B-8

Development of a Real-time Luminescent Sensor for Detecting Serotonin Levels in Neuroendocrine Tumors

Dane Tow, Deeraj Manika, Courtney A. Kaemmer, Michael Henry, Dawn Quelle, James Howe, Po Hien Ear
University of Iowa Carver College of Medicine, Iowa City, IA

BACKGROUND: Small bowel neuroendocrine tumors (SBNETs) are one of the most commonly occurring neuroendocrine tumors (NETs) that originate from transformed enterochromaffin cells. SBNETs are considered as rare cancers but the incidence is rapidly rising. Current standard of care drugs have limited efficacy at controlling tumor progression. Patients with SBNET metastases experience poor quality of life due to excess production of serotonin secreted by SBNET cells causing them to experience frequent diarrhea, flushing, and cause carcinoid heart valve fibrosis. There are critical needs to identify new medical therapies for treating SBNET progression and symptoms. Yet, research in serotonin regulation has been challenging because serotonin is very difficult to measure and highly sophisticated methodology based on mass spectrometry is required.

METHODS: Our goal is to develop an alternative strategy for measuring serotonin level in NETs in real-time. We developed various Serotonin-Luciferase Sensors (iSero-Luc) using the Renilla Luciferase and Firefly Luciferase as reporter proteins. The activity of the iSero-Luc sensors was characterized in the presence or absence of exogenous serotonin addition and with telotristat treatment.

RESULTS: We have engineered and characterized the activity of various serotonin sensors based on the Renilla Luciferase and Firefly Luciferase as reporter proteins in cell-based assays. Current effort is to evaluate the activity of this sensor in a xenograft model and use it for identification of new drugs targeting serotonin pathway in real-time or use as a diagnostic tool for detecting SBNETs.

CONCLUSION: SBNETs specifically express high levels of serotonin which is responsible for causing carcinoid syndrome in patients. Here, we report on

the development of novel serotonin sensors that allow the measurement of serotonin in live cells in real-time. This novel tool can potentially be used as a biomarker for tumor progression and serve as an imaging platform for assessing serotonin levels in vivo.

ABSTRACT ID: 179