**The School of Natural Sciences**

**Ph.D. Defense**

**The Regulation of Fuel Metabolism and Substrate Availability During the Prolonged Fast of the Northern Elephant Seal**

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**ABSTRACT:**

Food deprivation in mammals results in profound changes in fuel metabolism and substrate regulation. Among these changes, is a decreased reliance on the counter-regulatory dynamics by insulin-glucagon due to the reduced glucose utilization, and increased concentrations of lipid substrates in plasma to meet the energetic demands of peripheral tissues. Prolonged food deprivation also increases lipid oxidation and utilization, which may contribute to the onset of the insulin resistance associated with fasting. Because insulin resistance promotes the preservation of glucose and oxidation of fat, it has been suggested to be an adaptive response to food deprivation. As the primary storage site of lipid substrates, adipose serves as a primary contributor to the regulation of metabolism in food deprived states. Through its regulation of lipolysis, adipose influences the availability of carbohydrate, lipid, and protein, and so, may potentially be a key regulator of fasting metabolism.

The northern elephant seal pup (*Mirounga angustirostris*) naturally undergoes a 2-3 month post-weaning fast during which it depends primarily on the oxidation of fatty acids to meet its energetic demands. As such, it makes an ideal model to study the effects of prolonged food deprivation on the regulation of metabolism and to assess the contributions made by adipose tissue. Results from this work suggest that long-term fasting induces shifts in the regulation of lipolysis and lipid metabolism that contribute to the onset of insulin resistance in adipose, all-the-while maintaining insulin sensitivity in muscle. Furthermore, fasting leads to decreased glucose tolerance that may facilitate the onset of a whole-body insulin resistance-like condition despite the maintenance of skeletal muscle insulin sensitivity that serves to promote the preservation of metabolic substrates. These findings contribute to our understanding of the adaptive mechanisms used by fasting mammals to endure prolonged food deprivation.

**BIOGRAPHY:**

Jose Viscarra is a biologist studying the regulation of metabolism in fasting elephant seals. He was born and raised in California’s Central Valley and received his Bachelor’s Degree from UC Merced in 2009. Since entering the Ph.D. Program, Jose has worked on several projects assessing metabolic function in seals, as well as in rodent models of metabolic syndrome. Results of these investigations have led to the publication of eight peer-reviewed articles.

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