Endogenous effects of Leptin on Leydig stem cell differentiation are specific to patient's BMI

Himanshu Arora[1,2,3#]; Rehana Qureshi[4]; Kajal Khodamoradi[1]; Madhumita Parmar[1]; Derek J Van Booven[3]; Marilia Sanches Santos Rizzo Zutti[1]; Anastasia Vedenko[2]; Joshua Bitran[1]; Dolores Lamb[5]; Joshua M. Hare[2,5]; Ranjith Ramasamy[1,2#]

- [1]Department of Urology, Miller School of Medicine, University of Miami, Miami, Florida, USA
- [2]The Interdisciplinary Stem Cell Institute, Miller School of Medicine, University of Miami, Miami, Florida, USA
- [3]John P Hussman Institute for Human Genomics, Miller School of Medicine, University of Miami, Miami, Florida, USA
- [4]Braman Cancer Center, Miller School of Medicine, University of Miami, Miami, Florida, USA
- [5]Department of Urology, Weill Cornell Medicine, New York, NY
- [6]Department of Medicine, Cardiology Division, Miller School of Medicine, University of Miami, Miami, Florida, USA

UNIVERSITY OF MIAMI

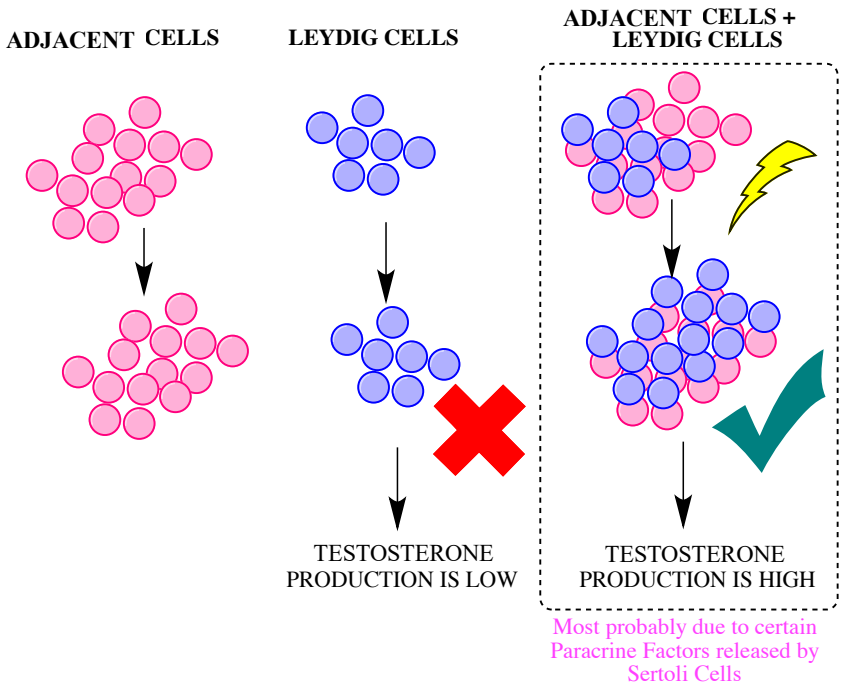
STEM CELLS TRANSLATIONAL MEDICINE

ENABLING TECHNOLOGIES FOR CELL-BASED CLINICAL TRANSLATION

Subcutaneous Leydig Stem Cell Autograft: A Promising Strategy to Increase Serum Testosterone

HIMANSHU ARORA,[a,b] MARILIA SANCHES SANTOS RIZZO ZUTTION,[b] BRUNO NAHAR,[a] DOLORES LAMB,[c] JOSHUA M. HARE,[b] RANJITH RAMASAMY[a,b]

Key Words. Leydig cell • Hypogonadism • Fertility • Sertoli cell • Myoid cell

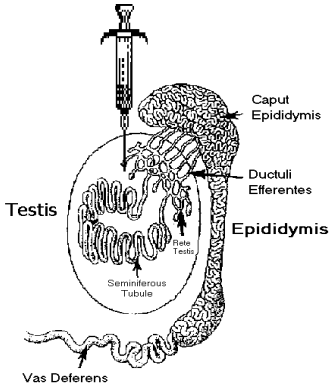


Odeh HM, Kleinguetl C, Ge R, Zirkin BR, Chen H. Regulation of the proliferation and differentiation of Leydig stem cells in the adult testis. Biology of reproduction. 2014;90(6):123. doi: 10.1095/biolreprod.114.117473. PubMed PMID: 24740597; PMCID: PMC4094000.

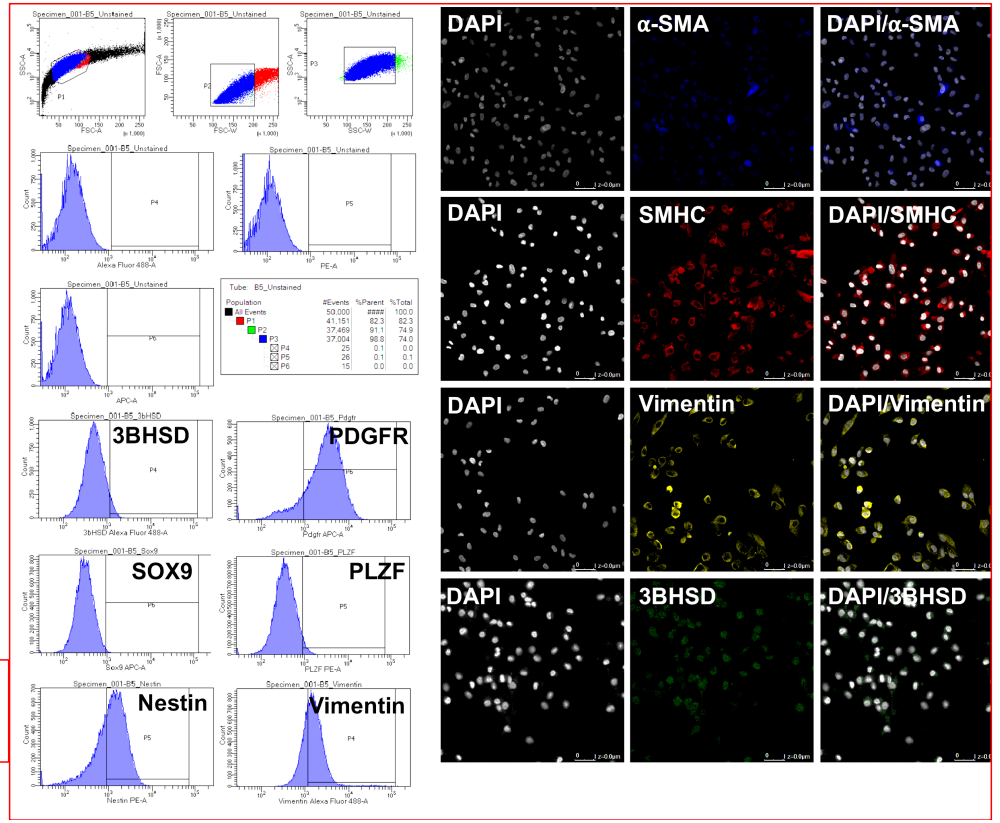
Recreated Figure by – Ramasamy Lab

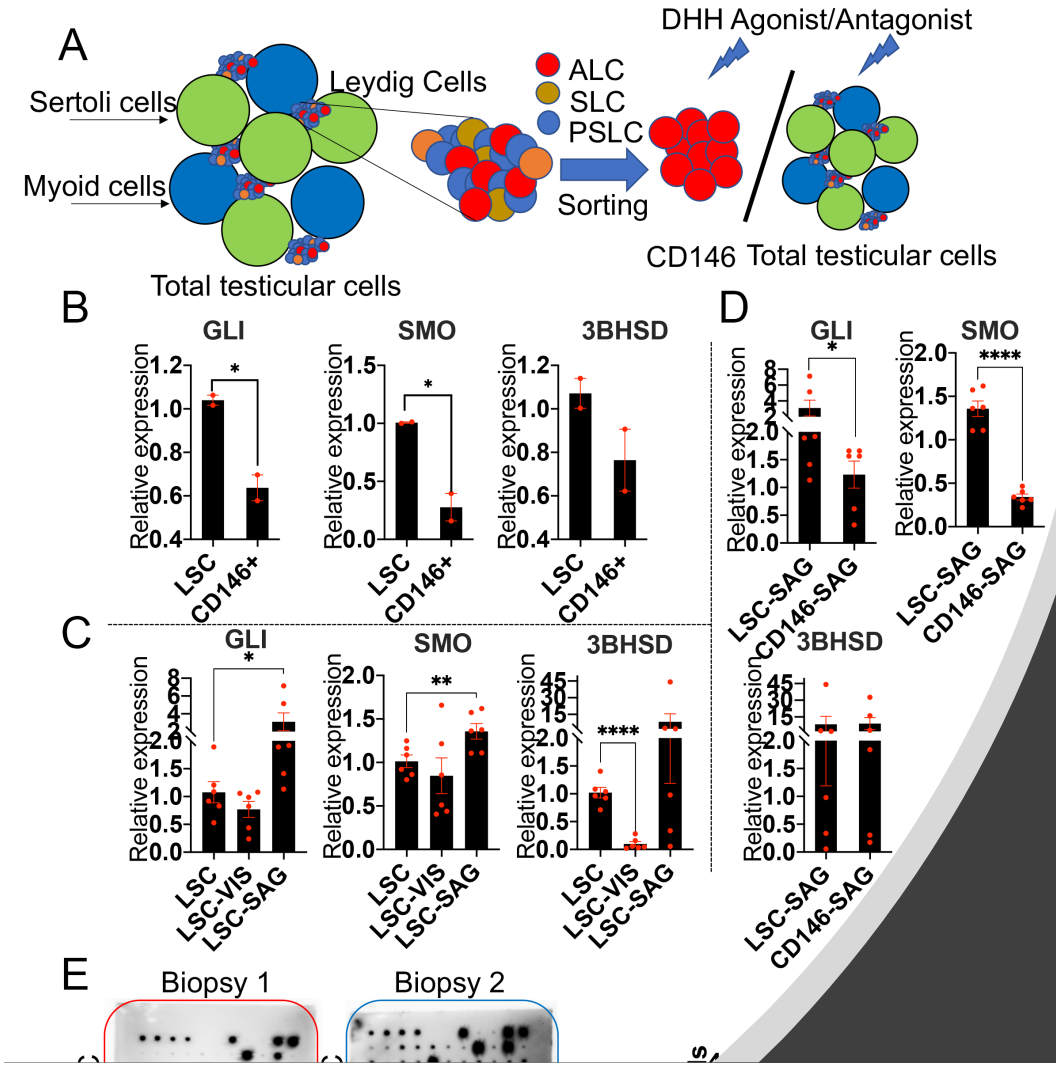
Isolation and characterization of Human Leydig Stem Cells

Testis biopsies were harvested from 10 men with oligo/azoospermia, undergoing sperm retrieval



LSCs were successfully cultured in-vitro, characterized

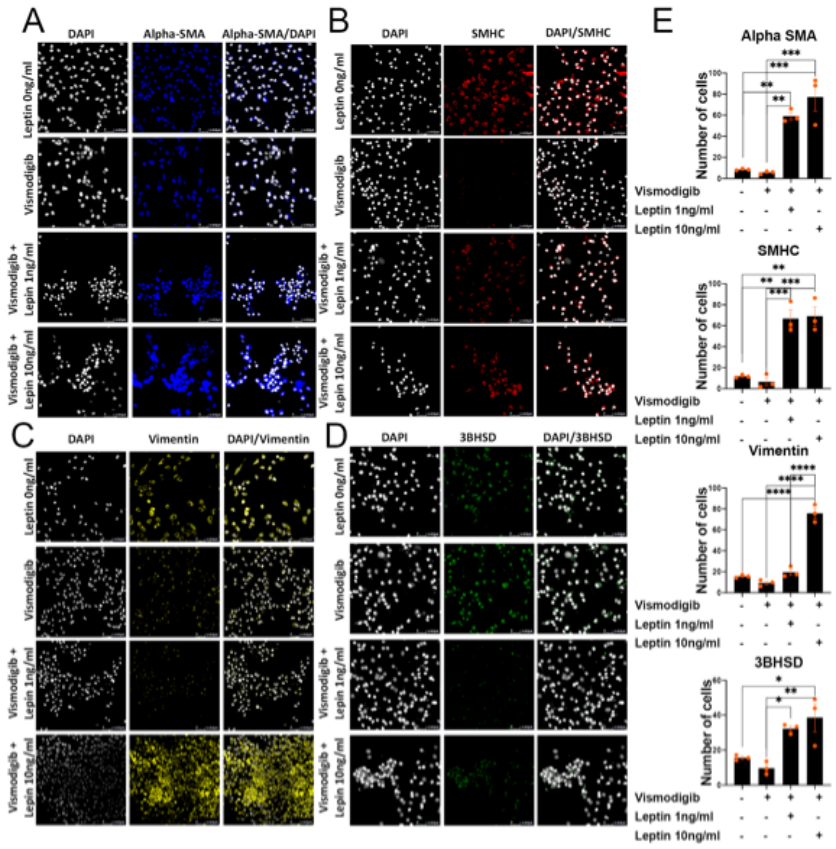




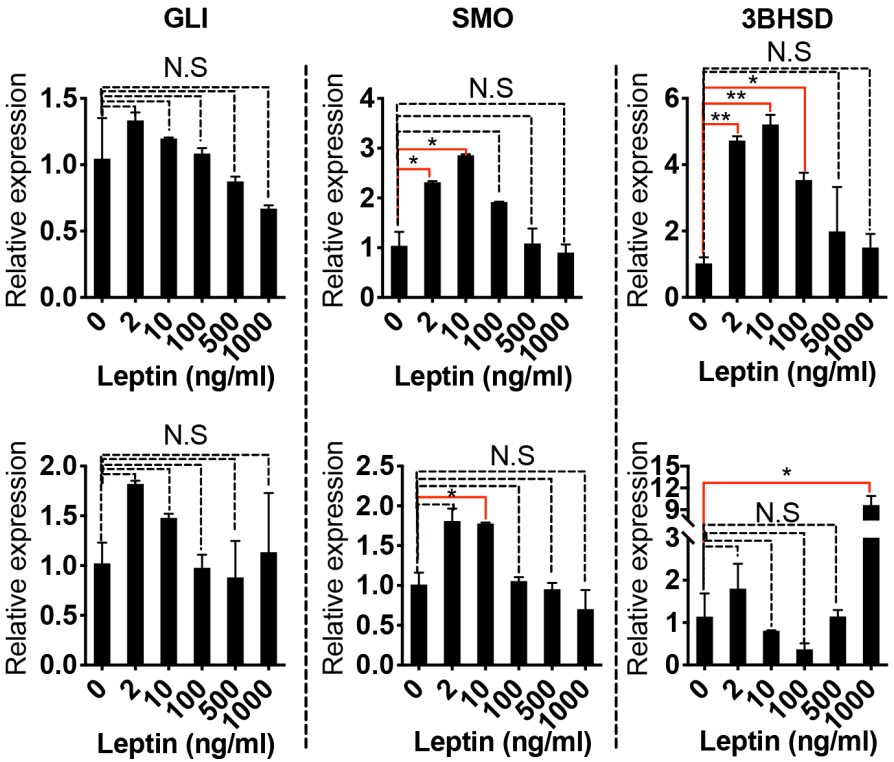
Paracrine factors

- Condition media was used from LSC cultures with or without Testicular microenvironment.
- Cytokine antibody array
- Leptin was the only cytokine whose levels were substantially suppressed in the absence of TME

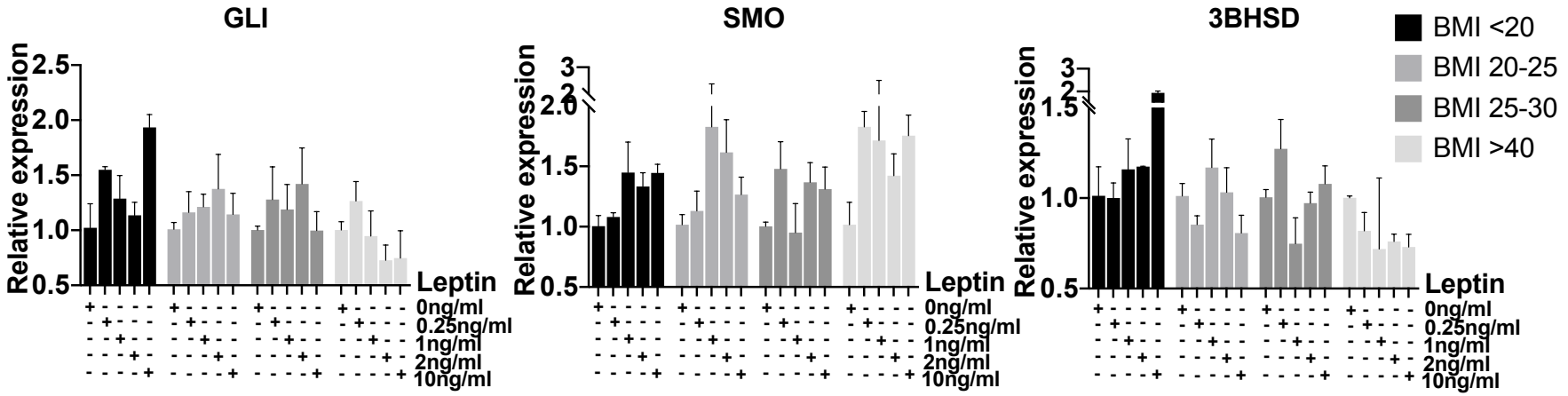
Leptin was found to be upstream of DHH Signaling and this interaction was found to be unidirectional



- Leptin was found to induce the differentiation of LSCs in a dose dependent manner
- Low doses of Leptin have an inducing and high Leptin doses have an inhibiting impact on LSC differentiation



Impact of Leptin wrt BMI



- Increasing does of Leptin have an inducing impact on LSC differentiation and DHH signaling in cells extracted from patients with BMI<20 (lean patients)
- Increasing does of Leptin have an inhibiting impact in cells extracted from patients with BMI>35 (obese patients)
- In patients with BMI between 20-30, low does of Leptin have a positive and high doses of Leptin have an inhibiting impact on LSC differentiation and DHH signaling.

Conclusion

- Leptin is a paracrine factor which is critical for LSC differentiation.
- Impact of Leptin on LSCs are dose dependent

Thank you!

- For more information contact: hxa287@med.miami.edu