Journal of Oncology Translational Research

Adipocyte amino acid sensing in the control of ovarian germline stem cell maintenance

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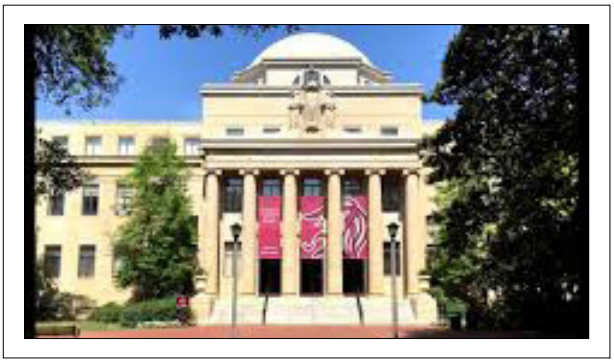
Abstract

Inter-organ communication plays a pivotal role in regulating whole organism physiological responses to changes in environmental factors such as nutrition. Over nutrition, or obesity, can lead to adipocyte dysfunction and is often associated with human diseases, including type 2 diabetes and many cancers. The Drosophila melanogaster ovary, a stem cell-supported organ, is highly responsive to dietary changes, showing a severe reduction in egg production when female flies are fed a protein-poor diet. This effect on egg production is mediated by nutrient-sensing pathways acting within the ovary and remote nutrient sensing by other tissues such as the fat body. We have previously shown that amino acid sensing specifically in adipocytes, the major cellular component of the Drosophila fat body controls germline stem cell (GSC) maintenance in adult ovaries. Reduced adipocyte amino acid transport leads to loss of GSCs by activation of the amino acid response pathway. We hypothesize that the amino acid response pathway mediates GSC loss by reducing translation of factors necessary for maintenance. The highly conserved AAR pathway further activates two downstream effects that may mediate its control on GSC maintenance: a global reduction in translation and selective up-regulation of ATF4 dependent transcription. We find that RNAi-mediated knock down of translational machinery to reduce global translation specifically in adult adipocytes phenocopies the GSC loss earlier shown by adipocyte specific amino acid transporter knockdown. We also find increased germline cyst cell death leading to a reduction in germarium size. Conversely, crc, Drosophila ATF4, over-expression specifically in adipocytes does not influence GSC maintenance. Taken together, these data suggest that AAR pathway activation in adipocytes reduces expression of proteins that may be directly or indirectly involved in maintenance of stem cells. In the future, our goal is to identify adipocyte factors secreted downstream of AAR pathway activity that modulates GSC maintenance. This work will illustrate translational inter-dependency between organs to maintain stem cell-supported tissues.

Biography

Subhshri Sahu is a research scientist with over 9 years of multidisciplinary experience in clinical and basic research in stem cells, regenerative biology and nutrient sensing in stem cell physiology. I am interested in using my training in islet biology, human gallbladder derived insulin positive progenitors and stem cell research to advance clinical and preclinical studies in diabetes.



14th World Congress on Stem Cell Research, Cell and Gene Therapy
October 30, 2020

Citation: Subhshri Sahu, Adipocyte amino acid sensing in the control of ovarian germline stem cell maintenance, Stem Cell Congress 2020, 14th World Congress on Stem Cell Research, Cell and Gene Therapy October 30, 2020, 03