Hexokinase and insulin expression patterns in canine insulinomas

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Canine insulinoma is an insulin-secreting endocrine tumor of pancreatic islet beta cells that causes hyperinsulinemia and hypoglycemia. Little is known about the pattern of insulin expression in canine insulinoma and the cellular mechanisms that lead to excess insulin production. Human insulinomas have lower insulin content than normal islets but secrete a larger proportion of insulin. Previously, we found increased glucokinase:hexokinase 1 (GCK:HKI) ratio in canine insulinoma compared with normal pancreas, suggesting aberrant HK1 expression or GCK overexpression as possible causes for abnormal glucose sensing and hyperinsulinemia. This study aimed to 1) compare the colocalization of GCK and HKI with insulin using immunofluorescence (IF) microscopy and 2) determine the total distribution of insulin through immunohistochemical (IHC) analysis of normal versus neoplastic islet cells. Sixteen insulinomas from an archived tissue bank were studied. IF was completed with a polyclonal guinea pig anti-swine insulin primary antibody (ab) with a goat anti-rabbit 568 nm secondary ab and dual stained with either GCK (G-6) or HKI (G1) primary abs with a goat anti-mouse 647nm secondary ab and imaged by confocal microscopy. IHC slides were prepared by the Veterinary Diagnostic Lab Histology Lab and insulin expression quantitated using HALO image analysis software. Data analysis will examine 1) colocalization of GCK or HK1 with insulin in tumor cells through confocal imaging and 2) to perform morphometric analysis of insulin quantity and distribution in insulinoma cells and normal pancreatic islets.

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