APRESENTAÇÃO DE PÔSTER - GENÉTICA ANIMAL E EVOLUÇÃO

GENERATION OF XENOGRAFT MODELS IN ZEBRAFISH FOR THE STUDY OF BONE TUMORS

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Children and adolescence tumors that arise from bone tissue comprise 4% to 8% of cases of pediatric cancers and present high mortality and morbidity rates. Osteosarcomas (OS) are the most prevalent bone tumors, comprising 50% of the cases. Genetics features of OS are genetics and epigenetics instability resulting in genome disorganization, aneuploidy and dysregulation of several cellular pathways. Despite advances in the survival rate of patients with OS, in the last 30 years there have been no changes in treatment and, due to the genetic complexity of this type of tumor, treatments are not always effective. The use of zebrafish as a model organism presents several advantages including the high morphological and genetic similarities with humans, the possibility of reproducing the characteristics of tumors and the possibility of carrying out drug tests on a large scale. In this work, we are going to study OS using xenotransplantation of immortalized and primary culture cells in zebrafish. The immortalized MG-63 and U-2OS cell lines derived from OS were injected into the yolk sac or into the cuvier's duct of zebrafish embryos at 2 days post fertilization (dpf) and the xenotransplanted embryos were analyzed for the next

4 days. The membranes of the injected cells were previously stained with the lipophilic dye CM-DIL to track the tumor cells in the zebrafish larvae. We observed that the cells proliferated and spread to the eyes and the caudal hematopoietic tissue regions, establishing metastatic sites in zebrafish.

Using antibodies specific for human cells, we are going to perform immunohistochemistry for Ki67 and laminin, to confirm that the fluorescence in the zebrafish corresponds to the injected cells. Then, primary OS culture cells, obtained from Boldrini's hospital tumor patients (CEP 28386820.7.0000.5376), will be injected in the zebrafish embryos to verify if they adopt the same pattern behaviors as the immortalized culture. Also, once the exome of the primary OS culture cells is sequenced, we are going to look for druggable molecular alterations and, the xenotransplanted zebrafish will be treated with the target drug in order to verify the effectiveness of this target therapy on the tumor cells behavior. These data will provide information for a better understanding about OS biology and how this tumor develops and behaves. Also, it can help in directing an individualized therapy for OS patients. The preliminary experiments demonstrated that OS-derived tumor cells can survive, proliferate and invade tissues when transplanted in zebrafish embryos.