Does the osteomimicry of breast cancer cells translate to the release of extracellular vesicles with different biogenesis and function?

Giada CORTI – *Tor Vergata University of Rome*

Previous studies have shown that breast cancer cells can acquire an osteoblast-like phenotype under osteogenic culture conditions, a phenomenon referred to as “osteomimicry”. However, a complete characterisation of the phenotype acquired by breast cancer cells in an osteogenic environment has not yet been described. It has not been described how osteomimicry affects the nanomechanical properties of breast cancer cells. Changes in the nanomechanical properties of cells can be mediated by different physical and molecular mechanisms at the membrane and cytoskeleton levels, which translate into changes in the cell behaviour, for example in the ability to release different types of extracellular vesicles. In this study we used atomic force microscopy to investigate the morphological and nanomechanical properties of two breast cancer cell lines, MCF-7 and MDA-MB-231, cultured in the absence and presence of osteogenic medium for different times (3, 7, 10 and 14 days). Our results showed that both types of cells had an elasticity that did not change significantly with culture time in the central area (nucleus) while it increased in the more peripheral area (cytoskeleton). Furthermore, our studies showed that MDA-MB-231, but not MCF-7, exhibited in the more peripheral area indentation curves typical of those of extracellular vesicles starting from the tenth day of culture, suggesting the presence of vesicles or vesicle-like protrusions on the membrane of these cells. Study of single nanoindentation curves showed that the elasticity of these surface structures increased in the presence of an osteogenic medium and with culture time. Morphological studies validated the increase in membrane roughness of MDA-MB-231, but not MCF-7, cultured in the presence of an osteogenic medium. Our results would suggest that MDA MB-231, but not MCF-7, use microvesicles, instead of exosomes, to mediate their biological functions. Furthermore, our results would suggest that “osteomimetic” MDA-MB-231 could use microvesicles to participate in mineralization processes. Our findings shed light on potential vesicle-mediated mechanisms used by breast cancer cells to communicate with other cells and contribute to the formation of microcalcifications.