City University of Hong Kong
Department of Biomedical Sciences
presents a seminar

"Missing Links between Stem Cell Differentiation and Tumorigenesis"

by

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Time: 11.00am to 12.30pm
Venue: Meeting room 2-130, 1/F, Block 2, To Yuen Building, CityU

Abstract

Mesenchymal stem cells (MSCs) are non-hematopoietic stem cells with the capacity to differentiate into tissues of both mesenchymal and non-mesenchymal origins. MSCs can differentiate into osteoblastic, chondrogenic, and adipogenic lineages although recent studies have demonstrated that MSCs are also able to differentiate into other lineages, including neuronal and cardiomyogenic lineages. Since their original isolation from the bone marrow, MSCs have been successfully harvested from many other tissues. While the detailed mechanisms governed MSC lineage-specific commitment and the eventual terminal differentiation remain to be fully understood, it is well recognized that MSC proliferation and differentiation is tightly regulated. Dysregulations of the growth differentiation process may lead to the development of mesenchymal tumors, mostly called sarcomas such as osteosarcoma (OS). OS is the most frequent primary bone sarcoma and is the most common non-hematologic malignant tumor of bone in children and adults. Most OS tumors are of high grade and tend to develop pulmonary metastases with a poor prognosis. OS tumors typically arise around the growth plate of long bones. The unifying histologic features present in all types and subtypes of OS is the presence of malignant osteoid produced by neoplastic cells. While the pathogenesis of OS is poorly understood, emerging evidence suggests that disruption of osteoblast terminal differentiation may lead to OS development. We demonstrated that osteogenic BMPs regulate a distinct set of target genes during osteogenic differentiation, many of which are involved progenitor expansion and highly expressed in tumor cells. We subsequently found that, unlike normal osteoblastic progenitors or MSCs, OS cells are refractory to osteogenic BMP-induced osteogenic differentiation, and that OS tumors grow much faster upon BMP stimulation, suggesting that OS may be regarded as a differentiation disease caused by genetic and epigenetic interruptions in osteoblast differentiation from MSCs. Based on this knowledge, we have recently embarked a genome-wide screening for regulatory noncoding RNA molecules using a high-content short RNA library and established a subpopulation of MSCs that are refractory to osteogenic stimuli and form OS-like tumors in *vivo*. More details about the findings and implications will be discussed.

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All are welcome