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Major Professor: Dr. Joan Jorgensen

Degree Objective: Ph.D, Endocrinology and Reproductive Physiology

Background: BS, Psychology, The Ohio State University

MA, Psychology-Neuroscience and Behavior, University of Virginia

Current Research Project:

Ovarian follicle integrity and healthy development depends on appropriate communication between somatic cells and the oocyte within the follicle. Previously, we reported that global knockout (KO) of two Iroquois homeobox transcription factors, *Irx3* and *Irx5* (*Irx3/5*, *Irx3^ΔIrx5^{EGFP}/Irx3^ΔIrx5^{EGFP}*) caused abnormal follicle morphology with disrupted somatic cell – oocyte contacts that led to massive oocyte death. The objective of the current study was to characterize *Irx3/5* expression profiles over time and investigate their roles in fertility. We hypothesized that cell- and time-specific expression of both *Irx3/5* is required to promote follicle integrity for optimal fertility. Whole mount *in situ* hybridization results supported previous data indicating robust *Irx3/5* RNA expression in mouse ovaries during development (embryonic day, E15.5 – postnatal day, P0), which diminished after P3. Further, immunofluorescence results showed that IRX3 and IRX5 were co-expressed within the pre-granulosa cell sub-population of ovarian somatic cells during development. After birth, IRX3 and IRX5 were co-expressed in both pre-granulosa cells and oocytes in primordial follicles, but their expression patterns diverged as follicles matured. From mature primordial to pre-antral follicle stages, IRX5 was restricted to granulosa cells while IRX3 was expressed exclusively in oocytes. Based on these patterns, we hypothesized that IRX3 and IRX5 play distinct roles in follicle health. To investigate the role of somatic cell-specific expression of *Irx3/5* during ovary development, we used *Sf1*-Cre to generate mice with somatic cell deletion of *Irx3* in the context of the *Irx5* global knockout [*Sf1Cre*^{+/-}; *Irx3^{fllox}Irx5^{EGFP}/Irx3^{fllox}Irx5^{EGFP}* (*Irx3/5* sFF)]. Breeding studies were conducted to compare fertility between *Irx3/5* sFF, *Irx5^{EGFP/EGFP}* (*NoCre*; *Irx3/5* sFF, = global *Irx5* KO) and *Irx3^{LacZ/LacZ}* (global *Irx3* KO) mice. After 6-months, *Irx3/5* sFF, *Irx5^{EGFP/EGFP}* and *Irx3^{LacZ/LacZ}* females produced significantly fewer pups per litter than their respective controls (9 vs. 11, P<0.01; 8 vs. 11, P<0.01; and 7 vs. 13, P<0.01). Notably, there was no significant difference in fertility between *Irx3/5* sFF and *Irx5^{EGFP/EGFP}* females (9 vs. 8, P>0.05). Based on these results, we concluded that somatic cell expression of *Irx3* was irrelevant; however, *Irx3^{LacZ/LacZ}* females were also subfertile suggesting that *Irx3* expression in germ cells was important. Experiments are currently underway to validate the requirement for germ cell-specific *Irx3* expression using *Ddx4*-Cre. Understanding the requirement of cell type – specific expression of *Irx3/5* in ovary will shed light on the mechanism of *Irx3/5* function within developing follicles that ensures their integrity and, ultimately, fertility.



Awards:

Student Research/Conference Grant, Student Research Grants Competition (SRGC) Conference Presentation Fund, University of Wisconsin – Madison, November 2016

Best Poster Presentation Award, ERP Research Symposium, University of Wisconsin – Madison, June 2016

Larry Ewing Memorial Trainee Travel Fund (LEMTTF) Award, Society for the Study of Reproduction, May 2016

Best Oral Presentation Award, ERP Research Symposium, University of Wisconsin – Madison, June 2015

ERP Student Research Grant Award, Endocrinology & Reproductive Physiology Program, University of Wisconsin – Madison, May 2015

Larry Ewing Memorial Trainee Travel Fund (LEMTTF) Award, Society for the Study of Reproduction, April 2015

Publications:

Holtz, S. L., **Fu, A.**, Loflin, W., Corson, J. A., & Erisir, A. (2015). Morphology and connectivity of parabrachial and cortical inputs to gustatory thalamus in rats. *Journal of Comparative Neurology*, 523(1), 139-161.

National Presentations:

Anqi Fu. (July 2016) Evaluation of *Irx3* and *Irx5* Contributions to the Somatic Cell – Oocyte Interactions in the Developing Mouse Ovarian Follicle. Short oral talk presented at Society for the Study of Reproduction 2016 Annual Meeting. San Diego, California. (Larry Ewing Memorial Trainee Travel Award and UW – Madison SRGC Student Research/Conference Grant)

Anqi Fu, Kathleen Krentz, Jessica Muszynski, Claire Holdreith, Mamawa Konuwa, Cristel Kpegba, Chi-chung Hui, Joan S. Jorgensen. (June 2015) *Irx3* and *Irx5* Promote Healthy Contacts Between Somatic and Germ Cells to Ensure Oocyte Survival and Proper Follicle Maturation. Poster presented at Society for the Study of Reproduction 2015 Annual Meeting. San Juan, Puerto Rico. (Larry Ewing Memorial Trainee Travel Award)

Anqi Fu, Stephen L Holtz, James A Corson and Alev Erisir (November 2011). *Ultrastructural Morphology and Synaptic Organization of Gustatory Thalamus*. Poster presented at the 41st Annual Meeting of Society for Neuroscience. Washington, DC.

Other Presentations:

Anqi Fu, Kathleen Krentz, Jessica Muszynski, Chi-chung Hui, Joan S. Jorgensen. (July 2016) Evaluation of *Irx3* and *Irx5* Contributions to the Somatic Cell – Oocyte Interactions in the Developing Mouse Ovarian Follicle. Short oral talk presented at Society for the Study of Reproduction 2016 Annual Meeting. San Diego, California. (Best Poster Award)



Anqi Fu, Kathleen Krentz, Jessica Muszynski, Claire Holdreith, Mamawa Konuwa, Cristel Kpegba, Chi-chung Hui, Joan S. Jorgensen. (October 2015) *Oocyte Survival and Follicle Maturation Requires Irx3 and Irx5 to Promote Communication Between Somatic and Germ Cells in the Mouse Ovary*. Poster presented at the 7th Illinois Symposium on Reproductive Sciences. University of Illinois Urbana- Champaign, Champaign, IL.

Anqi Fu. (June 2015) *Oocyte Survival and Follicle Maturation Requires Irx3 and Irx5 to Promote Communication Between Somatic and Germ Cells in the Mouse Ovary*. Oral presentation at Endocrinology and Reproductive Physiology 2015 Annual Research Symposium. University of Wisconsin – Madison, Madison, Wisconsin. (Best Oral Presentation Award)

Anqi Fu, Kathleen Krentz, Jessica Muszynski, Claire Holdreith, Mamawa Konuwa, Cristel Kpegba, Chi-chung Hui, Joan S. Jorgensen. (April 2015) *Irx3 and Irx5 Promote Healthy Contacts Between Somatic and Germ Cells to Ensure Oocyte Survival and Proper Follicle Maturation*. Poster presentation at the 3rd School of Veterinary Medicine Phi Zeta Research Day. University of Wisconsin – Madison, Madison, Wisconsin.

Anqi Fu. (October 2014). *Irx3 and Irx5 Promote Somatic Cell - Germ Cell Communication to Ensure Oocyte Survival and Facilitate Follicle Maturation*. Oral presentation at the 6th Illinois Symposium on Reproductive Sciences. Chicago, IL.

Service:

Endocrinology and Reproductive Physiology (ERP) Student Committee Member, 2016-2017

SRGC Student Research Travel Award Competition Peer Reviewer, October 2016