in total preproglucagon expression. Interestingly, the L-cells were found evenly distributed throughout the proximal and distal part of the jejunoileum and colon, in correlation to a similar marked hypertrophy of the epithelial mucosa. The gut volumes demonstrated a marked (250%) increase in mucosa volume as well as in total epithelial surface area.

Discussion: We show high plasticity of the gut in animal models of T2D. More importantly, and in contrast to the general opinion, GLP-1 releasing L-cells are shown numerous in both the proximal and distal part of the gut.

doi:10.1016/j.regpep.2012.05.038

Liraglutide and linagliptin improve glycemic control but show differential anti-obesity and hypolipidemic efficacy in a novel hamster model of diet-induced obesity and hypercholesterolemia

H.B. Hansen, G. Hansen, P.J. Pedersen, F. Hansen, J. Jelsing, N. Vrang
Gubra aps, Agern Allé 1, DK-2970 Hørsholm, Denmark

Introduction: The Golden Syrian hamster has unique features that make it a suitable animal model to study lipoproteins, atherosclerosis and evaluate hypolipidemic agents. Unlike mice and rats, hamsters fed a high-fat diet with cholesterol supplementation quickly develop hyperlipidemia and hypercholesterolemia, thus showing closer similarity to human lipoprotein metabolism.

Aims: We developed a novel hamster model of diet-induced obesity (DIO) and subsequently evaluated the anti-obesity, insulin sensitizing and hypolipidemic efficacy of the glucagon-like peptide-1 (GLP-1) analog liraglutide and DPP-IV inhibitor linagliptin, respectively.

Methods and results: Hamsters fed a high fat-high carbohydrate diet with cholesterol supplementation for 12 weeks developed an obese phenotype with impaired oral glucose tolerance and significantly elevated baseline levels of insulin, triglycerides, total cholesterol, LDL and HDL cholesterol. Pancreatic and atherogenetic markers are currently being evaluated. Chronic treatment with liraglutide (0.2 mg/kg, b.i.d, s.c., 4 weeks) normalized the body weight of the DIO hamster and also reflected a complete reversal of whole-body fat mass gain. Moreover, liraglutide significantly reduced plasma triglyceride and cholesterol levels. Both liraglutide and linagliptin (3.0 mg/kg, q.d., p.o, 4 weeks) fully normalized glucose tolerance in the DIO hamster.

Discussion: Hence, in addition to improved glycemic control upon liraglutide and linagliptin treatment, liraglutide also showed robust anti-obesity and cholesterol-lowering effects in the DIO hamster, which supports the view that chronic GLP-1 receptor agonism may also lower cholesterol-associated cardiovascular risk factors in diabetes and obesity. The present DIO hamster model is particularly useful for preclinical evaluation of novel anti-obesity, lipid modulating and insulin sensitizing agents.

doi:10.1016/j.regpep.2012.05.039

Change in Chromogranin A correlates with computed tomography imaging in pancreatic neuroendocrine tumors

K.H. Jensen[a,d], L. Hilsted[b], J.F.B. Andersen[c], T. Mynster[a,e], U. Knigge[a]
[a]*Department of Surgery C, Neuroendocrine Tumor Center of Excellence, Rigshospitalet, Denmark*
[b]*Department of Clinical Biochemistry, Neuroendocrine Tumor Center of Excellence, Rigshospitalet, Denmark*
[c]*Department of Radiology, Neuroendocrine Tumor Center of Excellence, Rigshospitalet, Denmark*
[d]*Department of Surgery, Region Sjælland, Slagelse Hospital, Faculty of Health Sciences, University of Copenhagen, Denmark*
[e]*Department of Surgery K, Bispebjerg Hospital, Faculty of Health Sciences, University of Copenhagen, Denmark*

Introduction: In addition to being an excellent marker for NET and tumor volume, plasma CgA is suggested as the most reliable marker in follow-up of patients with some types of NET. However, only few studies have been published on this issue.

Aim: We investigated the diagnostic accuracy of plasma CgA as a predictor for progression, regression or stable disease compared to changes on CT scan.

Methods: 76 patients with CgA positive pancreatic neuroendocrine tumors (NET) were included in the study. Each patient was evaluated by events. An event was recorded when a CT scan was followed by another corresponding scan. Change in tumor burden was defined as regression, progression or stable disease using RECIST criteria 1.1. There were 305 events: 46 progressions, 195 stable diseases and 65 regressions. Based on ROC curves a cut-off value of 25% change was selected as the discriminatory value for testing the power of neutral, increase and decrease in plasma CgA, using a radioimmunoassay specific for the hCgA(340–348) sequence.

Results: In the 46 events showing progression the diagnostic sensitivity and specificity of an increase in plasma CgA were 77% and 87%, respectively. The positive and negative predictive values were 61% and 93%, respectively. In the 195 events showing stable disease the diagnostic sensitivity and specificity of an unchanged plasma CgA were 71% and 80%, respectively. The positive and negative predictive values were 86% and 61%. In the 65 events showing regression the diagnostic sensitivity and specificity of a decrease in plasma CgA were 76% and 89%, respectively. The positive and negative predictive values were 56% and 95%, respectively.

Discussion: In conclusion, with this RIA, plasma CgA has a high diagnostic accuracy in monitoring patients with pancreatic NET. In particular an increase in plasma CgA was very useful in predicting tumor progression.

doi:10.1016/j.regpep.2012.05.040

Glucagon like peptide-2 (GLP-2) differentiated the intestinal proteome of pigs with short bowel syndrome

P. Jiang[a], A. Vegge[b], J.M. Wan[a], T. Thymann[b], P.T. Sangild[b]
[a]*School of Biological Sciences, The University of Hong Kong, SAR, China*
[b]*Department of Human Nutrition, Faculty of Science, University of Copenhagen, Denmark*

Introduction: Intestinal adaption occurs in response to intestinal resection in patients with short bowel syndrome (SBS). Part of this adaptation may depend on local release of glucagon-like peptide 2 (GLP-2) from the distal small intestine and colon. The molecular mechanisms facilitating intestinal adaptation, with and without GLP-2, remain poorly understood.

Aim: We investigated the total intestinal proteome in the remnant intestine of newborn pigs subjected to distal intestinal resection with and without GLP-2 supplementation (SBS + GLP-2, SBS; $n = 6$) and compared this with the proteome in un-operated controls (control, $n = 6$).

Methods: Six days after resection, intestinal tissue was subjected to proteomic expression profiling by 2 DE-gel electrophoresis and identification of differentially regulated proteins by MALDI-TOF-TOF/MS.

Results: GLP-2 induced a significant increase in weight of the remnant intestine in SBS piglets (+70%, $p<0.05$). In total, 45 proteins differed in expression among the SBS + GLP-2, SBS and control pigs ($p<0.05$). The biological functions of the identified protein covered cell proliferation, protein synthesis, processing and degradation, stress response, anti-oxidation, metabolism of carbohydrates, energy