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Spot on - Raman Trapping Microscopy for manufacturing and quality control of advanced therapy medicinal products

Schütze, K[1], Kremling, H[1], Vaes, B[2], Vlaming, MLH[3], Braam, S[3]

[1]CellTool GmbH, Bernried, Germany
[2]Regenesys, Bio-Incubator Leuven, Belgium
[3]Ncardia, Leiden, The Netherlands

Introduction

Raman spectroscopy (RS) is a highly specific method, extensively used in physics, chemistry and pharmacology. Here we provide evidence that RS is also a reliable and easy-to-use tool to monitor biological samples. Our Raman Trapping Microscope allows label-free and non-invasive analysis of cellular behavior on single cell level, keeping cells unharmed during analysis. With this, Raman Trapping Microscopy (RTM) provides a universal tool to answer a large variety of biomedical questions. In addition, it can support manufacturing processes of advanced therapy medicinal products (ATMPs) facilitating quality control of intermediates and final products whilst saving time and money.

Materials and Methods

First, the influence of culture conditions on bone marrow stem cells was analyzed. To do so, cells were grown in different media for several days, fixed in 3% PFA and analyzed using RTM. In a second approach, differentiation of heart stem cells was monitored. For this, Raman spectra were taken from cardiomyocytes which were differentiated for 0, 11 and 21 days. In both experiments, Principal Component Analysis (PCA) was used for analysis of spectral data.

Results and Discussion

Using bone marrow stem cells grown in different culture media, RTM was able to detect variances between the differently cultured samples and group them into several subgroups although samples were blinded. In case of heart cell differentiation, RTM allowed discrimination between differentiated and undifferentiated cardiomyocytes. Main variations in spectra were related to differences in RNA/DNA and protein content of the samples. Experiments show that RTM allows to see biological samples in a whole new light, providing highly specific information while keeping cells intact. To do so, RTM requires less than 100 cells. With this, RTM has great potential to supplement traditional approaches in manufacturing and quality control of ATMPs.

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Presenters Biography

Dr. Schuetze is a biologist and expert in non-contact cell handling and label-free cell analysis using innovative photonic technologies. She did her PhD work at the Institute for Applied Physical Chemistry in Heidelberg and her postdoc research at the University of California in Berkeley where she assembled her first Optical Trap. In 1993 she and her husband founded the PALM company, which was successfully sold to Zeiss. In 2008, they both founded their second company, the CellTool GmbH, where they develop Raman microscope systems for biomedical applications, providing physicians and biologists an easy to handle tool for label-free and non-invasive cell analysis.