



PhD. Defence

**The effect of choline supplementation and miR-29b in porcine ovarian follicular development**

Susan Zhan

Date: May 1st 2023 at 10:00am

The PhD Defence for Susan Zhan has been scheduled for May 1st, 2023 at 10:00am. The defence will be held online via Teams and in 141: [https://teams.microsoft.com/l/meetup-join/19%3ameeting\\_ZmNhYWQ3ZDUtZjE3YS00M2JkLWI5YmYtMzZhMzU5Y2UyYzE1%40thread.v2/0?context=%7b%22Tid%22%3a%22be62a12b-2cad-49a1-a5fa-85f4f3156a7d%22%2c%22Oid%22%3a%22fbd28915-dda5-478f-8ecb-a3682dcf0c3a%22%7d](https://teams.microsoft.com/l/meetup-join/19%3ameeting_ZmNhYWQ3ZDUtZjE3YS00M2JkLWI5YmYtMzZhMzU5Y2UyYzE1%40thread.v2/0?context=%7b%22Tid%22%3a%22be62a12b-2cad-49a1-a5fa-85f4f3156a7d%22%2c%22Oid%22%3a%22fbd28915-dda5-478f-8ecb-a3682dcf0c3a%22%7d)

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**The exam committee will consist of:**

Examining Chair: Dr. John Cant

Advisor: Dr. Julang Li

Adv. Committee Member: Dr. Lee-Anne Huber

Additional Graduate Member: Dr. Jonathan LaMarre

External Examiner: Dr. Chandrakant Tayade

**Abstract:**

Ovarian follicular development is an important process that ensures female reproductive health and ovarian function. Many nutrients and microRNAs are known to play a role in regulating follicular cell proliferation, differentiation, extracellular matrix formation and ovulation during follicular development. Choline is an essential nutrient that has been shown to play critical roles in the development and function of organs such as the brain and liver. It is reported that aberrant choline metabolism occurs in many ovarian-related diseases. However, the specific role of choline in ovarian development and its underlying mechanism is not well understood. My Ph.D research was to evaluate the *in vivo* effect of choline supplements on porcine ovarian development and the levels of miRNAs that are known to be important in ovarian function. In addition, I also further studied the role of miR-29b-3p, one of the choline-responsive miRNAs, in regulating oocyte and granulosa cell function *in vitro*. Gilts were fed with choline supplement feed from the age of 90 days to 187 days, and their reproductive development was assessed after euthanization. Our results revealed that choline additive increased the number of corpus luteum in the ovary as well as increased the vagina-cervix-length. RT-qPCR showed that choline supplement regulates the steroid biosynthesis-related gene expression and ovarian development-related miRNAs expression (in the ovarian tissue). Moreover, gut microbiome sequencing showed that choline increased the alpha diversity of the gut microbiome and activated the pathways of the gut microbiota that are associated with steroid hormone biosynthesis and infertility-causing environmental pollutants degradation. In addition, choline also regulates the proliferation, apoptosis and innate immunity-related gene expression of the intestinal cells. Our study demonstrated choline's influence on ovarian function *in vivo*, and offered insights into the mechanisms behind its positive effect on ovarian development phenotype.

To further investigate the role of miR-29b in ovarian follicular development, gain- and loss-function studies were performed in cumulus-oocyte complex (COC). It was found that over-expression of miR-29b-3p inhibits COC expansion and oocyte maturation *in vitro*. These were accompanied by the inhibition of extracellular matrix formation-related genes including SHAS2, ADAMTS1, ADAMTS2 and ADAMTS17 in cumulus granulosa cells. Further *studies* revealed that miR-29b-3p induced ROS accumulation by targeting the 3'UTR of CYCS, which ultimately resulted in the suppression of *in vitro* maturation. In addition, miR-29b-3p over-expression initiate autophagy in granulosa cell, by reducing AKT level. I also demonstrated the possible involvement of CYCS/ ROS pathway in this regulating process by the miRNA.