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Raman Trapping Microscopy for label-free and fast cell analysis in 2D-cell cultures, 3D tissue models and within liquid blood products

Schütze, K.[1], Vaes, B[2] , Steinke, M.[2], Kronstein-Wiedemann, R.[4],Tonn, T.[4]
Presenting author: Karin Schütze karin.schuetze@celltool.de
[1]*CellTool GmbH, Tutzing, Germany*
[2]*Regenesys, Bio-Incubator Leuven, Belgium*
[3]*University Hospital Würzburg, Tissue Engineering and Regenerative Medicine and Fraunhofer Institute for Silicate Research ISC Würzburg, Germany*
[4]*Experimental Transfusion Medicine – Medical Faculty Carl Gustav Carus, TU Dresden*

INTRODUCTION: Increasingly there is a need to test functionality, integrity and sterility of cell-based products during manufacture and of the final product prior to transplantation. Raman trapping microscopy (RTM) is a non-invasive, label-free, highly sensitive analytical method for fast identification and monitoring of single cells in solution, within 2D or 3D-tissue. Here, we present RTM as a novel tool for gentle yet highly precise cell analysis in three independent experiments, providing an overview about the large versatility of this method. First, the influence of culture conditions on bone marrow stem cells was analyzed. Second we investigated the characteristics of primary human tracheo-bronchial epithelial cells (hTEC) used to build an engineered 3D human airway mucosa tissue model. And third we used RTM to monitor condition of blood products.

METHODS: First bone marrow stem cells were grown in different media for several days, fixed in 3% PFA and analyzed using RTM. Second Raman spectra were collected within cytoplama of human airway adenocarcinoma Calu-3 cells and isolated hTEC cells seeded on cell culture dishes with glass bottom. Third a few microliters of erythrocyte and thrombocyte concentrates, respcetively were diluted in PBS buffer and Raman spectra were taken at different time points. In all experiments, Principal Component Analysis (PCA) was used for analysis of spectral data.

RESULTS: 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. Second: Comparing Raman spectra of living hTEC and adenocarcinoma Calu-3 cells relevant differences were identified in distinct wave number ranges. Furthermore, we could show that both erythrocytes and thrombocytes have their own Raman profile. In addition, change of Raman spectra with time was consistent with routine quality control studies of decrease in platelet activation capacity as well as with the correlation in metabolic consumption.

DISCUSSION & CONCLUSIONS: RTM is a fast and non-invasive method requiring less than 500 cells for analysis. Thus, RTM has the potential to become a standard for quality control of cell products and may lead to essential improvements in the field of transfusion medicine.

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