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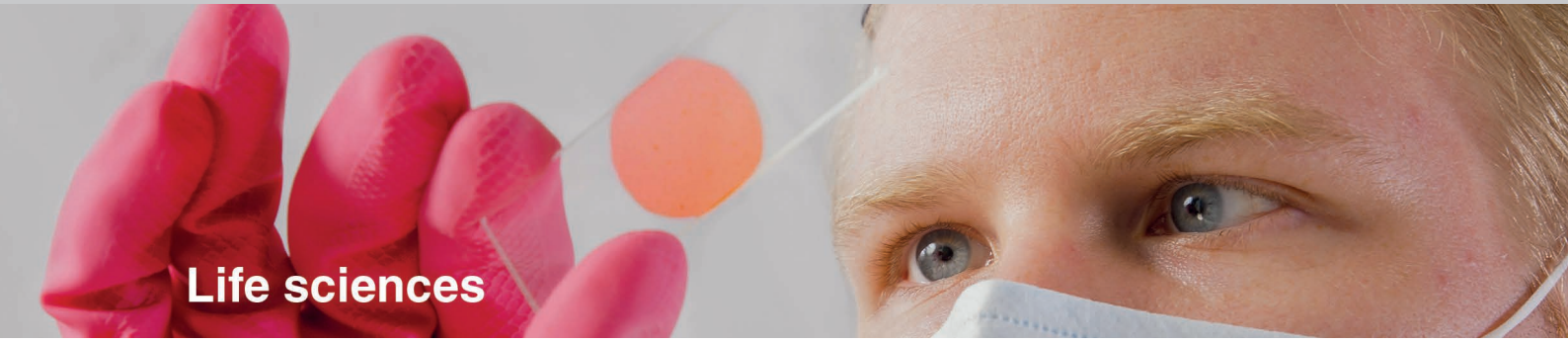
Surface enhanced Raman spectroscopic (SERS) imaging using the inVia™ confocal Raman microscope



Raman imaging is a powerful research tool for understanding the molecular composition, structure and distribution of different chemical species. Nano silver/gold colloids and roughened metallic substrates can be used to amplify the intensity of the Raman scattering of adsorbed molecules via SERS. This can increase the sensitivity and/or the specificity of the analysis.

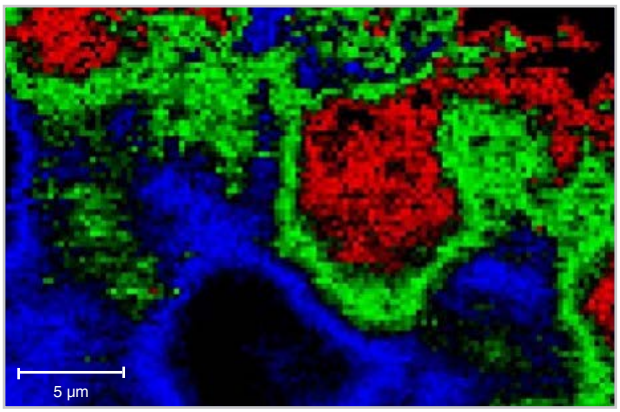
SERS imaging can be used to evaluate the efficacy of delivery of nanoparticles (NPs) into cells/animals. SERS measurement of labelled or surface-modified NPs can also be used for biosensing, multiplexing and theranostics.

Cell monitoring and rapid disease agent identification

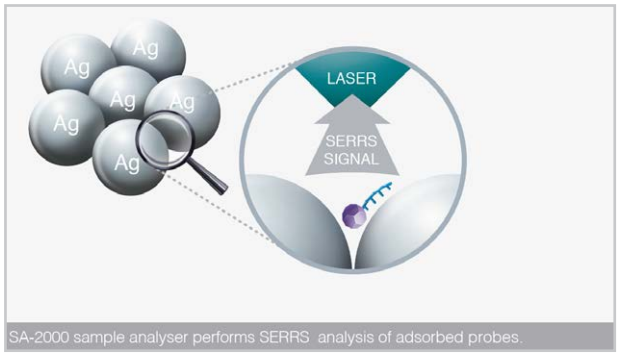
- Differentiate normal and cancer cells, and disease stages, by their intracellular SERS signals
- Monitor stem cell differentiation. Reveal changes in their biochemical profiles
- Identify microbes by their cell wall SERS signatures
- Screen with high sensitivity for circulating tumour cells using functionalised NPs and SERS analysis
- Create nanotags by coating NPs with reporter molecules, such as small molecules. SERS peaks are many times sharper than fluorescence bands. They allow nanotag identification through the reporter SERS signatures in a multiplex
- Identify pathogenic agents rapidly by detection of specific DNA sequences using a SERS multiplex

Locate tumours and enable therapy *in vivo*

- Identify tumour cells *in vivo* by means of their higher metabolic rates, and therefore their elevated rate of NP uptake
- Tag NPs with antibodies and deliver intravenously into animals to target certain tumours
- Evaluate the efficacy of tumour targeting using *in vivo* SERS imaging
- Use tumour-targeting NPs for thermal therapy or as surgical guide for tumour resection



Obtain cell compartment-specific chemical information by immunolabeling NPs to target specific cell compartments, e.g. cell membrane – SERS image revealing varying levels of cell surface proteoglycan in corneal epithelial cells (red to green to blue – high to low density)[vii]. Image courtesy of Dr Nigel Fullwood, University of Lancaster, UK.



Identify pathogen species by genotyping and reporting their species-specific DNA sequence using surface enhanced resonance Raman spectroscopy – schematic of oligonucleotides with reporter dye (purple) bound to silver NPs for read-out. Courtesy of Renishaw Diagnostics Ltd.

Renishaw plc

Spectroscopy Products Division
New Mills, Wotton-under-Edge,
Gloucestershire GL12 8JR
United Kingdom

T +44 (0) 1453 524524
F +44 (0) 1453 524901
E raman@renishaw.com

www.renishaw.com/raman

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Nano biosensing using labelled NPs

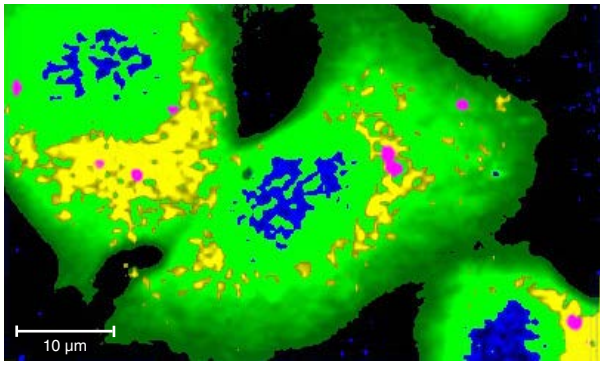
- Shed light on redox biology and health regulation by SERS measurements of cells/organelles
- Use NPs ≤100 nm diameter, which are readily endocytosed
- Measure intracellular redox potentials – the ratios of reporters' SERS peaks can be used as a metric for local redox potentials
- Enhance the normally weaker oxidised cytochrome Raman signals in living mitochondria by SERS

Report the intracellular distribution of nanotags in a multiplex

- Use NPs for drug delivery
- Utilise multiplexed nanotags for delivering particles to different cellular compartments
- Visualise the nanotags locations within cells via SERS imaging
- Combine 3D SERS and Raman imaging of cells to locate NPs in relation to the cellular compartments
- Obtain powerful insight into the NPs uptake mechanisms, and a means of evaluating the success of delivery/ targeting

Renishaw inVia; ideal for SERS imaging

- Research grade confocal Raman microscope
- StreamLine™ imaging technology for high speed screening of NPs without causing sample damage
- High confocality StreamHR™ imaging to precisely locate NPs in 2D and 3D
- StreamHR *Rapide* imaging to optimise speed and sensitivity
- Automated excitation wavelengths changing facilitates combined Raman and SERS imaging
- Component Analysis to enable live recognition of nanotags



Locate endocytosed NPs in relation to the organelles – Golgi network-targeting nanotags (pink) co-localised with membrane-bound organelles (yellow), rather than the nuclei (blue), in Chinese hamster ovarian cells (green).

The Renishaw inVia confocal Raman microscope

Relevant reading:

i. Brazhe et al, 2015, Probing cytochrome c in living mitochondria with surface-enhanced Raman spectroscopy. Sci. Rep. 5:13793
ii. White et al, 2014, Evaluation of a Commercially Developed Semiautomated PCR-Surface Enhanced Raman Scattering Assay for Diagnosis of Invasive Fungal Disease. J. Clin. Microbiol., 52(10): 3536-3543
iii. Karaber et al, 2014, Guiding Brain Tumor Resection Using Surface Enhanced Raman Scattering Nanoparticles and a Hand-Held Raman Scanner. ACS Nano, 8(10): 9755-9766
iv. McAughtrie et al, 2013, 3D Optical Imaging of Multiple SERS Nanotags in Cells. Chem. Sci. 4: 3566-3572
v. Huefner et al, 2013, Intracellular SERS Nanoprobes for Distinction of Different Neuronal Cell Types. Nano Letts, 13: 2463-2470
vi. Auchinvole et al, 2012, Monitoring Intracellular Redox Potential Changes Using SERS Nanosensors. ACS Nano 6: 888-896
vii. Hodges et al, 2011, Combining Immunolabeling and Surface-Enhanced Raman Spectroscopy on Cell Membranes. ACS Nano 5: 9535-9541
viii. Kahraman et al, 2011, On Sample Preparation for Surface-Enhanced Raman Scattering (SERS) of Bacteria and the Source of Spectral Features of the Spectra. Appl. Spectrosc. 65: 500-506
ix. Keren et al, 2009, Multiplexed Imaging of Surface Enhanced Raman Scattering Nanotags in Living Mice Using Noninvasive Raman Spectroscopy. PNAS 105 (15): 5844-5849

A range of related Renishaw literature is available. Please ask your local Renishaw representative for more information.

The RenDx® Multiplex Assay System and Fungiplex Assay are CE marked and provide automated, multiplex, high sensitivity *in vitro* diagnostics of infectious disease. Please visit **www.renishaw.com/diagnostics** for more information.

Renishaw. The Raman innovators

Renishaw manufactures a wide range of high performance optical spectroscopy products, including confocal Raman microscopes with high speed chemical imaging technology, compact process monitoring Raman spectrometers, structural and chemical analysers for scanning electron microscopes, solid state lasers for spectroscopy and state-of-the-art cooled CCD detectors, for both end-user and OEM applications.

Offering the highest levels of flexibility, sensitivity and reliability, across a diverse range of fields and applications, the instruments can be tailored to your needs, so you can tackle even the most challenging analytical problems with confidence.

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