## Irisin administration restores beta-cell functional mass in a mouse model of type 2 diabetes

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**Aim:** Irisin is a hormone secreted by skeletal muscle able to improve metabolic homeostasis. Serum irisin levels are reduced in type 2 diabetes (T2D), while exogenous irisin administration improves glycemic control in diabetic mice. We have previously demonstrated that irisin promotes beta-cell survival and function both in vitro and in vivo in healthy wild type mice. We have also demonstrated that irisin restores the defective glucose-stimulated insulin secretion (GSIS) and reduces apoptosis in human pancreatic islets from patients with T2D. Nevertheless, the beta-cellular effects of in vivo irisin administration to T2D mice are still unknown.
**Methods:** C57Bl/6 mice (n = 8) were fed a high-fat diet (HFD, 60% of energy deriving from fat) for 10 weeks and then intraperitoneally injected with streptozotocin (STZ, 100 mg/kg) to induce diabetes. Four standard diet (SD)-fed mice were used as control. HFD/STZ mice were treated with 0.5 µg/g irisin (n = 4) or vehicle (n = 4), for 14 days. Fasting glycemia, insulinemia, body weight, glucose tolerance, and pancreatic islet function were assessed. Pancreatic islet architecture was also evaluated through immunofluorescence analyses.
**Results:** Compared to SD mice, HFD/STZ mice showed higher fasting glycemia and body weight, glucose intolerance, and reduced GSIS; in addition, HFD/STZ mice showed reduced islet volume (-78%), beta-cell area (-35%), and insulin content (-60%), and increased alpha-cell area (+54%). Irisin administration significantly restored glycemia (-31%), body weight (-13%), glucose tolerance (-27%), GSIS (+23%), islet volume (+61%), beta-cell area (+34%) and alpha-cell area (-49%), and insulin content (+36%). Of note, irisin induced a 9-fold increase in beta-cell proliferation rate.
**Conclusions:** These results show that irisin improves glycemic homeostasis and restores the functional beta-cell mass when administered in vivo to diabetic mice, probably by promoting beta-cell proliferation.

## Acute ischemic stroke: how to investigate the association between disease etiology and gene expression profiles

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**Background:** Acute ischemic stroke (AIS) represents one of the principal causes of neurological morbidity and mortality worldwide. For a prompt and efficient cerebral blood restoration, intravenous treatment with rt-PA is often combined with mechanical thrombectomy (MT) which provides cerebral thrombi (CT) as study material, allowing the investigation of its cellular composition, morphological and histopathological features. Indeed, the determination of stroke etiology, typically defined by the TOAST classification, is paramount for prognostic factors, outcome, and management of the event. Aim of the study is therefore to highlight and analyze gene expression profiles in thrombotic tissue and peripheral blood (PB) in the comparison between strokes of cardioembolic (CE) and atherosclerotic (LAA) origin.
**Methods:** We performed gene expression profiles of 92 patients. CT were stored in RNA later and RNA was extracted by PAX gene blood miRNA kit. The global gene expression profile was assessed by Affymetrix technology using GeneChip Human Transcriptome Array 2.0 combined with Affymetrix Transcriptome Analysis Console (TAC) Software.
**Results:** Currently, we focused our attention on CT data analysis. The analysis revealed a significant difference (p-value<0.05 and Fold-Change=2 as threshold) in gene expression when comparing LAA and CE stroke. In particular, from CT of atherosclerotic origin emerges an overexpression of 1766 genes. Prominent among them are genes such as MMP-9, TGFB, TGFBR and CXCL1, primarily involved in neutrophil-mediated immunity, Blood-Brain Barrier (BBB) disruption processes, and associated with atherosclerotic plaque instability and related to poor neurological outcome, suggesting a deleterious role in human brain injury. As concerns CE patients, 57 genes mainly involved in transcriptional regulatory processes turn out to be significantly overexpressed.
**Conclusions:** Transcriptome profiling is a powerful weapon for revealing expression patterns associated with complex disorders. The variation of gene expression profiles confirmed and extended several known pathophysiological mechanisms and may be one way of delineating different stroke etiology.