CD36/Thrombospondin (THBS2) signaling Axis and Neuroendocrine Neoplasms

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Background: CD36 is a transmembrane receptor for the glycoprotein thrombospondin 2 (THSB2) and influences cell-to-cell and cell-to-matrix interactions linked to cancer. Currently the impact and mechanisms for CD36 and THSB2 in neuroendocrine cancer is unknown. Preliminary proteomic studies by our group identified TSHB2 as a potential biomarker and/or target for intervention. The purpose of this study was to build on this initial finding and investigate the involvement of CD36/TSHB2 axis in neuroendocrine cancers by quantifying THSB2 and CD36 in liquid biopsies collected and stored within our dedicated biorepository. **Methods:** Plasma collected from 1) patients with NETs prior to surgery (n=18) and 2) living renal donors (controls) prior to surgery (N=6) were quantified for TSB2 by commercially available ELISA. Peripheral blood mononuclear (PBMC) cells collected from, 1) patients with progressing NET tumors prior to Protein Receptor Radionucleotide Therapy (PRRT) (N=10), and 2) living renal donors (controls) prior to surgery (N=6) were quantified for CD36 expression by flow cytometry. **Results:** TSB2 protein levels in plasma from patients with NET tumors were significantly lower (10.3±2.5pg/ml) when compared to controls (68.2±35pg/ml)($p=0.003$)($p<0.01$). In contrast, CD36 expression levels in circulating lymphocytes was significantly higher in NET patients (25%), when compared to controls (1%)($p<0.01$). **Conclusion:** Reduced TSP2 levels is consistent with literature showing that 1) loss of TSP2 is associated with increased angiogenesis, and 2) long-term gene therapy, to increase THSP2, inhibits angiogenesis. Moreover, increased CD36 levels in circulating lymphocytes correlates with reduced rate of receptor removal from the cell surface in response to lower ligand concentrations. Increased lymphocyte CD36 is potentially detrimental to NET patients as CD36 is also a receptor for lipids that are known stimulate tumor growth.