Mimicking breast cancer-induced bone metastasis in vivo: current transplantation models and advanced humanized strategies.

Bone metastasis is a complication that occurs in 80 % of women with advanced breast cancer. Despite the prevalence of bone metastatic disease, the avenues for its clinical management are still restricted to palliative treatment options. In fact, the underlying mechanisms of breast cancer osteotropism have not yet been fully elucidated due to a lack of suitable in vivo models that are able to recapitulate the human disease. In this work, we review the current transplantation-based models to investigate breast cancer-induced bone metastasis and delineate the strengths and limitations of the use of different grafting techniques, tissue sources, and hosts. We further show that humanized xenograft models incorporating human cells or tissue grafts at the primary tumor site or the metastatic site mimic more closely the human disease. Tissue-engineered constructs are emerging as a reproducible alternative to recapitulate functional humanized tissues in these murine models. The development of advanced humanized animal models may provide better platforms to investigate the mutual interactions between human cancer cells and their microenvironment and ultimately improve the translation of preclinical drug trials to the clinic.