O-18.4 Short talk

Brillouin Microscopy reveals altered biomechanics in Kabuki Syndrome murine bone tissues

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Kabuki Syndrome (KS) is a rare genetic disease resulting from altered mechano-signalling during cell lineage commitment, leading to growth retardation. It is mainly caused by a loss-of-function mutation of MLL4, an epigenetic modifier of chromatin relaxation. Our previous work demonstrated that this MLL4 mutated protein irreversibly alters the mechanical properties of mesenchymal stem cells in an in-vitro KS model. In this new study, we generated an in-vivo murine model of KS (where mice exhibited same growth delays as KS individuals) and measured the mechanical properties of the growth plate of tibia, the site of bone development. We used our custom-made Brillouin Microscope (BM), equipped with a new calibration technique, that allowed for non-contact, high resolution, label-free and reliable mechanical imaging of tissues.

Our results show that cells and extra-cellular matrix (ECM) stiffness both varied in a precise spatial pattern across the growth plate of control tissues. In contrast, nuclear stiffnesses of cells from KS tissues were completely unresponsive to external ECM properties, showing altered mechanical morphologies. This study highlights the strict connection between biomechanics and cell lineage commitment and confirm the use of Brillouin Microscopy as a fundamental technique for mechanobiology.