The Poster Awards of the 54th ICBL: "Linking transcription to physiology in lipidomics"

During the gala dinner at the Nicolaus Hotel Roof Garden the traditional Poster Award winners were announced. Members of the 2013 Poster Award Jury were: Laszlo Vigh (chairman), Hungary, Makoto Ito (Japan), Norma Sterin-Speziale (Argentina), Christian Wolfrum (Zurich), Donatella Caruso (Italy), Emma De Fabiani (Italy) and Chiara Degirolamo (Italy). From about 75 posters, 36 were eligible as finalists by the Poster Award Jury. The pre-selected posters were more closely inspected by all members of the Poster Award Jury during the Conference poster sessions. Criteria for selecting the top posters were the relevance of the topic, originality of the subject, the quality of the presentation, the visual appearance, and discussions with the presenter. In this year's two Poster Award presentations were sponsored by Progress in Lipid Research. The abstracts of the two winning posters are shown below. The ICBL community is proud of the high quality of the posters presented at the Bari meeting and congratulates the winners.

Laszlo Vigh, Vice President of ICBL

The winners of the 2013 ICBL Poster Awards were: Erika Fiorino (Università degli Studi di Milano, Milano, Italy) and Katarzyna Malenczyk (Nencki Institute of Experimental Biology, Warsaw, Poland)

Progress in Lipid Research Poster Awards

HISTONE DEACETYLASES REGULATE CHOLESTEROL 7a-HYDROXYLASE AND HEPATIC LIPID METABOLISM

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Cholesterol 7a-hydroxylase (CYP7A1) is the major check-point of bile acid (BA) synthesis, quantitatively the most important route of cholesterol disposal in mammals. BA returning to the liver repress CYP7A1 expression. We showed that BA induce the sequential recruitment of HDAC7, 3, 1 and of the corepressor SMRTα on the CYP7A1 promoter. Previous results showed that non-selective HDAC inhibitors increase CYP7A1 expression in vitro and in vivo by preventing the negative feedback exerted by BA and reduce serum cholesterol in mice. Based on these seminal findings, our aim was to define the role of specific HDACs and corepressors in the regulation of CYP7A1. To this end, we tested class selective HDAC inhibitors in vitro and in vivo. By using a human reporter cell line containing CYP7A1 promoter upstream of luciferase gene, we demonstrated that the class I selective HDAC inhibitor MS275 prevented the repressive effect of BA on CYP7A1. In addition, MS275 increased liver Cyp7a1 expression in C57Bl/6J
mice. To unravel the role of specific HDACs and corepressors we cloned shRNA against Hdac1, 3, 4, 5, 7 and Smrt in adenovectors and we tested them in primary hepatocytes. Hdac1, 7 and Smrt silencing significantly increased Cyp7a1 transcription, highlighting their involvement in the regulation of this gene. To investigate the role of HDAC7 in vivo we generated a HDAC7 liver-specific KO mouse (H7LivKO) and observed 10% reduction of total plasma cholesterol in this mouse model. Preliminary results in H7LivKO mice on western diet showed reduction of body weight and of LDL-cholesterol, lower liver lipid accumulation and liver size compared to wild type mice suggesting a role of HDAC7 on hepatic cholesterol and lipid metabolism. Collectively, our results show that specific HDACs affect CYP7A1 transcription and underscore their role in the regulation of BA and lipid homeostasis.

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CB1 CANNABINOID RECEPTOR ACTIVATION LEADS TO FOCAL ADHESION KINASE-DEPENDENT CYTOSKELETAL REMODELING IN PANCREATIC BETA-CELLS AND INDUCES INSULIN RELEASE

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The pancreatic β cells exhibit remarkable abilities to change their function in response to altered tissue insulin demands. The increasing body of evidence suggests important role of lipid neuromodulators, endocannabinoids (eCBs) in regulation of this process. However, the molecular cascade coupling agonist-induced cannabinoid receptor activation to insulin release remains unknown. In the present study we aim to elucidate the role and mechanism of eCBs’ action on insulin secretion. We combine molecular pharmacology and genetic tools carrying the experiments out in INS-1E β cell line and pancreatic islet isolated from wild type and cannabinoid receptor 1 (CB1R) knockout mice. RT-PCR, western blot analysis, immunochemistry and insulin secretion measurements are used to investigate presence, role and mechanism linking eCBs signaling to insulin release. Both β cells and pancreatic islets exhibit functional and autonomous eCBs signaling (receptors and enzymatic machinery tuning anandamine (AEA) and 2-arachidonoylglycerol (2-AG) bioavailability). We show that AEA and 2-AG potentiate insulin secretion. Observed eCBs’ effect depends on CB1R activation since it is absent in the pancreatic islets isolated from CB1R-/- mice and impeded only when its antagonist (O-2050) or reverse agonist (AM251) are applied. CB1R stimulation leads to activation of Akt and extracellular signal-regulated kinases 1/2 and further phosphorylation of focal adhesion kinase (FAK). CB1R-mediated FAK activation induces the formation of focal adhesion plaques and stress fibers, facilitating the second-phase of insulin release. We show that inhibition of endocannabinoid synthesis of FAK activity foreclose insulin release. The obtained results show FAK downstream from CB1Rs mediates eCBs-induced insulin release by allowing cytoskeletal reorganization that required for the exocytosis of secretory vesicles.
