BALÁZS GEREBEN

Institute of Experimental Medicine

Address: Szigony u. 43., H-1083 Budapest, Hungary

RESEARCH AREA

Thyroid hormones (TH) are master regulators of cellular metabolism and proliferation and consequently exert a fundamental impact on brain development and function predominantly due to their impact on transcriptomic activity. The Laboratory aims to (i) identify and modulate cell-type specific molecular pathways responsible for the regulation of TH economy in the brain and coupled peripheries; (ii) translate these mechanisms to specific brain functions under physiological and pathophysiological conditions; (iii) develop transgenic approaches to assess and modulate cell-type specific TH action. They combine molecular, cell biological, anatomical and transgenic techniques to study regulation and consequences of TH signalling. (1) They study the molecular regulation of deiodinase enzymes mediating TH metabolism with special respect to the complex and tight regulation of type 2 deiodinase (D2) to identify molecular elements and protein-protein interactions allowing the rapid regulation of D2 activity along the ubiquitin/proteasome pathway and its role in the generation of tissue-specific hypothyroidism. The studies also target the regulation of the D2-encoding dio2 gene during hypothalamic response to inflammation, a phenomenon they described as a component of the pathogenesis of the nonthyroidal illness syndrome. (2) They investigate the mechanisms and biological consequences of D2 and type 3 deiodinase (D3) mediated neuro-glial coupling of TH metabolism and its impact on the hypothalamo-pituitary-thyroid axis and thyroid hormone signaling of the nervous system. (3) The Laboratory is involved in the generation of transgenic mouse models for cell-type specific modulation and assessment of TH signalling and also aims to identify human markers representing tissue TH economy. This resulted in the generation and patenting of the Thyroid Hormone Action Indicator (THAI) Mouse, allowing tissue-specific assessment of TH action in vivo.

TECHNIQUES AVAILABLE IN THE LAB

Recombinant DNA techniques, cell culturing, recombinant protein expression, transgenics, quantification of gene expression, detection of proteins and mRNA, microscopy, deiodination and biochemical assays, work with rodent models.

SELECTED PUBLICATIONS

Jo, S., Fonseca, T.L., Da Costa Bocco, B.M., Fernandes, G.W., McAninch, E.A., Bolin, A.P., Da Conceição, R.R., De Castro, J.P.W., Ignacio, D.L., Egri, P., Németh, D., Fekete, C., Bernardi, M.M., Leitch, V.D., Mannan, N.S., Curry, K.F., Butterfield, N.C., Bassett, J.H.D., Williams, G.R., **Gereben, B.,** Ribeiro, M.O., Bianco, A.C. (2019) Type 2 deiodinase polymorphism causes ER stress and hypothyroidism in the brain. **J Clin Invest 129:** 230-245.

Mohácsik, P., Erdélyi, F., Baranyi, M., Botz, B., Szabó, G., Tóth, M., Haltrich, I., Helyes, Zs., Sperlágh, B., Tóth, Zs., Sinkó, R., Lechan, R.M., Bianco, A.C., Fekete, Cs., **Gereben B.** (2018) A transgenic mouse model for detection of tissue-specific thyroid hormone action. **Endocrinology 159:** 1159–1171.

Kollár, A., Kvarta, Papp, Zs., Egri, P., **Gereben, B.** (2016) Different Types Of Luciferase Reporters Show Distinct Susceptibility To T3-Evoked Down-Regulation. **Thyroid 2016 26:** 179-82.

Gereben, B., McAninch, E.A., Riberio, M.O., Bianco, A.C. (2015) Scope and limitations of iodothyronine deiodinases in hypothyroidism. Nature Rev Endo 11: 642-52.

Dentice, M., Bandyopadhyay, A., **Gereben, B.,** Callebaut, I., Christoffolete, M.A., Kim, B.W., Nissim, S., Mornon, J.P., Zavacki, A.M., Zeold, A., Capelo, L.P., Curcio-Morelli, C., Ribeiro, R., Harney, J.W., Tabin, C.J., Bianco, A.C. (2005) The Hedgehog-inducible ubiquitin ligase subunit WSB-1 modulates thyroid hormone activation and PTHrP secretion in the developing growth plate. **Nature Cell Biology 7:** 698-705.