

# FSHR N680S (A2039G) POLYMORPHISM (FSH RECEPTOR)

## ORDERING INFORMATIONS

REF: GEN-021-25  
RDM Code: 1730074/R  
Tests: 25 Reactions: 31  
CND Code: W0106010499  
Manufacturer: BioMol Laboratories s.r.l.

## CONTENTS OF THE KIT

The kit consists of reagents for Real-Time PCR amplification  
\*reagents for the extraction of genomic DNA are not supplied in the kit

For in vitro diagnostic use



## PRODUCT CHARACTERISTICS

Device belonging to the family of in vitro medical devices **REAL-TIME QUALITATIVE PCR-GENETIC VARIANTS**. Detection of N680S (A2039G) polymorphism of the FSHR gene by Real-Time PCR technique. Kit optimized for Real-Time PCR instrumentation Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx.

## SCIENTIFIC BACKGROUND

In assisted reproductive technology programs, the ovulatory response of women to exogenous follicular hormone (FSH) stimulation exhibits interindividual variability. It is difficult to predict the ovarian response to intense gonadotropin stimulation, but it is known that a deficient ovarian response results in under stimulation and cycle cancellation and conversely, an overresponse can potentially lead to a serious and life-threatening complication such as ovarian hyperstimulation (OHSS). The analysis of the genotype of the FSH receptor therefore allows to individually modulate the administration of FSH and therefore to increase the efficacy and safety of the therapy. Several studies support a role for the FSHR rs6166 (c.2039A>G, p. Asn680Ser) variant as a prognostic indicator of ovarian response to FSH stimulation. The Ser/Ser variant was associated with higher basal levels of FSH, a higher total dose of gonadotropins required during ovarian stimulation, lower peak estradiol levels and fewer retrieved oocytes. Collectively these studies suggest that the Ser/Ser variant is associated with a reduced sensitivity of the FSHR to exogenous FSH. A randomized controlled trial (RCT) demonstrated that this reduced sensitivity of the FSHR may be overcome by increasing the FSH dose. Furthermore, many scientific works have recently been published on the correlation between FSH receptor polymorphisms (FSHR) and the risks of non-physiological spermatogenesis, correlating them with a functional deficit in the spermatogenesis process and therefore with a possible contributing cause in the phenomena of oligospermia or azoospermia.

## CLINICAL SIGNIFICANCE

Follicle Stimulating Hormone (FSH) performs its ovarian function through important effects on granulosa cell proliferation, oocyte maturation and estrogen synthesis. Multiple studies have shown that a decrease in FSH concentration followed by a high concentration of estrogen plays an important role in the selection of the dominant follicle. In humans, on the other hand, FSH is important for the regulation of the metabolic functions of Sertoli cells, an essential stage for the maintenance of normal spermatogenesis from a qualitative and quantitative point of view. The physiological action of the FSH hormone depends on the activation of its receptor (FSHR). The FSH receptor is expressed in ovarian granulosa cells and Sertoli cells and is encoded by the FSHR gene located on chromosome 2p21-p16. Inactivating mutations of the FSHR gene have been described, but also multiple gene polymorphisms (about 900). The most common are the rs6165 and rs6166 polymorphisms, which correspond to the FSHR substitutions Thr307Ala and Asn680Ser respectively. Both polymorphisms are present in the same exon 10 and were found to be in «linkage disequilibrium». The two isoforms are considered variants of the glycosylation/phosphorylation sites of the FSH receptor; Indeed, Asn680 represents a consensus sequence for glycosylation while Thr307 represents a potential site of phosphorylation. Variants of post-translational modification sites can affect ligand-dependent signal transduction.

- § J Clin Med. 2024 Apr 13;13(8):2261. doi: 10.3390/jcm13082261. Application of Biomarkers in Obese Infertile Women: A Genetic Tool for a Personalized Treatment
- § J Reprod Infertil. 2023 Oct-Dec;24(4):240-247. The Effect of FSHR (G2039A) Polymorphism on Müllerian Duct Development and Hormonal Profile of Women with Primary Amenorrhoea
- § J Ovarian Res. 2023 Sep 1;16(1):183. doi: 10.1186/s13048-023-01238-7. Polymorphisms in FSHR modulating susceptibility to polycystic ovary syndrome: an updated meta-analysis
- § Multicenter Study Genes (Basel). 2023 Jun 15;14(6):1269. doi: 10.3390/genes14061269. Genetic Variants of Gonadotropins and Their Receptors Could Influence Controlled Ovarian Stimulation: IVF Data from a Prospective Multicenter Study
- § Int J Mol Sci. 2023 Jan 5;24(2):1080. doi: 10.3390/ijms24021080. The Polymorphism Asn680Ser on the FSH Receptor and Abnormal Ovarian Response in Patients with Normal Values of AMH and AFC
- § Front Endocrinol (Lausanne). 2022 Feb 1;12:797365. doi: 10.3389/fendo.2021.797365. eCollection 2021. Effect of Genetic Variants of Gonadotropins and Their Receptors on Ovarian Stimulation Outcomes: A Delphi Consensus
- § The susceptibility of FSHB -211G > T and FSHR G-29A, 919A > G, 2039A > G polymorphisms to men infertility: an association study and meta-analysis. BMC Med Genet. 2017 Aug 1; 18(1):81.
- § FSH receptor gene p. Thr307Ala and p. Asn680Ser polymorphisms are associated with the risk of polycystic ovary syndrome. J Assist Reprod Genet. 2017 Aug; 34(8):1087-1093. Epub 2017 May 25.
- § Follicle-Stimulating Hormone Receptor (FSHR): A Promising Tool in Oncology? Mol Diagn Ther. 2016 Dec; 20(6):523-530. Review.



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DESCRIPTION	LABEL	VOLUME	STORAGE
		<b>GEN-021-25</b>	
Mix oligonucleotides and probes	Mix N680S FSHR 10X	1 x 77,5 µl	-20°C
Mix buffer and Taq polymerase enzyme	Mix Real-Time PCR 2X	1 x 387,5 µl	-20°C
Deionized H <sub>2</sub> O	Deionized H <sub>2</sub> O	1 x 1 ml	-20°C
Genomic DNA or recombinant DNA	Control 1	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 2	1 x 22 µl	-20°C
Genomic DNA or recombinant DNA	Control 3	1 x 22 µl	-20°C

## TECHNICAL CHARACTERISTICS

### COD. GEN-021-25

STABILITY	18 months
REAGENTS STATUS	Ready to use
BIOLOGICAL MATRIX	Genomic DNA extracted from whole blood, tissue, cells
CONTROLS	Recombinant DNA for at least 3 analytical sessions
VALIDATED INSTRUMENTS	Biorad CFX96 Dx, Biorad Opus Dx and Agilent AriaDx
TECHNOLOGY	Real-time PCR; oligonucleotides and specific probes; 2 FAM/HEX fluorescence channels
RUNNING TIME	85 min
THERMAL CYCLING PROFILE	1 cycle at 95 °C (10 min); 45 cycles at 95 °C (15 sec) + 60 °C (60 sec)
ANALYTICAL SPECIFICITY	Absence of non-specific pairings of oligonucleotides and probes; absence of cross-reactivity
LIMIT OF DETECTION (LOD)	≥ 0,016 ng of genomic DNA
LIMIT OF BLANK (LOB)	0% NCN
REPRODUCIBILITY	99,9%
DIAGNOSTIC SPECIFICITY / DIAGNOSTIC SENSITIVITY	100%/98%