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MAIN FIELDS OF RESEARCH; ABSTRACT

Osteosarcoma (OS) is the most common primary malignant bone tumor in children and adolescents with a high propensity for pulmonary metastasis. This is also the major cause of death in these patients. Significant clinical improvements over the past decades have led to a dramatic increase in the survival of patients with localized disease. However, patients with metastasis have a very poor prognosis. Therefore, it is vital to understand the underlying mechanisms involved with increased metastatic potential. Exosomes are small membrane extracellular vesicles (30-100nm) that mediate local and systemic cell communication through transfer of their cargo (mRNA, microRNAs and proteins). Accumulating evidence in carcinomas indicate that exosomes dictate metastasis by educating the host tissues towards a pre-metastatic phenotype. The overall goal of this project is to investigate the biological relevance of tumor-derived exosomes in OS progression and metastasis development and to explore the biology of the communication between the primary tumor and distant target organs of metastasis. We will perform isolation and comparative molecular cargo profiling of exosomes derived from established OS cell lines with differential metastatic potential. The identification of relevant factors will be achieved through next-generation sequencing, mass spectrometry or qRT-PCR. The roles of particular exosomal miRNAs or proteins will be examined through in vitro functional assays (proliferation, migration, adhesion, invasion, soft agar assays) as well as in an in vivo setting using established xenograft OS mouse models. The study will include the elucidation of exact mechanisms underlying the contribution of tumor-derived exosomes to the pre-metastatic niche establishment. Acquiring insight into the basic biology of OS progression will lead to development of effective drugs for prevention of systemic dissemination of cancer cells or to eliminate overt metastasis.

SPECIAL TECHNIQUES AND EQUIPMENT

Nanoparticle tracking analysis (NTA) – Malvern Nanosight NS300