Docket #: S11-477

Fertility treatment to stimulate ovarian follicles by inhibiting Hippo signaling

Researchers in Prof. Aaron Hsueh's laboratory have discovered a technique to promote fertility by stimulating the growth of ovarian follicles (functional units that produce oocytes) through disrupting the Hippo signaling pathway. The conserved Hippo pathway normally functions to maintain optimal size across organs and species. Disrupting the pathway in the ovaries (either through direct or downstream inhibitors) promotes the growth of follicles that can then be induced to produce mature oocytes through conventional FSH and hCG treatments. This approach has both human and veterinary applications and may be particularly well-suited for treating conditions of diminished ovarian reserve (such as primary ovarian insufficiency, polycystic ovary syndrome, or peri-menopause).

Applications

- **Human infertility treatment** - therapeutic agents that inhibit Hippo signaling (including HSP90 inhibitors, PTEN inhibitors or PI3 kinase activators) to stimulate ovarian follicles for obtaining oocytes from patients with:
    - polycystic ovary syndrome
    - primary ovarian insufficiency
    - peri-menopause
- **Veterinary medicine** - stimulate ovarian follicles to obtain mature oocytes in farm animals or endangered species

Advantages

- **Alternative to standard treatment** - Hippo signaling inhibitors may provide an alternative to patients who do not respond to conventional FSH treatment because they have few follicles

Publications

- Y. Cheng et al Actin polymerization-enhancing drugs promote ovarian follicle growth mediated by the Hippo signaling effector YAP *The FASEB Journal* June 2015.
- Kawamura K, Cheng Y, Suzuki N, Deguchi M, Sato Y, Takae S, Ho CH, Kawamura N, Tamura M, Hashimoto S, Sugishita Y, Morimoto Y, Hosoi Y, Yoshioka N, Ishizuka B, Hsueh AJ., Hippo signaling disruption and Akt stimulation of ovarian follicles for infertility treatment. *Proc Natl Acad Sci U S A.* 2013 Oct 22;110(43):17474-9. Epub 2013 Sep 30.
- Stanford-developed technique induces egg growth in infertile women, and one gives birth *Stanford Report* Sept. 30, 2013.

Patents

- Published Application: WO2014043568
- Published Application: 20150231209

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