B-8

Novel Mouse Models of Pancreatic Neuroendocrine Tumor Metastasis

Courtney Kaemmer[1]; Umesalma Shaik[1]; Chandra Kumar Maharjan[1]; Devon Moose[1]; Goutham Narla[2]; Benjamin Darbro[1]; Andrew Bellizzi[1]; Micheal Henry[1]; Dawn Quelle[1]

[1]The University of Iowa; [2]University of Michigan

BACKGROUND: Pancreatic neuroendocrine tumors (PNETs) are rare, slow growing cancers that lack effective treatments once they become metastatic. Unfortunately, 60% of PNET patients have distant metastatic disease (mainly in the liver) at diagnosis and current therapies fail to improve overall survival. Pre-clinical models of PNET metastasis are greatly needed to advance our understanding of mechanisms driving NET metastasis and to develop/test novel therapeutic interventions.

METHODS: PNET cell lines stably expressing luciferase (BON1.luc and Qgp1.luc) were generated and transwell assays performed to measure in vitro migration. Bioluminescent cells were introduced into NSG immunodeficient mice by intravenous (IV, tail vein) or intracardiac (IC) injection. Tumor growth was monitored longitudinally on a weekly basis by non-invasive bioluminescence imaging (BLI). Animals with tumor burden exceeding 10^9 photons/sec or low body conditioning scores were euthanized, and tumor bearing tissues subjected to ex vivo BLI, histopathology and genetic analyses.

RESULTS: One hundred percent tumor incidence was achieved for both IV and IC metastasis models. Qgp1.luc cells preferentially metastasized to the liver regardless of delivery route, mimicking the predominant site of PNET metastasis observed in patients. By comparison, BON1.luc cells always formed tumors in the lung regardless of administration route and colonized a wider variety of tissues compared to Qgp1.luc, including liver but also adrenal glands, kidney and ovaries with high frequency. Pre-clinical studies evaluating drugs with predicted anti-metastatic activities are ongoing.

CONCLUSION: We successfully developed new bioluminescent mouse tumor models of PNET metastasis. Qgp1.luc cells preferentially formed tumors in the liver while BON1.luc cells displayed a broader metastatic distribution. This system represents a rapid and relatively inexpensive platform for testing candidate metastasis genes and novel PNET therapies.