHRK583R plasmid and a constant amount (6 μg) of the LHRL20A or LHRK583R plasmid. The cells were assayed first for hCG binding to determine the relationship of the surface concentration of LHRK583R with the plasmid concentration (Fig. 5). The results show that the surface concentration of LHRK583R increased in parallel to the plasmid concentration used for transfection. The range of the LHRK583R concentration was 5,000–21,000 receptors/cell, which compares favorably...
The observations described in Figs. 5 and 6 indicate that the rescue, although the maximum cAMP levels remained high.

One may question whether the surface expression levels of the LHR–hCG mutants shown in Fig. 5 were constant, although 6 µg of the plasmids was used for transfection of the cells throughout the experiment. To address this problem, we took another approach to keep the expression level of cells throughout the experiment. To address this problem, we took another approach to keep the expression level of cells throughout the experiment. To address this problem, we took another approach to keep the expression level of cells throughout the experiment.

The nonbinding receptors tested so far have mutations in the exodomain that impair hormone binding. In addition to these nonbinding receptors with a defective exodomain, there are nonbinding receptors that have a normal exodomain but mutation in the endodomain, such as P479A and P479G of the transmembrane helix 4 (31). These mutations in the endodomain block hCG binding to the exodomain by constraining the exodomain although the exodomain itself is intact (34, 35). To test whether these mutants could pair with LHRK583R and induce cAMP production, LHRK583R was co-expressed with LHRP479A or LHRP479A. The cells co-expressing LHRK583R and LHRP479A or LHRP479A and LHRP479A failed to induce cAMP production although they were capable of binding hCG (Fig. 7). These results indicate that not all of the mutant pairs of LHR–hCG and LHR–hCG/–cAMP are capable of rescuing the hCG dependent cAMP induction, suggesting a specificity for pairing. Furthermore, these results suggest that LHR–hCG with a mutation in the exodomain, but not in the endodomain, could be rescued.

In addition, we tested the affect of another receptor species on the activity of wild type LHR. When LHREwt was co-expressed with FSHREwt, the functional FSHR did not impact the hCG binding affinity or the EC50 value and maximum level of cAMP induction by LHREwt (data not shown). These results show that the cAMP induction by LHR–hCG and LHR–hCG/–cAMP was not rescued by accidental collisions between them or with different hormone receptor species.

with the in vivo LHR concentration on porcine granulosa cells, several thousand per cell.2 In addition, the variation in the receptor concentration does not appear to impact the hormone binding affinity. However, the maximum cAMP levels show an interesting trend. When 6 µg of the LHRK22A plasmid was cotransfected with 6, 12, or 18 µg of the LHRK583R plasmid, the maximum cAMP levels were 52.3, 71.1, and 36.5 fmol/1000 cells, respectively. The differences among the three values are statistically significant with p values of <0.05 to <0.001. Therefore, the maximum cAMP level increased by 36% at 12 µg and then decreased by 30% at 18 µg as compared with the cAMP level at 6 µg of the plasmid. The result was similar when 6 µg of the LHRK22A plasmid was co-transfected with 6, 12, or 18 µg of the LHRK583R plasmid. These observations suggest that the cAMP rescue requires LHRK583R and is dependent on the concentration of this mutant receptor.

One may question whether the surface expression levels of the LHR−hCG mutants shown in Fig. 5 were constant, although 6 µg of the plasmids was used for transfection of the cells throughout the experiment. To address this problem, we took another approach to keep the expression level of LHR−hCG mutants constant. Cell lines were established after stably transfecting them with the LHRK22A plasmid or LHRK583R plasmid. These cell lines were transfected again with varying concentrations (6, 12, and 18 µg) of the LHRK583R plasmid. The doubly transfected cells showed increasing concentrations of LHRK583R (Fig. 6). Transfection with 12 µg of the LHRK583R plasmid increased the maximum cAMP level by 29–58% over that of the cells transfected with 6 µg of the plasmid. Transfection with 18 µg of the plasmid resulted in a 3-fold increase in the EC50 value for the cAMP rescue, although the maximum cAMP levels remained high. The observations described in Figs. 5 and 6 indicate that the cAMP rescue is dependent on the LHRK583R concentration. However, there is a notable difference in the results of Figs. 5 and 6. In Fig. 5 the maximum levels of cAMP peaked as the LHRK583R concentration increased, whereas it plateaued in Fig. 6. The difference in the two experiments was LHR−hCG, which was transiently expressed in the Fig. 5 experiment and stably expressed in the Fig. 6 experiment. A molecule is expressed in stable cell lines generally more than in transiently expressing cells because of the associated antibiotic selection. Therefore, another experiment was performed using the stable cell line expressing Flag-LHRK22A, which appears to express less than 12,800 receptors/cell. It was transiently transfected with increasing concentrations of the LHRK583R plasmid from 3 to 18 µg. The cells produced cAMP in response to hCG, and the maximum cAMP levels peaked (Fig. 3). These results taken together with the data shown in Figs. 5 and 6 show that there are optimal concentrations of LHRK583R to pair with LHR−hCG and rescue cAMP induction. They indicate the importance of the number of the hCG binding receptor and/or the ratio of the hCG binding receptor to the nonbinding receptor.

### Table I

**Surface expression of Flag-LHRS**

| Cells | Kd (nM) | Receptor/Cell | EC50 (nM) | Max (fmol/1000 cells) |
|-------|---------|---------------|-----------|-----------------------|
| Wild-type | 0.05 ± 0.01 | 152.4 ± 1.7 | 80.6 ± 3.7 |
| LHRK22A | 0.32 ± 0.04 | 5,000 ± 1,100 | 1,24 ± 0.91 |
| LHRK583R | 0.05 ± 0.01 | 152.4 ± 1.7 | 52.3 ± 11.3 |

2 C. Lee, I. Ji, and T. H. Ji, unpublished observation.
DISCUSSION

Our observations described in this work show that cells co-expressing a pair of two differently defective mutants, one defective in hCG binding at the exodomain (LHR<sup>K583R</sup>/H11002<sup>hCG</sup>) and the other defective in signal generation at the endodomain (LHR<sup>L9262/aCG</sup>/H11001<sup>hCG</sup>/H11002<sup>cAMP</sup>), can induce cAMP production. This successful rescue of cAMP induction requires both types of mutant receptors. However, not all LHR<sup>K583R</sup> were capable of pairing with LHR<sup>L9262</sup>/H11001<sup>hCG</sup>/H11002<sup>cAMP</sup>, and rescuing cAMP induction. Rescue is observed when hormone binding of an LHR<sup>K583R</sup> is impaired by a mutation in the exodomain but not by mutations in the endodomain. These results suggest specificity for the rescue of CAMP induction. For example, the rescue is dependent on hCG dose, the surface concentration of the mutant receptors, and the amino acid positions of the mutations. Furthermore, random collisions among mutant receptors are not involved in the rescue.

It is known that LHR binds hCG first at the exodomain (12–14), and the resulting hCG-exodomain complex undergoes conformational changes (21, 36, 37) and modulates the endo-
main (38, 39). This secondary interaction is responsible for signal generation and receptor activation (4–6). Based on these observations and the results described in this work, the cooperation between the two types of mutant LHRs includes the exodomain of LHRK583R and the endodomain of LHR L20A or LHR C22A. Furthermore, the two domains most likely interact with each other. Therefore, our results suggest an intermolecular interaction between the exodomain of one receptor and the endodomain of another receptor and implicate at least partial substitution of the hCG-functional exodomain complex of a receptor for the defective exodomain of another receptor. This is supported by several pieces of evidence. The rescue is observed when hormone binding of an LHR -hCG is impaired by a mutation in the exodomain but not by mutations in the endodomain. The exodomain and endodomain are dependent on each other (34, 35) and after hormone binding. The exodomain modulates signal generation using a suppressor in the hinge region (38, 39) and an activator in Leu-rich repeat 4 (40). On the other hand, the endodomain constrains hormone binding at the exodomain through exoloops and transmembrane helices (31, 34, 35). The interaction between the exodomain and endodomain involves exoloop 2 of the endodomain and the hinge region of the exodomain (22, 39). In addition, other exoloops are likely to be involved (35).

The intermolecular exodomain-endodomain interaction is also consistent with the dependence of the rescue on receptor concentrations and the existence of optimal concentrations. The observation that too few or too many LHR -hCG can

**Fig. 6.** Coexpression of stable LHR -hCG and transient LHR -hCG -cAMP. Cells stably expressing LHR -hCG were transiently transfected with increasing concentrations of the LHR -hCG plasmid. The cells were assayed for hormone binding and cAMP production as described in the legend for Fig. 1.

**Fig. 7.** cAMP rescue is dependent on the location of mutation in LHR -hCG. Cells were transiently coexpressed with LHR -K583R and LHR -P479A or LHR -K583R and LHR -P479G. The cells were assayed for hormone binding and cAMP production as described in the legend for Fig. 1.
interfere with the collaboration between LHR$^{+\text{hCG}}$–cAMP and LHR$^{-\text{hCG}}$ is of interest and reminiscent of the antibody and antigen interaction. One wonders whether too many LHR$^{+\text{hCG}}$–cAMP might nonproductively compete for a limited number of LHR$^{-\text{hCG}}$, which could lead to less effective induction of cAMP. It also suggests the intriguing possibility of pleiotropic activation of other LHRs by a liganded LHR, in addition to intramolecular activation of its own endodomain. The intermolecular exodomain-endodomain interaction would allow a heterozygote consisting of LHR$^{+\text{hCG}}$–cAMP and LHR$^{-\text{hCG}}$ to rescue the LHR activity.

The rescue observed in this study differs from experiments performed by the Hsueh group (20). They have elegantly demonstrated the rescue of two defective mutant LHRs: one with the exodomain connected to the transmembrane domain 1 and lacking the rest of the transmembrane helices; and the other possessing the first five transmembrane helices without an exodomain (20). The first transmembrane helix played a crucial role in the cAMP rescue, apparently by its interaction with the exodomain (20). Perhaps because of the different mechanisms of rescue in the previous report (20) and this study, the maximum cAMP levels rescued differ considerably; it was 12% of the wild type value in the previous study and 50% in this study. This is also substantially (~9-fold) higher than the normal basal cAMP level. This is a significant difference when compared with the maximum cAMP level of activating mutant LHRs, which is 5–8-fold greater than the normal cAMP basal level (41).

REFERENCES
1. McGee, E. A., and Hsueh, A. J. (2000) Endocr. Rev. 21, 200–214
2. Lase, L. L., Wu, S. M., Kudo, M., Bourdony, C. J., Cutler, G. B., Jr., Hsueh, A. J., and Chan, W. Y. (1996) Mol. Endocrinol. 10, 987–997
3. Wu, S., Hallermeier, K. M., Lase, L., Braun, C., Berry, A. C., Grant, D. B., Griffin, J. E., Wilson, J. D., Cutler, G. B., and Chan, W. (1998) Mol. Endocrinol. 12, 1651–1660
4. Ji, T. H., Murdoch, W. J., and Ji, I. (1995) Endocrine 3, 187–194
5. Ji, T. H., Grossmann, M., and Ji, I. (1998) J. Biol. Chem. 273, 17299–17302
6. Dufau, M. L. (1998) Annu. Rev. Physiol. 60, 461–496
7. McFarland, K., Sprengel, R., Phillips, H., Kohler, M., Rosembliit, N., Nikolic, K., Segaloff, D., and Seeburg, P. (1989) Science 245, 525–526
8. Loosfelt, H., Misrahi, M., Atger, M., Salesse, R., Thi, M., Jolivet, A., Guichon-Mantel, A., Sar, S., Jailal, B., Garnier, J., and Milgrom, E. (1989) Science 245, 525–526
9. Nagayama, Y., Kaufman, K. D., Seto, P., and Rapoport, B. (1989) Biochem. Biophys. Res. Commun. 165, 1184–1190
10. Sprengel, R., Braun, T., Nikolic, K., Segaloff, D. L., and Seeburg, P. H. (1990) Mol. Endocrinol. 4, 525–530
11. Tilly, J. L., Ahara, T., Nishimori, K., Jia, X. C., Billig, H., Kowalski, K. I., Perlas, E. A., and Hsueh, A. J. (1992) Endocrinology 131, 799–806
12. Tsai-Morris, C. H., Buezzo, E., Wang, W., and Dufau, M. L. (1990) J. Biol. Chem. 265, 19385–19388
13. Xie, Y. B., Wang, H., and Segaloff, D. L. (1990) J. Biol. Chem. 265, 21411–21414
14. Ji, I., and Ji, T. H. (1991) Endocrinology 128, 2648–2650
15. Davis, D., Liu, X., and Segaloff, D. (1995) Mol. Endocrinol. 9, 159–170
16. Braun, T., Schofield, P. R., and Sprengel, R. (1991) EMBO J. 10, 1885–1890
17. Moyle, W. R., Campbell, K. R., Myers, R. V., Bernard, M. P., Han, Y., and Wang, X. (1994) Nature 366, 251–255
18. Liu, X., DePasquale, J. A., Grisswold, M. D., and Dias, J. A. (1994) Endocrinology 135, 692–691
19. Remy, J. J., Bozon, V., Couture, L., Goex, B., Salesse, R., and Garnier, J. (1993) Biochem. Biophys. Res. Commun. 183, 1023–1030
20. Osuga, Y., Hayashi, M., Kudo, M., Canti, M., Kobilka, B., and Hsueh, A. (1997) J. Biol. Chem. 272, 25906–25912
21. Ji, I., Pan, Y.-N., Lee, Y.-M., Phang, T., and Ji, T. H. (1995) Endocrine 3, 907–911
22. Nishi, S., Nakabayashi, K., Kobilka, B., and Hsueh, A. J. (2002) J. Biol. Chem. 277, 3958–3964
23. Kosugi, S., Van Dop, C., Geffner, M. E., Rabi, W., Carel, J. C., Chausanna, J. L., Mori, T., Merendino, J. J., Jr., and Shenker, A. (1996) Hum. Mol. Genet. 4, 183–188
24. Bhowmick, N., Huang, J., Puett, D., Isaacs, N. W., and Laptahorn, A. J. (1996) Mol. Endocrinol. 10, 1147–1159
25. Tillas, D., Rozell, T., Liu, X., and Segaloff, D. (1996) Mol. Endocrinol. 10, 760–768
26. Misrahi, M., Meduri, G., Pissard, S., Bovvattier, C., Beau, I., Loosfelt, H., Jolivet, A., Eppaport, R., Milgrom, E., and Bougneres, P. (1997) J. Clin. Endocrine Metab. 82, 2159–2165
27. Ji, I., and Ji, T. H. (1991) J. Biol. Chem. 266, 14953–14957
28. Chen, C., and Okayama, H. (1987) Mol. Cell. Biol. 7, 2745–2752
29. Ji, I., and Ji, T. H. (1980) Proc. Natl. Acad. Sci. U. S. A. 77, 7167–7170
30. Ryu, K.-S., Gilchrist, R. L., Ji, I., Kim, S.-J., and Ji, T. H. (1996) J. Biol. Chem. 271, 7301–7304
31. Hong, S., Ryu, K.-S., Oh, M.-O., Ji, I., and Ji, T. H. (1997) J. Biol. Chem. 272, 4166–4171
32. Hong, S., Phang, T., Ji, I., and Ji, T. H. (1998) J. Biol. Chem. 273, 13835–13840
33. Song, Y. S., Ji, I., Beauchamp, J., Isaacs, N. W., and Ji, T. H. (2001) J. Biol. Chem. 276, 3428–3435
34. Ryu, K., Lee, H., Kim, S., Beauchamp, J., Tung, C., Isaacs, N. W., Ji, I., and Ji, T. H. (1998) J. Biol. Chem. 273, 6285–6291
35. Ryu, K., Gilchrist, R. L., Tung, C., Ji, I., and Ji, T. H. (1998) J. Biol. Chem. 273, 30264–30271
36. Xiong, D., Roux, M., and Oubert, M. (1997) J. Biol. Chem. 272, 25012–25019
37. Ryu, K.-S., Gilchrist, R. L., Tung, C., Ji, I., and Ji, T. H. (1999) J. Biol. Chem. 274, 18851–18856
38. Nakabayashi, K., Kudo, M., Kobilka, B., and Hsueh, A. J. (2000) J. Biol. Chem. 275, 30264–30271
39. Zeng, H., Phang, T., Song, Y. S., Ji, I. I., and Ji, T. H. (2001) J. Biol. Chem. 276, 3451–3458
40. Song, Y. S., Ji, I., Beauchamp, J., Isaacs, N. W., and Ji, T. H. (2001) J. Biol. Chem. 276, 3436–3442
41. Kosugi, S., Mori, T., and Shenker, A. (1996) J. Biol. Chem. 271, 31813–31817
Two Defective Heterozygous Luteinizing Hormone Receptors Can Rescue Hormone Action
ChangWoo Lee, Inhae Ji, KiSung Ryu, YongSang Song, P. Michael Conn and Tae H. Ji

J. Biol. Chem. 2002, 277:15795-15800.
doi: 10.1074/jbc.M111818200 originally published online February 21, 2002

Access the most updated version of this article at doi: 10.1074/jbc.M111818200

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 41 references, 20 of which can be accessed free at
http://www.jbc.org/content/277/18/15795.full.html#ref-list-1