

Field Report

Institution:

The Shulman Lab

Department of Internal Medicine

Endocrinology Section

PO Box 208020, TAC S269

333 Cedar Street

New Haven, 06510, United States

Gerald I. Shulman, MD, PhD – Principal Investigator

Gary W. Cline, PhD – Principal Investigator

Johanna Json-Toft – Lab Secretary

Kun Lyu – Graduate student, colleague

1. General impression of the stay

The laboratory group of Dr. Shulman and Dr. Cline is located in The Anlyan Centre (also known as TAC building) in New Haven in the state of Connecticut. The group consists of more than 20 members, most of whom are PhD students and post-doctoral fellows. The laboratory is divided into two sections: the Analytic Core and the Mouse Metabolic Phenotyping Core. The Analytic Core employs 10 members who operate instruments of gas and liquid chromatography coupled to mass spectroscopy, and nuclear magnetic resonance apparatus. The section carries out chemical tissue analysis on demand from the outside source, as well as from the Mouse Metabolic Phenotyping Core. This part designs and carries out individual animal studies on non-alcoholic liver disease and type 2 diabetes. Dr. Shulman leads the Phenotyping Core and Dr. Cline the Analytic Core.

Before the work in the laboratory, I had to pass several preparatory courses such as Radiation Safety, Animal Care, Biosafety or HIPAA training modules. A specific protocol had to be signed and approved from the Office of Environmental Health and Safety, which allowed me to handle animals.

My overall evaluation and impression of my stay is very positive. All laboratory members were willing to apprentice me and guide me through all the individual steps necessary to either successfully design an experiment, or conduct chemical analysis. My primary duty was conduction of hyperinsulinemic-euglycemic clamps to assess insulin resistance in mice and rats in vivo, after specific hormonal adjustments or therapeutic treatments with variant dosing of distinct drugs. Tracers were infused simultaneously, to trace hepatic and peripheral glucose and fatty acid fluxes, in specific organs and hence assess the treatment's influence on hepatic metabolism. The tracer enrichment ratios were analysed by me on GC-MS instruments, before

each analysis, animal plasma and tissue samples had to be chemically derivatized; such a derivatization involved a series of organic chemical reactions which modulate the structure of traced compound to allow for separation in the gaseous phase. The attitude of the laboratory group to my position was open, but rewarding – I was freely allowed to participate in what I was interested in, every post-doc or PhD student was assigned a study project with which I could help, and after 2 months of training I was assigned my own project. PIs wanted me to learn as much as was technically possible, the aim was to have me engaged in every scientific method, which they employed in order to bring back a plethora of analytical practical skills with improved theoretical background in biochemistry, metabolism and chemical analysis. I realized that performing studies in vivo might sometimes be a challenge, due to a pile of physiological aspects of the living organism that come into play, along the animal housing costs at YARC – Yale Animal Resource Centre. For this reason, most of the experiments were stressful due to time and finance constraints. This research stay greatly improved my scientific and critical thinking, and cleared the focus of my career path after graduation.

2. Quality of the host institution

The technical equipment was at the highest level – GC-MS and LC-MS analytic instruments were novel and up to date, regularly maintained by professional staff of the producer. Stock chemicals and experimental tools such as pipette tips or heparinized haematocrit capillary tubes were continuously ordered. Animal models were ordered from producer laboratory (eg. a mouse model with a specific mutation) and bred at YARC – this was the most expensive element of the laboratory costs, which can rise to 100.000 dollars/month. YARC was directly located in the TAC building. Yale Section of Endocrinology carried out scientific conference talks and clinical case study presentations every Friday, which included incoming doctors and scientists giving talks on various clinical dilemmas of the Internal Medicine department and research innovations of their laboratories. The Department of Internal Medicine held “Medical Grand Rounds” – scientific presentations of doctors from all over the country on a weekly basis. I was given access to all these.

3. Contacts within the host institution

I have made a personal connection with all laboratory members, however, the most relevant and appreciated ones are specified in the report’s heading.

4. Recommendations for future Marshall Plan fellows

I would absolutely recommend students this laboratory, but only with sufficient knowledge of biochemistry, metabolism and cellular and molecular physiology. Tracer studies require a lot of mathematical understanding and experiments require knowledge of organic chemistry. Lab is open to take students with similar background, in case of a free vacancy.