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Stratification of neuroendocrine tumors for ecto-5-nucleotidase expression for clinical trials

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BACKGROUND

The recent development of small molecules inhibitors and neutralizing antibodies targeted against the enzyme ecto-5-nucleotidase (NT5E) is potentially applicable to the treatment of neuroendocrine neoplasms (NEN). NT5E is known to convert AMP to adenosine. Increased levels of NT5E are linked to worse outcomes in lung, pancreas, and stomach cancer. Phase 2 clinical trials for NT5E inhibitors are currently ongoing for the treatment of gastrointestinal cancers. We have previously quantified circulating levels of adenosine, AMP and NT5E levels in NEN patients and reported significant differences between patients with NEN tumors and control non cancer patients. The purpose of this study was to quantify NT5E levels in NEN tumors directly, determine cohort variations, and demonstrate patient/tumor specific screening for clinical trials.

METHODS

The Louisiana State University Health Science Center – New Orleans Neuroendocrine Cancer tissue repository was queried for unfixed cryopreserved 1) primary small bowel NEN tumors (N=30), 2) matched small bowel primary and liver metastatic NEN tumors (N=9), and 3) normal small bowel tissue (N=10). Available tumors and normal tissues were homogenized and quantified for NT5E by commercial ELISA.

RESULTS

NT5E levels were significantly higher in G2 and G3 primary small bowel NEN tumors ($p<0.01$) but not in G1 tumors ($p=0.41$) when compared to normal small bowel tissue. In contrast, liver NEN metastaic tumors NT5E levels did not increase with grade and were significantly lower when compared to matched G2 and G3 small bowel primary tumors.

CONCLUSIONS

NT5E expression levels correlated with primary NEN tumor grade but not metastatic liver grade. This observation corolates with literature proporting NT5E role in cancer progression and metastasis. Consequently, NT5E small molecule inhibitors or NT5E neutralizing antibodies have the potential to benefit patients with moderate and high-grade primary tumors by targeting metastatic growth.

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