ETUDE DU RÔLE DE L'HORLOGE CIRCADIENNE DANS LA FONCTION DE L'ILÔT PANCRÉATIQUE HUMAIN

*TIPHAINE MANNIC, *DANIEL SAGE, PATRICK SALMON, JACQUES PHILIPPE, MICHAEL UNSER, PHILIPPE HALBAN, DOMENICO BOSCO, CHRISTOPH BAUER AND CHARNA DIBNER
DIVISION OF ENDOCRINOLOGY, DIABETES AND NUTRITION, GENEVA UNIVERSITY HOSPITAL (HUG), SUISSE
* equal contribution

Auteur correspondant : charna.dibner@hcuge.ch

Circadian oscillation of biological processes has been described in organisms ranging from photosynthetic bacteria to vertebrate and reflects the existence of underlying intrinsic biological clocks with near 24 hour oscillation periods. There is a growing evidence for the connection between a number of metabolic syndromes, including obesity and diabetes, and circadian clockwork. Glucose homeostasis and the insulin secretion are tightly controlled by the circadian system. Furthermore, patients with circadian misalignments show profound perturbations of plasma glucose and insulin levels. An outstanding goal is therefore to provide further insights into the emerging roles of circadian genes in the regulation of pancreas function and glucose metabolism. The overall purpose of our research is to study the physiological importance of a functional pancreatic islet clock, and its role in metabolic diseases and type 2 diabetes. Our experiments provide the compelling evidence for robust circadian oscillations recorded in cultured human islets, as well as in dispersed islet cells. To get the insights into pancreatic islet clockwork, we employed continuous bioluminescence recording by Actimetrics Lumicycler, as well as combined bioluminescence-fluorescence time lapse microscopy. Robust islet cell autonomous self sustained clocks were detected in human islets, and in ß-cells marked by rat insulin promoter fluorescent lentiviral construct. Moreover, robust oscillatory patterns of endogenous core clock genes in human islets were recorded. Using islet perifusion system connected to the photomultiplier tubes, we are currently working on obtaining insulin and glucagon secretion profiles "around-the clock". Dissection of the endocrine pancreas oscillator function will advance the understanding of emerging link between pancreas circadian clockwork, metabolic disorders and type 2 diabetes.