Ciências Básicas

(1165) - PATIENT DERIVED XENOGRAFTS OF BRAIN METASTASES: A TOOL FOR TRANSLATIONAL MEDICINE

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Objectives: Approximately 40% of patients with any given cancer will develop metastases in the brain. Despite the current available treatments, brain metastastic disease is incurable and patients have a dismal outcome. Therefore, we developed animal models of human brain metastases in order to validate novel therapies.

Methods: Patient derived xenografts (PDXs) of human brain metastases were originated from diverse primary tumors. Surgical samples were obtained from patients treated at Hospital de Santa Maria (Lisbon) and implanted in the flank of immunodeficient mice. We evaluated the tumor take rate, time to tumor formation (mean latency time), presence of metastases and ability to serially passage the tumor.

Results: Tumor tissue from 17 human brain metastases was implanted in mice. Primary tumor location was lung (n=10), bladder (n=2), colon (n=1), melanoma (n=1), breast (n=1), osteosarcoma (n=1) and pancreas (n=1). The overall take rate was 76%. The mean latency time was 37 days for lung, 55 days for bladder and 24 days for osteosarcoma brain metastases. The time for tumor growth decreased with serial passaging, suggesting a more aggressive disease phenotype. Interestingly, animals implanted with three different samples of lung brain metastases, developed spontaneous metastases in the lung, suggesting that these tumor cells maintain the ability to disseminate and to return to the primary organ. The histological and immunohistochemical comparison between the patient's tumor and the tumors engrafted, showed similar tumor morphology and staining.

Conclusion: PDXs from human brain metastases recapitulate patient's disease and can be utilized as preclinical models for drug screening.

Palavras-chave : patient derived xenografts, brain metastases, preclinical models