

Silva Laboratory

Research Interests: *Thyroid hormone physiology, Thermogenesis, Temperature Homeostasis*

Our laboratory's long time interest is in how hormones, particularly the hormones of the thyroid gland (thyroid hormone, TH), regulate thermogenesis and energy balance. Homeothermic animals spend a large amount of energy generating heat (thermogenesis) to maintain body temperature. The fuel efficiency of the homeothermic "machine" is much lower than that of the poikilothermic machine for the sake of temperature homeostasis. Being a wasteful process, the need for thermogenesis has competed through evolution with food availability. Probably because of these competing pressures on our remote ancestors, thermogenesis is major source of variability of energy expenditure in humans. It is known that low metabolic rate (due to low thermogenesis) is a risk factor for obesity. Furthermore, thermogenesis is promptly turned down in starvation and caloric restriction, which limits the efficiency of low-calorie diets. TH acquired a new role with the advent of homeothermy in evolution, which is to stimulate and sustain thermogenesis. In the absence of TH, homeothermic species regress to a nearly poikilothermic status. Therefore, understanding how thyroid hormone controls thermogenesis and energy balance is likely to provide valuable insight to understand the variability of energy expenditure in humans and eventually may provide clues to medical interventions, and this knowledge is relevant to obesity and type-2 diabetes, two major health problems of our time.

Over recent years, our laboratory has turned to transgenic mouse models with deletion of genes likely to be involved in the control of thermogenesis and temperature homeostasis. Mice with deletion of one of the TH receptors (TR), the TR α , have lower body temperature and are cold intolerant. To compensate, they stimulate another form of thermogenesis, which is more energy demanding and makes them eat more and gain less weight. However, this mechanism is not sufficient to protect them from severer cold (e.g. 4-10°C). Another model, lacking a mitochondrial enzyme, is more prone to diet-induced obesity and loses less weight when calorie-restricted. Interestingly females are much more affected than males, who compensate better for the lack of the gene.

Selected Publications

Marrif,H.; Schifman,A.; Stepanyan,Z.; Gillis,M.A.; Calderone,A.; Weiss,R.E.; Samarut,J.; **Silva,J.E.** 2005. Temperature Homeostasis in Transgenic Mice Lacking Thyroid Hormone Receptor Alpha Gene Products. *Endocrinology* 146: 2872-2884

Alfadda,A.; DosSantos,R.A.; Stepanyan,Z.; Marrif,H.; **Silva,J.E.** 2004. Mice with Deletion of the Mitochondrial Glycerol-3-Phosphate Dehydrogenase Gene Exhibit a Thrifty Phenotype. Effect of Gender. *Am. J. Physiol. (Regul. Integr. Comp Physiol.* 287: R147-R156

Silva,J.E. 2006. Thermogenic Mechanisms and Their Hormonal Regulation. *Physiological Reviews* 86:435-464

Professional Highlights

Van Meter Award of the American Thyroid Association (outstanding contributions to thyroid research)

Latin American Thyroid Society Award (contributions to thyroid research and mentoring young investigators in thyroid physiology and disease)

President Canadian Society of Endocrinology and Metabolism



Jorge Enrique Silva, MD

Chief, Endocrinology and Metabolism, Baystate Medical Center

Adjunct Professor, Biology, University of Massachusetts, Amherst

Education

M.D., University of Chile

Postdoctoral

Internal & Experimental Medicine, Hospital del Salvador, U Chile, 1968-1971

Endocrinology Research, Montefiore Hospital Medical Center, 1974-1976

Endocrinology Research, Peter Bent Brigham Hospital, Harvard Medical School, 1976-1977

Contact Information

J. Enrique Silva, MD

3601 Main Street

Springfield, MA 01199

Phone: 413.794.9571 or 0207

Fax: 413.794.0857 or 9329

enrique.silva@bhs.org