parenchyma. However, the reduction in functional tissue as a result of diabetes tended to decrease vessels-to-pancreatic cells ratio compared to control parenchyma. Diabetes determined a significant increase in interstitial fibrosis and vascular remodeling also in the myocardium. Similarly, capillary and sinusoids density were significantly reduced in central and paratrabecular areas of diabetic bone marrow when compared to nondiabetic cases ($p < 0.05$). Compared to controls, lymphatic vessels were also significantly reduced in diabetic pancreas ($p < 0.05$) while arteriolar density was unaffected. Interestingly, CD34pos progenitor cells were significantly reduced ($p < 0.01$) in both bone marrow and pancreas of diabetic patients compared to controls.

Conclusions: Rearrangement of the blood and lymphatic network and reduction in CD34pos progenitors concur in multiple tissues with diabetes. Although we did not established whether this was a consequence or a cause of diabetes associated multiorgan damage, our approach may offer new insights on the understanding of the diabetic paradox of a tissue specific angiopathy.

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Novel anti-obesity quercetin-derived Q2 prevents metabolic disorders in rats fed with high-fat diet

C. Rocca[a,d], L. Albano[b,d], M.C. Granieri[a,d], D. Amelio[a,d], I.C. Nettore[c,d], P.E. Macchia[c,d], S. Sinicropi[a,d], P. Ungaro[b,d], T. Angelone[a,d,e]
[a]*Department of Biology, Ecology and ES, University of Calabria, Arcavacata di Rende (CS), Italy*
[b]*CNR Institute of Endocrinology and Experimental Oncology "G.Salvatore", Napoli, Italy*
[c]*Department of Clinical Medicine and Surgery, University of Napoli "Federico II", Napoli, Italy*
[d]*Department of Pharmacy, Health and Nutritional Sciences, University of Calabria, 87036 Arcavacata di Rende (CS), Italy*
[e]*National Institute of Cardiovascular Research (INRC), Bologna, Italy*

Objective: Obesity is often accompanied by an increased morbidity and mortality due to an increase of the cardiovascular disease risk factors, diabetes mellitus and dyslipidemia. Research is constantly working on protective molecules against obesity. In the present study, a novel Quercetin derivative Q2 was synthesized to overcome the poor bioavailability and low stability of Quercetin, a natural flavonoid with antioxidative and antiobesity properties.

Methods: Rats were fed (12ws) with normodiet (fat: 6.2%), High Fat Diet (fat:60%), HFD + Q2 in water (500 nM). Metabolic and anthropometric parameters were measured. 3T3-L1 preadipocytes were incubated with Q2 (1-25μM) and the differentiation program was evaluated by lipid accumulation through ORO staining. Gene and protein expression levels were assessed by RT-PCR and Western blot analysis.

Results: Compared to HFD, HFD + Q2 rats showed reduced body weight, abdominal obesity, dyslipidemia and improved glucose tolerance. This is associated to lower adipose and liver modifications compared to hypertrophy and steatosis observed in HFD. In 3T3-L1 cells, lipid accumulation was significantly impaired by treatment with Q2. Indeed, Q2 significantly decreased the expression of the main adipogenic markers, c/EBPα and PPARγ both at mRNA and protein level.

Conclusions: Our results indicate that Q2 markedly decreases differentiation of 3T3-L1 preadipocytes and contributes to prevent metabolic disorders as well as adipose and liver alterations typical of severe obesity induced by a HFD.

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MIR-182 is a Tbx5 effector during heart development in zebrafish

E. Guzzolino[a,b], R. D'aurizio[c], M. Pellegrino[d], D. Garrity[e], N. Ahujah[e], M. Groth[f], M. Baugmart[f], C. Hatcher[g], A. Mercatanti[b], L. Mariani[b], Monica Evangelista[b], F. Russo[c], R. Fukuda[h], D. Stainier[h], L. Pitto[b]
[a]*Scuola Superiore Sant'Anna of Pisa, Italy*
[b]*Institute of Clinical Physiology, CNR, Pisa, Italy*
[c]*University of Pisa, Italy*
[d]*Institute of Informatics and Telematics CNR, Pisa, Italy*
[e]*Colorado State University, Fort Collins, USA*
[f]*Fritz Lipmann Institute for Age Research, Jena, Germany*
[g]*Philadelphia College of Osteopathic Medicine, Department of Bio-Medical Sciences, Philadelphia, United States of America*
[h]*Max Plank institute, Bad Nahueim, Germany*

Objective: MicroRNAs, small molecules of 22-25 nt, inhibit translation of target mRNAs and with transcription factors comprise two major layers of gene regulatory networks with strictly interconnected activities. Tbx5, a dosage sensitive gene, is a pivotal player involved in heart/limbs development and its mutations are responsible of the Holt-Oram syndrome (HOS) in human, characterized by upper limb malformations and congenital heart defects (CHD)s both in morphology and electrophysiology.

Methods: With the hypothesis that Tbx5 and miRNAs can work cooperatively trough mutual cross-regulation, we performed *miRNA-profiling* on RNA extracted from E11.5–E12.0 hearts isolated from WT and HOS mice. By a bioinformatic approach we selected the miR-182 resulted differentially expressed in HOS and able to putatively target evolutionarily conserved genes related to heart development. The miR-182 was functionally tested *in vivo* in zebrafish with experiments of transient and stable mis-expression and by *in situ* hybridization analysis.

Results: miR-182 was found to be up-regulated in HOS mouse phenotype. In line with this data, miR-182 overexpression in zebrafish embryos resulted in a dose-dependent cardiac defects. miR-182 overexpression decreases the pool of cardiac progenitor cells by reducing their proliferation rate during early stages of development, affects myocardial cell morphology and ventricular muscle fiber at 48 hpf. By digital droplet PCR analysis we observed that miR-182 overexpression determines the downregulation of some calcium channel genes which were putative miR-182 targets. In *Tg(myl7:gCaMP)* zebrafish line the miR-182 overexpression caused an alteration of calcium wave across the heart suggesting an impact of miRNA activity on calcium handling. Both transient and stable overexpression of miR-182 caused events of strong arrhythmias and a reduction of heart rate on the whole. Finally, the downregulation of miR-182 was able to partially rescue HOS phenotype in zebrafish Tbx5 knockdown embryos and in Tbx5 mutants.

Conclusion: Our approach further support the importance of microRNA regulation in HOS pathology and demonstrate that miR-182 is a conserved Tbx5 effector with implications both in heart development and functions.

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Understanding the poor angiogenic capacity of the mammalian heart

T. Kocijan[a], A. Cappelletto[a], M. Rehman[a], Y.Q. Tang[a], S. Vodret[a], L. Zentilin[b], M. Giacca[b], S. Zacchigna[a]
[a]*Cardiovascular Biology Laboratory, International Centre for Genetic Engineering and Biotechnology, Trieste, Italy*
[b]*Molecular Medicine Laboratory, International Centre for Genetic Engineering and Biotechnology, Trieste, Italy*

Objective: The reason why a hypoxic tumor forms its own vasculature, mainly through the secretion of the Vascular Endothelial