SERS imaging of mesenchymal stromal cells differentiation

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Understanding differentiation pathways of mesenchymal stromal cells (MSCs) is essential for implementation of such cells in regenerative medicine and cellular applications. MSCs, however, are heterogeneous populations of cells with varying capacities of self-renewal and differentiation potential between different tissue sources, donors, and inter-clonal variations, arising from non-standardized isolation and cryopreservation techniques. Since native MSCs demonstrate such variability, it is possible that their response to experimental manipulation may also vary, so it is of high importance to study cells with methods that interfere the least in their environment. The most commonly used procedures for following cell differentiation include e.g., immunofluorescence staining, qPCR, colorimetric assays. Nevertheless, a label-free method that does not require the termination of the cell culture prior the analysis, is still lacking. Surface-enhanced Raman scattering (SERS) is rapidly advancing as a non-invasive cell imaging method that reveals the chemical composition of a given sample based on inelastic scattering properties of the molecular bonds, which are significantly enhanced when in contact with the metallic nanostructured surfaces. Here, we show the direct and label-free approach for studying the extracellular matrix and membrane changes during differentiation in mesenchymal stromal cells with surface-enhanced Raman scattering. SERS is used as a sensitive tool to study the structure of cellular compounds, as it provides comprehensive information on the molecules in the nm-scale proximity of gold nanoisland substrates used as sensing platforms. We fabricated the substrates by repeated gold deposition and thermal annealing, which resulted in sufficient enhancement and homogenous distribution of "hot spots" [1]. To demonstrate their applicability as in vitro sensing platforms for long term cell cultivation, we cultured MSCs and recorded spectra of cellular membrane at selected timepoints during differentiation. The results indicate that SERS alone is sufficient to monitor the progress of extracellular matrix development and osteoblasts formation, selectively probing the outer membrane molecules adjacent to the surface of gold nanoisland substrates.

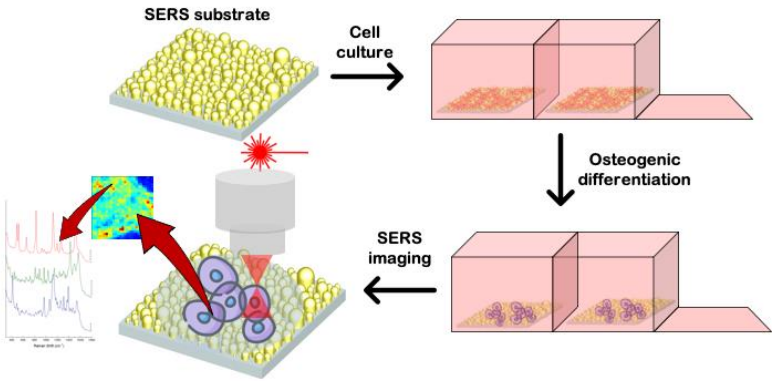

Figure 1. Schematic representation of protocol for SERS screening of MSC osteogenic differentiation on gold nanoisland substrates

[1] Milewska, A.; Zivanovic, V.; Merk, V.; Arnalds, U. B.; Sigurjónsson, Ó. E.; Kneipp, J.; Leosson, K. Biomed. Opt. Express 10, 6172-6188 (2019)