Analyzing living cells quickly and accurately

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The optical analysis system of IGB: the spectra recorded by the Raman spectroscope (back right) are displayed graphically on a monitor screen. The scientist controls the laser with the small box. Credit: Fraunhofer IGB

In order to investigate inflammation, tumors or stem cells, medical practitioners analyze living cells. Non-invasive optical procedures such as Raman spectroscopy accelerate this procedure. Researchers have now developed it to industrial scale.

The Fraunhofer Institute for Interfacial Engineering and Biotechnology IGB in Stuttgart can now analyze living cells quickly and accurately with the help of Raman spectroscopy. The non-invasive optical procedure, which recognizes the molecular fingerprint of different materials, has primarily been employed in quality control for medications and pharmaceutical substances. Now biologists and biomedical researchers can also use this technology thanks to the research work at IGB. The technology is suited to investigating living cells without invasive techniques or altering them with dyes. In order to characterize stem cells or identify changes to tissues that are caused by tumors, inflammations, fungi, or bacteria, it is now sufficient to determine the individual cells' Raman spectrum – a specialized energy spectrum having particular analytical capability,

"Under joint projects with universities, industrial partners, and the State of Baden-Württemberg, IGB has developed comprehensive know-how in this area over the last years and has advanced the technology from use in pure research to industrial implementation. We can now investigate not just individual cells in this manner, but entire tissue structures and organs. Next we want to further refine the technology and develop more applications," says Prof. Katja Schenke-Layland from IGB.

The unmistakable Raman spectrum

Cell biologists at IGB use a specially developed Raman spectroscope jointly designed and built with physicists at the Fraunhofer Institute for Physical Measurement Techniques IPM in Freiburg, Germany. The device is compact and can be conveniently used to investigate a wide range of scientific problems. The scientists are accumulating the spectra they have recorded into a database. "Each cell has a unique, unmistakable Raman spectrum. Doctors are able to compare the sample from their patients' cells with our data base and complete the diagnosis more quickly," says Schenke-Layland.

The technology is already being employed on a practical basis by industrial partners. The scientists are working at present on a rapid test for cancer diagnosis. "Doctors using mobile Raman spectroscopes during an operation could unambiguously say whether the patient has cancer or not simply by comparing the cell sample with the data base," according to Schenke-Layland.

Cancer diagnoses are still complicated and prolonged. After excising the tissue for biopsy, it first must be prepared for further analysis – for example by suitably sectioning or dying it to identify biomarkers. "But this always requires intervention in the specimen and manipulating it in some way," according to Schenke-Layland.

The specimen is then transferred to a pathologist who analyses whether the tissue contains malignant or benign cells. This method is error prone and can lead to the specimen being unusable for other tests in the end. "Human error is reduced by a software-based comparison with our data base," according to Schenke-Layland.

Employment in cancer diagnostics and regenerative medicine

There are numerous additional applications for this non-invasive optical technology – especially in regenerative medicine. Artificially grown tissue may replace diseased cells in patients and thereby help the tissue to heal. To accomplish this, tissue-specific cells from bone marrow, for instance, must be removed and the stem cells extracted. Bone marrow is made up of highly diverse cells and it is complicated to differentiate the adult stem cells from the ordinary tissue cells. In addition, the stem cells must be 100% correctly identified and separated. If this does not happen and other types of cells are cultured into the implant, the body may not react as hoped, causing implant rejection or tumor formation.

Raman spectroscopy is a process to unambiguously identify and differentiate various materials from one another. It is based on the interaction of electromagnetic radiation and matter. If matter is irradiated with light at a precisely defined frequency, some of the photons of this light interact with the molecules of the matter, which thereby shifts the photons' own energy spectrum. This frequency shift of the laser light, also known as inelastic optical scattering, is recorded by the Raman spectroscope. The effect is named after the Indian physicist C. V. Raman, who received the 1930 Nobel Prize in Physics for his work. The frequency shifts are a function of the material and every material possesses an unmistakable spectral fingerprint.

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