Parthenogenic blastocysts derived from cumulus-free in vitro matured human oocytes.

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Public Summary:

Scientific Abstract:
BACKGROUND: Approximately 20% of oocytes are classified as immature and discarded following intracytoplasmic sperm injection (ICSI) procedures. These oocytes are obtained from gonadotropin-stimulated patients, and are routinely removed from the cumulus cells which normally would mature the oocytes. Given the ready access to these human oocytes, they represent a potential resource for both clinical and basic science application. However culture conditions for the maturation of cumulus-free oocytes have not been optimized. We aimed to improve maturation conditions for cumulus-free oocytes via culture with ovarian paracrine/autocrine factors identified by single cell analysis. METHODOLOGY/PRINCIPAL FINDING: Immature human oocytes were matured in vitro via supplementation with ovarian paracrine/autocrine factors that were selected based on expression of ligands in the cumulus cells and their corresponding receptors in oocytes. Matured oocytes were artificially activated to assess developmental competence. Gene expression profiles of parthenotes were compared to IVF/ICSI embryos at morula and blastocyst stages. Following incubation in medium supplemented with ovarian factors (BDNF, IGF-I, estradiol, GDNF, FGF2 and leptin), a greater percentage of oocytes demonstrated nuclear maturation and subsequently, underwent parthenogenesis relative to control. Similarly, cytoplasmic maturation was also improved as indicated by development to blastocyst stage. Parthenogenic blastocysts exhibited mRNA expression profiles similar to those of blastocysts obtained after IVF/ICSI with the exception for MKLP2 and PEG1. CONCLUSIONS/SIGNIFICANCE: Human cumulus-free oocytes from hormone-stimulated cycles are capable of developing to blastocysts when cultured with ovarian factor supplementation. Our improved IVM culture conditions may be used for obtaining mature oocytes for clinical purposes and/or for derivation of embryonic stem cells following parthenogenesis or nuclear transfer.