(STZ+RS, n = 6), 2) recurrent hypoglycemia (STZ+RH, n = 7), and 3) recurrent hypoglycemia + metoclopramide (STZ+RH+MET, 3 mg/kg IP, n = 7). After 3 days, all rats underwent a hyperinsulinemic (50 mU/kg/min) and hypoglycemic (~45 mg/dl) clamp. In the clinical trial, adults with Type 1 diabetes (age 20–60, ≥5 years duration) were enrolled in a phase II, double-blinded, placebo-controlled trial. Awareness status was assessed via Gold score, and subjects maintained drug regimens and underwent two hyperinsulinemic-hypoglycemic clamps (where blood glucose was lowered to 100, 65, 55, and 45 mg/dl) to assess counterregulation. RESULTS/ANTICIPATED RESULTS: In the pre-clinical model, glucose infusion rates (GIR) to maintain hypoglycemia were higher in STZ+RH (27±0.9 mg/kg/min) than STZ+RS (19±0.8 mg/kg/min, p DISCUSSION/SIGNIFICANCE OF IMPACT: Metoclopramide improves glucoregulatory, sympathoadrenal, and counterregulatory responses to hypoglycemia in pre-clinical models, suggesting dopaminergic regulation. While clinical data are still blinded, increased epinephrine and growth hormone responses suggest treatment may preserve or restore counterregulation.

423

Peritoneal lesion and peri-metastatic rim classification using machine learning and image processing*

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OBJECTIVES/GOALS: The goal of this study is to investigate the peri-metastatic rims of peritoneal lesions to determine features that predict malignancy using both imaging processing techniques and machine learning. This information will subsequently be added to our existing knowledge of peritoneal lesions to improve classification accuracy as benign or malignant. METHODS/STUDY POPULATION: The study population consists of 521 imaged lesions from 163 subjects with cancers of GI-origin with biopsy results as well as the clinical subject information and follow up. All images were obtained during staging laparoscopy by the senior author (TS). On the images, the central lesion as well as the surrounding peri-metastatic rim will be segmented as regions of interest (ROIs). Image processing will be used to calculate a variety of metrics for these two regions. A general estimating equation approach will be used to determine significance of these metrics compared to the dependent outcome of malignancy determined on the pathology report as the ground truth. These ROIs and significant metrics will then be used to improve the accuracy of a machine learning model to classify these lesions as benign or malignant. RESULTS/ANTICIPATED RESULTS: Our previous research showed that experts performed this task at only a 52% accuracy rate (classifying lesions as malignant or benign based on imaging). A previous machine-learning model on a much smaller dataset was able to achieve by contrast an area under the curve of 0.78. We anticipate that by including a larger dataset in addition to including the peri-metastatic rim, we will be able to improve the accuracy of the the model in this task while uncovering significant biomarkers as well that can be used in future studies. DISCUSSION/SIGNIFICANCE OF IMPACT: Classifying peritoneal lesions determines the correct treatment for cancer patients whether chemo-radiation, definitive surgery or palliative surgery. This project aims to develop an improved model that can perform this task using nonlabeled laparoscopic imaging with a particular focus on the diagnostic value of the peri-metastatic rim.

424

Liraglutide protects against microvascular dysfunction and sepsis-mediated inflammation and organ injury

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OBJECTIVES/GOALS: • To determine the impact of liraglutide on inflammation and organ injury during sepsis. • To investigate the protective effects of liraglutide on microvascular dysfunction in a clinically relevant model of sepsis. • To provide evidence for the potential therapeutic use of GLP-1 receptor agonists in endothelial dysfunction in sepsis. METHODS/STUDY POPULATION: Sepsis was induced in mice (N = 34) by intraperitoneal injection of cecal contents (1.8 mg/g body weight) and 24-hour hyperoxia (FiO2 90–95%). Mice received saline or liraglutide (0.1 mg/kg) at 6 and 18 hours post-injection and fluids and antibiotics at 12 hours. At 24 hours, mice were euthanized for plasma, bronchoalveolar lavage (BAL), and tissue collection. Plasma inflammatory markers, organ injury markers, and BAL components were measured. In vitro, primary human lung microvascular endothelial cells (HLMVECs) were treated with saline or liraglutide for 24 hours before exposure to saline or LPS (100 ng/mL). HLMVEC barrier dysfunction was evaluated using express permeability testing (XPerT) and electric cell-substrate impedance sensing (ECIS) to measure transendothelial electrical resistance (TER). RESULTS/ANTICIPATED RESULTS: In murine sepsis, illness severity scores and lung injury were improved in mice pretreated with liraglutide (N = 10). Plasma blood urea nitrogen (BUN; P = 0.0036), alanine transaminase (ALT; P = 0.0311) and vascular inflammatory markers MCP-1 (P = 0.0172), ICAM-1 (P = 0.0356), and Pecam-1 (P = 0.0493) in plasma were reduced in mice treated with liraglutide. In HLMVECs, liraglutide (1.5 nM) significantly reduced LPS-induced barrier dysfunction measured by XPerT assay (P = 0.0030) and ECIS (P = 0.0075). DISCUSSION/SIGNIFICANCE OF IMPACT: Liraglutide reduces illness severity, vascular inflammation, and organ injury in a two-hit model of sepsis. Liraglutide has direct effects in the microvascular endothelium, limiting LPS-mediated barrier dysfunction. These findings support a protective role for GLP-1 receptor agonism in sepsis, mediated through the microvasculature.

425

Elucidating structure–function relationships driving immune aging in lymph nodes

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OBJECTIVES/GOALS: The aging population faces unique health issues, many of which are exacerbated by aging-associated immune function decline. However, the driving mechanisms behind this decline are poorly understood. We use a mouse model to study the relationship between extracellular matrix (ECM) stiffness and cell mobility within the lymph node (LN) as one potential driving mechanism. METHODS/STUDY POPULATION: We will collect

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