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Neuregulin belongs to the EGF family members and binds to tyrosine kinase receptors ErbB3 and ErbB4, which in turn, heterodimerize preferently with the orphan receptor ErbB2. Initially, neuregulin was described as a local factor released by multiple tissues to promote their differentiation, but also involved in contraction-related events that allows the muscle to increase glucose uptake in order to fulfill its energetic requirements.
Lately, it has been described that neuregulin is an endocrine factor released by adipose tissue, more extensively by brown adipocytes, impacting on liver metabolism by reducing its lipogenic activity, and therefore, diminishing the risk to develop hepatic steatosis. In the mice, when administering intraperitoneally a recombinant bioactive neuregulin fragment, the EGF-domain, it was observed that it acutely improved the glucose tolerance by decreasing hepatic glucose output, reducing gluconeogenesis and increasing glucose utilization, in an insulin independent manner. Moreover, when blocking hepatic ErbB3 receptors with specific antibodies, neuregulin effect on glucose tolerance was reversed. Interestingly, *in vivo* effect of neuregulin on glucose tolerance was deeper in insulin resistance according to studies in obese and diabetic rodent models. In obese and diabetic ZDF rats, neuregulin accentuated lactacidemia by increasing liver, but not muscle, lactate production, what ran in parallel with an increase in the hepatic fructose-2,6-bisphosphate content, the main inducer of glycolysis in the liver. Intriguingly, diabetic rodents have a decrease in liver neuregulin receptors that could be, somehow, compensated by an increase in the hepatic neuregulin production. Whereas skeletal muscle appears unaffected under systemic neuregulin action, it is unknown whether these adipokines may impact on the hypothalamic sensors of the basal energetic status, as well as on the own adipose metabolism. Future studies will have to determine the physiological role of neuregulin in the endocrine system that regulates glucose homeostasis.

P18-2

Gills glutathione metabolism allows detecting the segregation of *Petromyzon marinus* L. populations from the Lima and Vouga river basins of Portugal

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The *Petromyzon marinus* L. migration from the fresh water to the sea may trigger metabolic alterations in gills that modify its redox environment and its ability to remove xenobiotics by glutathione *S*-transferases (GST). Thus, the success of the trophic migration of this anadromous species may depend on functional expression of the gills conjugation enzymes which are modulated by chemicals of environmental circulation, present in their habitat during salinity acclimatization. Thus, the main purpose of this work was to evaluate, in detail, the response in tanks to the 0-35 salinity gradient, by oxidative stress markers and glutathione conjugation enzymes of gills of *P. marinus* juveniles, caught in the Lima and Vouga basins of Portugal, at the beginning of the trophic migration phase. Sampled juveniles were transported to the laboratory with LSS life-support system and subjected, for 28 days, to a gradual and increasing scale of salinity between 0 and 35. The content of glutathione and malonaldehyde was determined by fluorimetry and the mGST and cGST activities by UV/Vis spectrophotometry. Stats analysis include ANOVA I and Duncan test. The results showed that acclimation to salinity 35 did not affect the mGST and cGST activities of gills of the sea lamprey juveniles of both basins, differing of that detected only at salinity 35 for GSH+GSSG and GSSG contents.
The animals of the Lima and Vouga river basins were segregated in terms of mGST and cGST activities, higher in the Vouga juveniles, as well as by glutathione content and GSH/GSSG ratio, higher in the Lima individuals, a condition that suggest the influence of specific environmental factors of each basin on glutathione metabolism.

P18m-3

Glycogen metabolism is regulated through phosphorylation and inactivation of Glycogen Synthase Muscular Isoform (MGS) by Dual-specificity Tyrosine Phosphorylation-regulated Kinase Class I

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Glycogen is a multibranched polysaccharide of glucose that serves as a form of energy storage in various cell types. Among the mechanisms that regulate its synthesis are the changes of the phosphorylation state of Glycogen Synthase (GS). Muscular isoform of GS (MGS) is inactivated by phosphorylation, where site 3a is the most important (Ser640) and susceptible to be phosphorylated by different kinases. Glycogen levels in different tumour and cancer cells are negatively correlated with proliferation rates, suggesting that glycogen is consumed for sustaining cancer's growth and survival. DYRK family of kinases are proteins that phosphorylate their substrates in serine and threonine residues. There is *in vitro* evidence which suggests that DYRK1A, DYRK1B and DYRK2 phosphorylate site 3a of MGS, which could represent a novel regulation mechanism of glycogen synthesis. To determine whether DYRK1A/1B play a role in the regulation of glycogen metabolism in cancer cells, HeLa cell line was used as a study model. Using confocal microscopy, partial co-localization of DYRK1A with MGS was observed in cytoplasm. The interactions of DYRK1A and DYRK1B were further confirmed with co-inmunoprecipitación assays. The physiological relevance was assessed using INDY or harmine, specific inhibitors of DYRK1A/1B to evaluate both the phosphorylation state of MGS in site 3a using Western blot analyses and glycogen levels using an amyloglucosidase-based assay. Together, these results suggest that the inactivation of MGS by DYRK1A is an alternative pathway for MGS regulation in these cells.

P18-4

Malignancy impact on the melanocyte lipid barcode

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Current evidence suggests that lipid composition and metabolism are modified in cancer. Our hypothesis is that such alterations may drive the malignant transformation of melanocytes to melanoma. The aim of this work was to identify and compare the lipidome of melanoma, nevus and non-pathological melanocytes, in order to find out new tools that, broadening the knowledge of melanocyte malignant transformation, may help in the diagnosis and prognosis of melanoma. Using two different methodologies, we analyzed the lipotype of 27 primary and established cell lines: 3 skin melanocytes, 9 melanocytes isolated from nevi, 6 primary melanomas and 9 metastatic melanomas. We first obtained lipid extracts