

Role of the Keap1/Nrf2 antioxidant response system in the thyroid gland:

Cells are equipped with complex systems that help sustain protein homeostasis (proteostasis). Our group investigates the roles of proteostatic systems in the prevention and pathogenesis of endocrine diseases. Our main current focus is the Keap1/Nrf2 signaling pathway, which controls the expression of a battery of genes mediating antioxidant responses, detoxification of xenobiotics, degradation of damaged macromolecules, and various other proteostatic mechanisms. We are investigating the roles of Keap1/Nrf2 signaling in thyroid physiology and pathophysiology, including its implication in the response to exposure to pharmacological doses of iodine, in the pathogenesis of benign thyroid nodules, and in thyroid carcinogenesis. We are also characterizing the molecular cross-talks between the Keap1/Nrf2 pathway, the ubiquitin-proteasome system (UPS), and the unfolded protein response (UPR) in various physiological and pathological settings; and we are searching for compounds that can modulate thyroid physiology to prevent and treat common thyroid disorders. In our studies we adopt a multi-disciplinary and translational approach: we develop and use cellular models of endocrine physiology, rodent models of endocrine pathophysiology, and samples from patients with benign endocrine disorders or endocrine cancers. Our research is funded by the Swiss National Science Foundation, the Swiss Society for Endocrinology-Diabetology, the 3R Foundation Switzerland, the Leenaards Foundation and various pharmaceutical companies. At the European level, we represent Switzerland in international research networks (COST Actions). We also participate in international multi-center clinical studies for the diagnosis and treatment of thyroid diseases.