Role of the RNA binding protein Sam68 in leptin and insulin signaling in granulosa cells

Context: The RNA-binding protein Sam68 is expressed in granulosa cells and the knockout female mice for this gene are subfertile, with ovulation problems. Since we have previously found that Sam68 may be recruited to insulin and leptin receptors, we planned to study the participation of Sam68 in signaling and action of insulin and leptin receptors in granulosa cells.

Objective: We aimed to study the expression of Sam68 in granulosa cells in response to leptin and insulin in vitro.

Methods: Signaling was studied in Virgen Macarena University Hospital by immunoprecipitation and immunoblot of the phosphorylated proteins. The expression of Sam68 is inhibited by antisense strategy. The expression level of Sam68, and leptin and insulin receptors are quantified by qPCR and immunoblot.

Patients: Patients who underwent IVF cycles in the clinic IVI Sevilla

Interventions: Pick-up of the granulosa cells obtained during follicle puncture, as part of an IVF treatment

Main Outcome Measures: Sam68 expression levels

Results: We have found that Sam68 is tyrosine phosphorylated by insulin or leptin stimulation in granulosa cells, recruiting Sam68 to signaling complexes and decreasing its RNA binding capacity. In addition, both insulin and leptin increase the expression of Sam68 in granulosa cells. Finally, full expression of Sam68 is required for the activation of PI3K and MAPK signaling pathways by insulin or leptin in granulosa cells.

Conclusions: Sam68 is recruited to leptin and insulin receptor signaling, its expression is induced by both hormones, and Sam68 is necessary for the full activation of insulin and leptin receptor signal transduction in granulosa cells. Sam68 may be a new important element in the ovarian insulin resistance.
and the decreased fertility found in obese women.