## Label Free, Live Cell Immuno-therapy Enhanced Darkfield Hyperspectral Imaging

Research of immuno-therapy as an effective treatment for cancer has made tremendous progress over the past decade. While there are a large number of rapidly emerging approaches in this field, many involve the use of either CAR T-cells or NK (natural killer) immune cells. These cells are innate to the body and can be utilized to target and eliminate specific cancer cells. While significant progress has been made with blood based cancers, immuno-therapy is now experiencing good success with solid tumor cancer cells.

Understanding how immune cells such as the NK cells interact with cancer cells is vital to these research efforts. The ability to observe live immune cell and cancer interactions, along with the ability to measure the cancer cell response to the interaction, can be very insightful in determining efficacy of these treatments.

Recently, CytoViva's Enhanced Darkfield Hyperspectral Microscope has been utilized to provide in-vitro, label free, live cell imaging and spectral analysis of the interaction between targeted immune cells and breast cancer cells<sup>1</sup>.



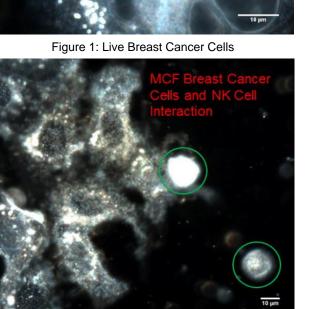
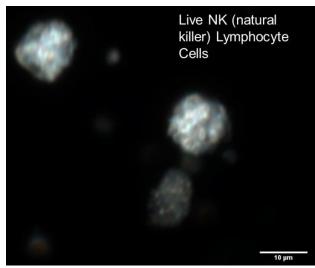


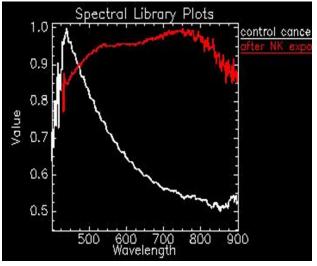
Figure 3: Live Cancer Cells - NK Cell Interaction

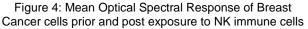


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Figure 2: Live NK (Natural Killer) Immune Cells





The CytoViva system incorporates patented enhanced darkfield (oblique angle) illumination optics that create a high signal-to-noise image of all components of the cell without the use of any fluorescent labels. This enables observation of all cell structures, not just those which are fluorescently labeled. For example, in figure 1, live MCF breast cancer cells are shown. In these cells, large endosomes are seen as bright white circles in the cells while the nucleus appears dark with a defined bright membrane. Figure 2 illustrates smaller NK cells. These cells appear granular in nature.

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In figure 3, the NK cells are incubated with MCF cancer cells. Note the two NK cells circled green with one of the cells clearly interacting with the confluent breast cancer cells. Also note a drastic change in the observed morphology of the breast cancer cells during this interaction, as they begin to decrease in size and granules appear in the cells.

Figure 4 illustrates a very significant measured change in the mean optical spectral response of the cancer cell. With hyperspectral imaging, you can capture the complete VNIR 400nm-1,000nm optical spectral response in each pixel of the image. This enables the ability to measure spectral data for individual sub-cellular elements or the mean spectral average of an entire cell area. The mean optical spectral response of the cells post interaction with the NK cells demonstrates a significant change in the spectral response of the cells. These measured spectral changes are also consistent with the observed morphological changes in the cells.

The CytoViva system can provide critical insight regarding the interaction of live NK cells and similar immune cells and their interaction with both live blood cells and live solid tumor cells such the MCF breast cancer cells shown here. To learn how the CytoViva system can advance your efforts in related immuno-therapy research, please contact us at info@cytoviva.com. We will be pleased to discuss test imaging of your samples or providing an onsite demonstration if appropriate.

<sup>1</sup> ONCOGEN Center (Timisoara, Romania), Chimeric Antigen Receptor Targeted Oncoimmunotherapy with NK Cells" (CAR-NK)