



# Micro RNA mRNA Series Defines a Translatable Molecular Outcome Phenotype in Osteosarcoma

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## DESCRIPTION

There are no well-validated biomarkers for osteosarcoma. Osteosarcoma is a rare, intractable disease whose treatment criteria have been stagnant for decades, with variable outcomes and poorly understood biological behavior. The only standard prognostic factor for osteosarcoma is the degree of pathological necrosis after preoperative chemotherapy, which does not adequately capture the biological complexity of the tumor and provides therapeutic stratification of the patient.

New robust biomarkers are needed to better understand the prognosis and better reflect the biological and molecular complexity underlying the disease.

Osteosarcoma is a primary malignant bone disease that is most common in adolescents and young adults. It peaks in late adulthood. During chemotherapy with a standard regimen of cisplatin / doxorubicin / methotrexate Combined with surgical resection (known as MAP), the prognosis of patients with localized tumors is significantly improved, with up to 40-50% of patients relapsed and eventually succumb to the disease and patients with metastatic disease. The prognosis is even worse. There have been no advances in new therapies in the last 30 years, and the progression of this disease is hampered by the lack of well-validated biomarkers that may promote patient stratification to new therapies. Pathological necrosis in response to neoadjuvant chemotherapy is prognostic but does not fully correlate with the outcome of a subset of patients with suboptimal responses. In addition, it is semi-quantitative and can only be evaluated by an experienced pathologist after several cycles of chemotherapy have been administered. Recent large-scale international randomized studies using pathological necrosis to stratify patients to add ifosfamide / etoposide or interferon to adjuvant therapy are currently available with the need for new therapies. The benefits of survival could not be demonstrated, reflecting both prognostic / stratified marker limitations. This leads to increased interest in molecular outcome markers. In this regard, miRNAs have recently received attention due to their recognized regulatory role in many downstream genes in cancer. Our group previously published pilot results suggesting that microRNAs are useful for stratifying the prognosis of osteosarcoma.

Osteosarcoma (OS) is the most common primary bone tumor in adolescents and young adults. The 5-year survival rate has been constant for the past 40 years, 70% in patients without metastases,

but only 30-40% in patients with recurrence and metastases. The effectiveness of traditional chemotherapy has not improved over the last few decades and new targeted and immunotherapies are of little expectation for successful OS treatment. This OS treatment dilemma requires further molecular investigation to elucidate the etiology and mechanism of progression of OS. This has the potential to enable the design of potential drugs.

Tumor Micro Environment (TME) plays an important role in the initiation and development of OS. Due to the mixture of cancer cells and their stroma, the characteristics of TME are abnormal, and normalizing TME enhances the effectiveness of cancer chemotherapy and immunotherapy. Therefore, investigating the key factors of TME in OS may reveal potential therapeutic targets.

## OSTEOSARCOMA

Osteosarcoma (osteosarcoma) is a type of cancer that begins in the bone. At first, cancer cells look like normal bone cells. Then they create tumors, which create immature and irregularly ill bones. This is most common in teens, with a median age at diagnosis of osteosarcoma of 15 years.

“Sarcoma” is a type of cancer that begins in connective tissues such as bone, cartilage, and muscle. “Osteo” refers to bone.

Osteosarcoma is most common in long bones such as the arms and legs. This usually occurs near the end of the bone (metaphysis) and near the knee. It grows fastest near the knees (for teens). The most commonly affected bones and areas include:

Femur near the knee (femur). Tibia near the knee (tibia). Humerus near the shoulder (humerus). It is rarely found in soft tissues and organs in the abdomen and chest. Other less common sites of osteosarcoma are: pelvis, skull and chin.

## TYPES

- Osteoblastic
- Chondroblastic
- Fibroblastic
- Small cell
- Telangiectatic

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