Abstract A157: Metastatic PDX modeling displays correlation between CTC and metastatic potential, both inhibited by chemotherapy.

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Abstract

Gastric carcinoma is a common cancer of high mortality and is particularly prevalent in East Asia. There are only a few treatment options: surgery, chemotherapy, as well as Herceptin® for a small subset of patients with erbb2 amplification. Metastasis usually renders surgery ineffective. Drug therapy becomes only meaningful option. One of the keys to a successful search for effective treatment is development of experimental model that truly mimics patient conditions. Patient derived xenograft (PDX or HuPrime®) is believed to be among the best mimicking human diseases (1). Recently, we have established a cohort of ~70 gastric cancers from Asian and Caucasian patients. This report describes that two of them (GA0046, GA0087), while established as subcutaneous xenografts, were confirmed to metastasize to lung at high frequency (100% for GA0087). GA0087 is a neuroendocrine cancer of gastric origin. Its high metastasis potential, as measured by counting the colony nudules in lung of subcutaneous tumor bearing mice, suggests that it would be a useful experimental model for studying cancer metastasis and exploring inhibitory agents. The observed metastasis is particularly significant since metastasis is rarely occurin subcutaneous xenograft. Circulating tumor cells, or CTCs, have been identified in the blood of some cancer patients and believed to be responsible for cancer metastasis (2, 3). We recently developed a new method, based on subtraction enrichment combined with immunofluorescence staining (anti-human cytokeratin 18 and CD45 monoclonal antibodies) and FISH (iFISH), for effective identification and enumeration of CTCs enriched from bloods of patients (4). In this study, we investigated the presence of CTCs in GA0087 metastatic PDX and their potential correlation to metastastic potential. As a result, we, for the first time, detected CTCs in PDX (GA0087), with a range of 1-61 CTCs per 200µL mouse blood. Our preliminary observation seems to also indicate that the CTC frequency is correlated to the numbers of metastasis nodules in lung. Furthermore, a chemotherapy agent can inhibited both CTC and metastasis. Our data seem to confirm the proposed correlation of metastasis and CTC in this first experimental metastasis/CTC PDX model.

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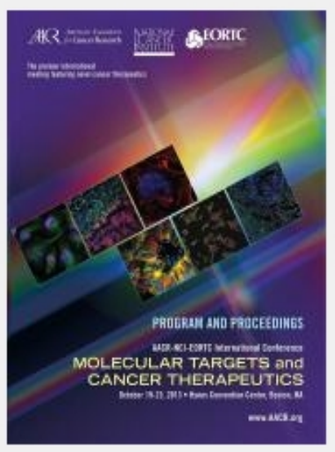

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