

# Is there a bridge between diminished ovarian reserve and inflammation ? A pilot study

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## ABSTRACT

### Study question & Summary answer:

Can diminished ovarian reserve (DOR) be linked to immunologic bias?

Immune mediators expressed by cumulus cells are significantly distinct in DOR women versus control (NOR), and specifically correlated with ovarian reserve markers.

**Introduction:** Diminishment of ovarian reserve (early or not) is recognized as a limiting factor in Assisted Reproductive Technology (ART). Throughout the growth of the ovarian follicle, the oocyte is in close contact with neighboring cells such as cumulus cells (CC), which contribute to the oocyte maturation and quality. Thereby, the oocyte-cumulus dialogue is representative of the quality of the oocyte, which in turn is indicative of the embryo quality and a crucial point in ART. However, the inflammatory environment in which the oocyte evolves is not clearly established, and it remains unclear how ovarian inflammatory background can impact the ovarian reserve.

**Results:** In this pilot study, we report that DOR affects the expression of interleukin (IL) 1 members in CC compared with NOR. Independently of age, mRNA expression of IL1R1 was significantly increased in DOR ( $p=0,0151$ ). This increase was significantly and negatively associated with AMH (serum level) ( $p=0,0383$ ). Interestingly, IL1B was also significantly and negatively correlated with AMH serum level ( $p=0,0001$ ). In turn, IL1RN (IL1 antagonist receptor) was significantly increased in DOR ( $p=0,0001$ ) and negatively correlated with AMH ( $p=0,0022$ ) and antral follicle count (AFC) ( $p=0,0020$ ). Because of both increase of IL1R1 and IL1RN, IL1R1/IL1RN balance was inverted in DOR patients, which can probably affect oocyte maturation. On the other hand, we observed that the percentage of circulating neutrophil was associated with AMH decrease ( $p=0,0279$ ). Curiously, the major neutrophil chemotactic factor, IL8, was significantly increased in DOR ( $p=0,0097$ ) and negatively correlated with AMH ( $p=0,0024$ ) and AFC ( $p=0,0001$ ). Statistical analysis were performed using Mann Whitney and Pearson correlation tests.

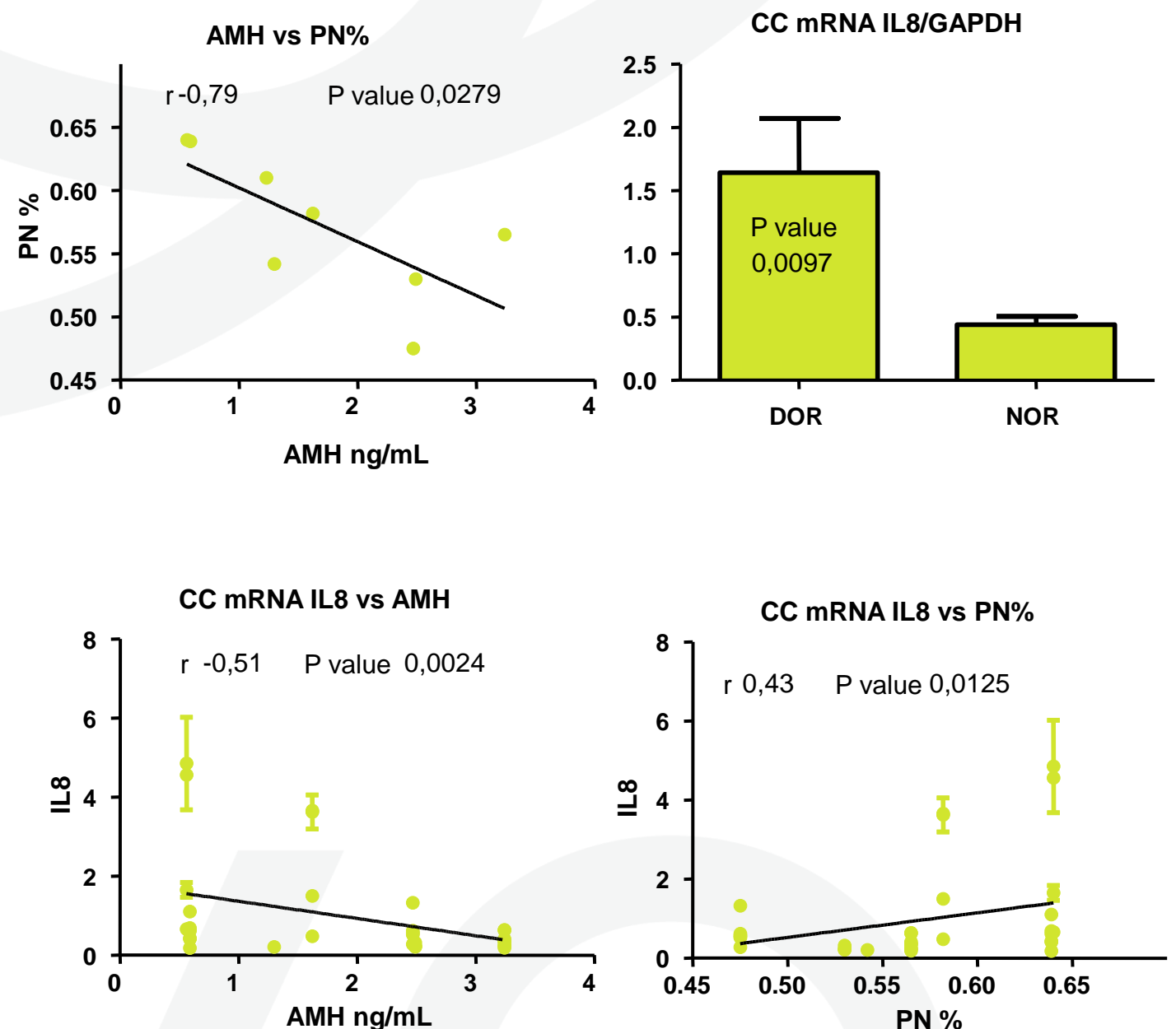
**Conclusions:** We observed that DOR skewed the balance of agonist and antagonist members of interleukin 1 family in a pattern that can impair oocyte maturation mechanism. Moreover, investigated immune mediators correlated with ovarian reserve markers, and can be linked with blood neutrophil count, indicating that there is an immune bias in DOR patients.

## RESULTS

### IL1 family members :

	Mean mRNA/GAPDH			Correlation AFC		Correlation AMH	
	DOR	NOR	<i>p</i>	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
IL1R1	3,58	1,50	0,0151	-0,21	0,1620	-0,32	0,0383
IL1B	0,88	0,73	0,1492	-0,35	0,0372	-0,53	0,0010
IL1RN	4,39	1,34	0,0001	-0,49	0,0020	-0,48	0,0022
R1/RN	0,51	1,32	0,0001	0,64	0,0001	0,60	0,0001

### IL8 and blood neutrophil count :



## Acknowledgement