Summer Student Research Program
Project Description

FACULTY SPONSOR'S NAME AND DEGREE:*Ioana Carcea, MD PhD*
PHONE: (347) 458 - 3519
DEPARTMENT AND INTERNAL MAILING ADDRESS:*Pharmacology Physiology and Neurosciemce, MSB H584*
E-MAIL: ***Ioana.carcea@rutgers.edu***
PROJECT TITLE (200 Characters max):

Susceptibility of Glucose Regulation to Social Isolation

HYPOTHESIS:

Social isolation induces glucose dysregulation by activating pre-autonomic brain centers controlling sympathetic input to liver and pancreas.

PROJECT DESCRIPTION **(Include design, methodology, data collection, techniques, data analysis to be employed and evaluation and interpretation methodology)**

Social isolation and loneliness have reached epidemic levels within the United States. Loneliness associates with increased incidence of type 2 diabetes and other metabolic disorders. However, recent efforts to assign directionality and causality to data collected from human populations led to contradictory findings. Animal models that allow mechanistic investigation and experimental control of social variables, are best suited to investigate if and how social isolation leads to glucose dysregulation.

In rodents, social isolation disrupts multiple metabolic endpoints, but the dynamics and mechanisms remain poorly understood. In recent work, we showed that chronic social isolation leads to **fasting hyperglycemia** in male mice. Isolation does not affect glucose dynamics in females and orchiectomized males. We find no effect of isolation on the plasma level of several major glucoregulatory hormones: insulin, epinephrine, and corticosterone. However, **glucagon** levels are distinctly modulated by social isolation in intact vs orchiectomized male mice. Glucagon release is in part regulated by neurons expressing the nitric oxide synthase nNOS-1 in the ventromedial hypothalamus (VMH), a brain structure that modulates autonomic input to the pancreas. We find that the vast majority (90-95%) of VMH nNOS-1 neurons co-express the receptor for oxytocin hormone (OTR). VMH-OTR+ neurons respond to social interactions, and we found that chronic isolation increases immediate early gene expression in these neurons. Furthermore, we show that chemogenetic activation of VMH-OTR+ neurons increases blood glucose levels. Together, these findings indicate that VMH-OTR+ neurons are ideally positioned to mediate the link between social isolation and glucose dysregulation.

Social isolation deprives animals of complex, multisensory communication signals. We tested the role of somatosensory vs non-somatosensory social communication in protecting against isolation-induced hyperglycemia. Mouse dyads separated by a perforated barrier which allows visual, auditory and olfactory but not somatosensory social communication show improved glucose regulation compared to animals deprived of all social signals. Separately, we show that thermosensation, a key but less recognized aspect of social communication, can also protect against isolation hyperglycemia. Our data indicate that multiple channels for social communication could redundantly feed into glucoregulatory mechanisms to impact glucose regulation.

Our recent work describes unexpected effects of social isolation on glucose homeostasis, and identifies three directions for mechanistic investigation: (1) does isolation affect the function of VMH-OTR+ neurons to induce glucose dysregulation? (2) how do testicular factors contribute to isolation susceptibility? and (3) how does thermosensation contribute to isolation hyperglycemia? We will answer these questions using photometry brain recordings, chemogenetic manipulation of neuronal activity, genetic deletion of specific genes, glucose measurements, ELISA hormonal measurements, etc.

SPONSOR'S MOST RECENT PUBLICATIONS RELEVANT TO THIS RESEARCH:

https://www.biorxiv.org/content/10.64898/2025.12.18.695168v1

Susceptibility of Glucose Regulation to Social Isolation
Hannah H. Lamont, Rumi Oyama, Paula Diaz Munoz, Dashiel Siegel, Paula Baringanire, Valentina Vargas, Miriam E. Bocarsly, Vanessa H. Routh, Ioana Carcea
doi: https://doi.org/10.64898/2025.12.18.695168

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THIS PROJECT IS: ☐ **Clinical** ☒ **Laboratory** ☐ **Behavioral** ☐ **Other**

THIS PROJECT IS CANCER-RELATED ☐
Please explain Cancer relevance

THIS PROJECT IS HEART, LUNG & BLOOD- RELATED ☐
Please explain Heart, Lung, Blood relevance

THIS PROJECT INVOLVE RADIOISOTOPES? ☐

THIS PROJECT INVOLVES THE USE OF ANIMALS ☒
PENDING ☐ **APPROVED** ☒ **IACUC PROTOCOL #201800225**

THIS PROJECT INVOLVES THE USE OF HUMAN SUBJECTS? ☐
PENDING ☐ **APPROVED** ☐ **IRB PROTOCOL # M**

THIS PROJECT IS SUITABLE FOR:

UNDERGRADUATE STUDENTS	☒	ENTERING FRESHMAN	☐
SOPHMORES	☐	ALL STUDENTS	☒

THIS PROJECT IS WORK-STUDY: **Yes** ☐ **or** **No** ☐

THIS PROJECT WILL BE POSTED DURING ACADEMIC YEAR
FOR INTERESTED VOLUNTEERS: **Yes** ☒ **or** **No** ☐

WHAT WILL THE STUDENT LEARN FROM THIS EXPERIENCE?
Critical thinking, experimental methods, troubleshooting, specific techniques, data interpretation, data presentation