

# The polymorphism Ala307Thr of the Follicle Stimulating Hormone Receptor (FSHR) gene is associated with different doses of recombinant FSH received during IVF/ICSI treatment

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## Study question

Is there an association between FSHR gene Ala307Thr polymorphism (rs6165) and ovarian reserve, ovarian response or clinical results in IVF/ICSI treatment?

## Methods

This prospective cohort study included 450 women who underwent IVF/ICSI cycles. The enrolled individuals met the following inclusion criteria: age of  $\leq 37$  years; normal karyotype; presence of two ovaries as observed by ultrasound examination; and no history of ovarian surgery, endometriosis, hydrosalpinx, infection, or endocrine disorders. DNA was extracted from peripheral blood, and the Ala-307Thr FSHR polymorphism (rs6165) was genotyped using TaqMan SNP genotyping assay. The results were associated with age, anti-Müllerian hormone (AMH) levels, antral follicle counts (AFC), total dose of r-FSH, follicle size, number of retrieved oocytes, and clinical outcome of IVF/ICSI cycles. The statistical analyses were performed using Fisher's exact test and Kruskal-Wallis test.

## Results

An association between the genotypes of the FSHR (Ala307Thr) polymorphism and different doses of r-FSH was observed. Patients with the Ala/Ala genotype received a higher r-FSH dose than patients with the Ala/Thr ( $P=0.0002$ ) and Thr/Thr ( $P=0.02$ ) genotypes. No other correlation was observed. Table 1 summarizes the results.

## Conclusion

Ala/Ala genotype was associated with the use of higher doses of recombinant FSH(r-FSH), suggesting that homozygosis of this allelic variant (Ala) provides lower sensitivity to r-FSH. The results suggest that FSHR Ala307Thr (rs6165) gene polymorphism is related to ovarian response but not to ovarian reserve. This SNP can be used as an additional tool in the individualization of ovarian stimulation protocols.



Table 1. Results

	FSHR (rs6165) genotypes			P
	Thr/Thr	Ala/Thr	Ala/Ala	
n (%)	141 (31.3%)	213 (47.4%)	96 (21.3%)	
Age (years)	35.0 $\pm$ 3.8	34.5 $\pm$ 4.1	34.5 $\pm$ 4.7	0.57
BMI (kg/m <sup>2</sup> )	24.3 $\pm$ 4.0	24.3 $\pm$ 4.0	24.4 $\pm$ 4.7	0.81
AMH (ng/ml)	1.7 $\pm$ 2.3	1.9 $\pm$ 2.1	1.6 $\pm$ 2.1	0.26
AFC (n)	12.6 $\pm$ 8.7	13.4 $\pm$ 7.4	12.3 $\pm$ 9.0	0.11
<b>Total dose r-FSH (UI)</b>	<b>2085<math>\pm</math>922<sup>a</sup></b>	<b>1946<math>\pm</math>955<sup>b</sup></b>	<b>2364<math>\pm</math>1060<sup>a,b</sup></b>	<b><sup>a</sup>0.02 <sup>b</sup>0.0002</b>
Time of stimulation (days)	10.3 $\pm$ 2.5	10.1 $\pm$ 2.4	10.5 $\pm$ 2.2	0.17
Follicles (n)				
Total	11.4 $\pm$ 6.6	12.0 $\pm$ 7.4	11.6 $\pm$ 7.4	0.86
$\geq 18$ mm	3.8 $\pm$ 2.2	5.7 $\pm$ 2.0	3.6 $\pm$ 2.5	0.64
Retrieved oocytes (n)				
Total	8.2 $\pm$ 5.4	8.1 $\pm$ 5.1	8.2 $\pm$ 5.4	0.98
Metaphase II	6.1 $\pm$ 4.3	5.9 $\pm$ 4.1	6.1 $\pm$ 4.8	0.92
Fertilization rate (%)	64.5 $\pm$ 26.4	64.6 $\pm$ 26.5	64.4 $\pm$ 29.9	0.96
Implantation rate (%)	23.9	26.1	25.7	0.82
Pregnancy rate/transfer (%)	34.6	39.9	39.8	0.65
Pregnancy rate/patient (%)	31.2	35.2	34.4	0.79