Resonance stimulated Raman microscopy for super-multiplex detection in living cell and animals

Technology #cu13332

This technology is a platform for multi-color detection of vibrationally-tagged small molecules for enhanced live imaging using resonance stimulated Raman microscopy.

Unmet Need: Super-multiplex vibrational imaging of a large number of targets at the single cell or single molecule level

The development of novel imaging techniques to simultaneously identify, image, and track multiple targets (such as protein, RNA, organelles, cells) below the Rayleigh limitation imposed by traditional fluorescence microscopy is increasingly crucial in biomedicine and biotechnology. This is underscored by the explosion in super-resolution microscopy techniques within the last decade. However, almost all the existing methods such as magnetic resonance imaging (MRI), positron emission tomography (PET) or fluorescence techniques face a fundamental limitation in terms of imaging small-molecule metabolites and drugs with high-enough resolution and fast enough acquisition speeds. This is because MRI and PET have inherently low spatial resolution and fluorescence imaging requires the use of large fluorophores which cannot label small molecules. Additionally, prevalent fluorescence microscopy exhibits limited multiplexity due to the broad and featureless fluorescence spectrum.

The Technology: Resonance stimulated Raman microscopy for multi-color small molecule detection in live cells

This technology uses bioorthogonal bond-edited tags that produce sharp and tunable vibrational signatures upon stimulation. These vibrational tags only consist of a few atoms, thereby they are capable of labeling small biomolecules such as such as amino acids, nucleic acids, fatty acids, choline, glucose, cholesterol, and drugs. By targeting the distinct vibrational signature of around 2100 cm⁻¹, established Raman imaging methods can all be used to map out the distribution of vibrational tags with high resolution and sensitivity in biological samples, including in living cells and animals. Due to the narrow resonance of the Raman peaks, a large number of mutually resolvable frequencies (“colors”) can be realized for these vibrational tags by fine tuning the...
molecular composition of the bond-edited organic molecules. As such, this technology offers a palette of Raman-active absorbing dyes, allowing multiple (up to 24) biomolecules such as proteins and organelles to be targeted and imaged concurrently in living cells and tissues. When combined with standard conjugation methods and advanced Raman microscopy, this technology enables the dynamic visualization of small biomolecules and drugs in live cells and organisms with high sensitivity, specificity, resolution and biocompatibility.

This technology has been validated in live mammalian cells, tissue samples, and model organisms such as C. elegans, zebrafish, and mice.

**Applications:**

- Tracking the distribution and dynamics of small bio-molecules
- Visualization of newly synthesized biomolecules (protein, RNA and DNA) in live cells and organisms
- Visualization of protein degradation, RNA and DNA in live cells and organisms
- Visualization of spatiotemporal dynamics of lipids inside live cells and animals
- Imaging of tumor metabolism
- Imaging of glucose uptake activity in live cells and tissues
- Monitoring of drug delivery in living tissue
- Simultaneously imaging and tracking multiple (up to 24) targets such as protein, RNA, organelles, cells

**Advantages:**

- Can be used to image live cells, tissues and organisms without the need to fix the sample
- Can track the distribution and dynamics of small biomolecules that cannot be studied by fluorescence
- Multicolor imaging of multiple Raman-tagged biomolecules due to specificity of Raman shift
- Does not disrupt biological processes in live cells
- Obviates the need for the genetic modifications required by other techniques
- Does not require radioisotope labels
- Is not prone to bleaching – Raman active tags can be imaged over an extended duration
- Can be used simultaneously with other imaging modalities such as fluorescence microscopy

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**Patent information:**

Patent Pending (US 20160243261)

**Related Publications:**


Tech Ventures Reference:

• IR CU13332, IR CU13346, IR CU15116

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