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Upconversion Nanoparticles as a tool for histopathological tissue evaluation with multiplexing and machine learning potential

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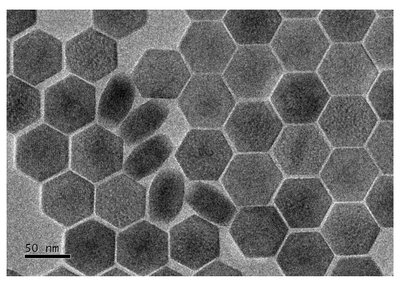
Background

In the field of histopathology misdiagnosis is a great risk. Haematoxylin and eosin (H&E) stain is a standard way to visualise the morphology of the cells. It is also common to detect proteins using a DAB chromogenic stain combined with a counterstain to visualise cell cytoplasm and nuclei. However, this method suffers from a narrow dynamic range, problems with quantitation and difficulties with multiplexing and co-localisation. Fluorescent IHC techniques generate a more quantitative readout but suffer from photobleaching. Here we present that the use of upconversion nanoparticles (UCNPs) allows to overcome problems associated with commonly used imaging techniques.

Upconversion Nanoparticles

Important properties of upconversion nanoparticles:



- Core made of rare earth minerals
- Erbium and Thulium used in most cases
- 30-80 nm in size
- Attractive for bioimaging because of the anti-stokes effect properties

Main advantages over IHC and IF:

- Possibility to combine with a counterstain in one slide
- Quantification is possible
- Potential for multiplexing - very narrow emission spectrum
- Can be used in standard automated IHC setup
- No background signal
- Very stable, no photobleaching

How it works

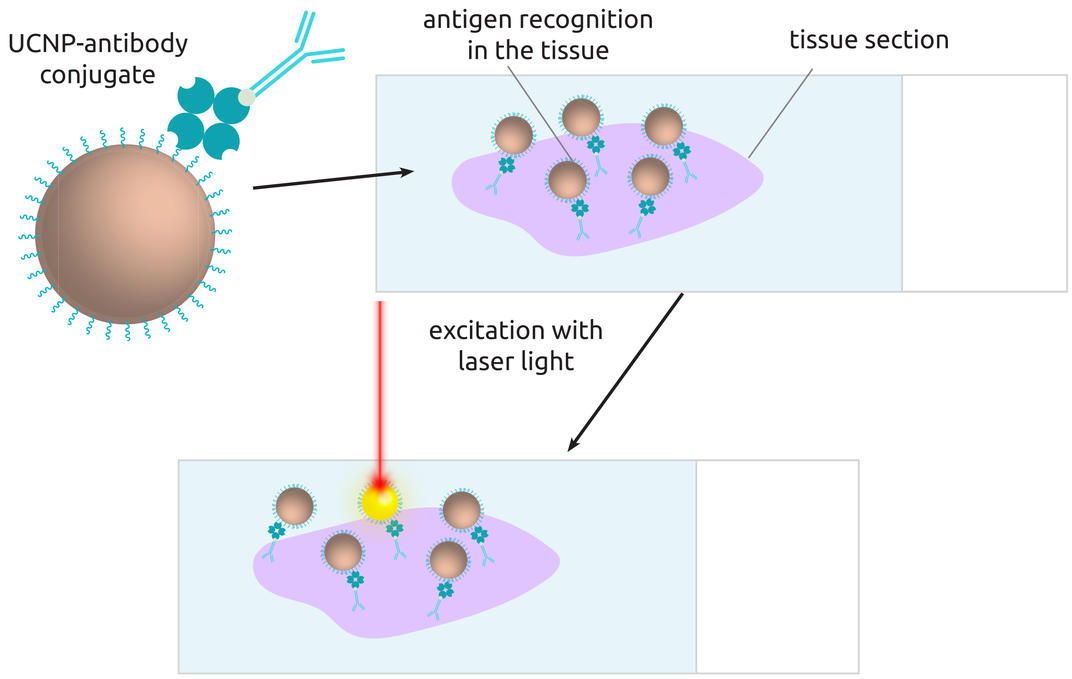


Figure 1. Staining workflow. Standard IHC workflow can be used with UCNPs. UCNP-antibody conjugates are formed and used to visualise antigens detected with standard primary antibodies. Fluorescent signal is obtained via UCNP excitation with a laser.

Our Solution

Lumito scanner

UCNP IHC staining kit

Figure 2. Our product line. We offer an automated slide scanner capable of brightfield and fluorescent imaging with DICOM output file. Our offer will contain a staining kit based on upconversion nanoparticles. The workflow is essentially the same as for standard IHC and an autostainer can be used.

Imaging

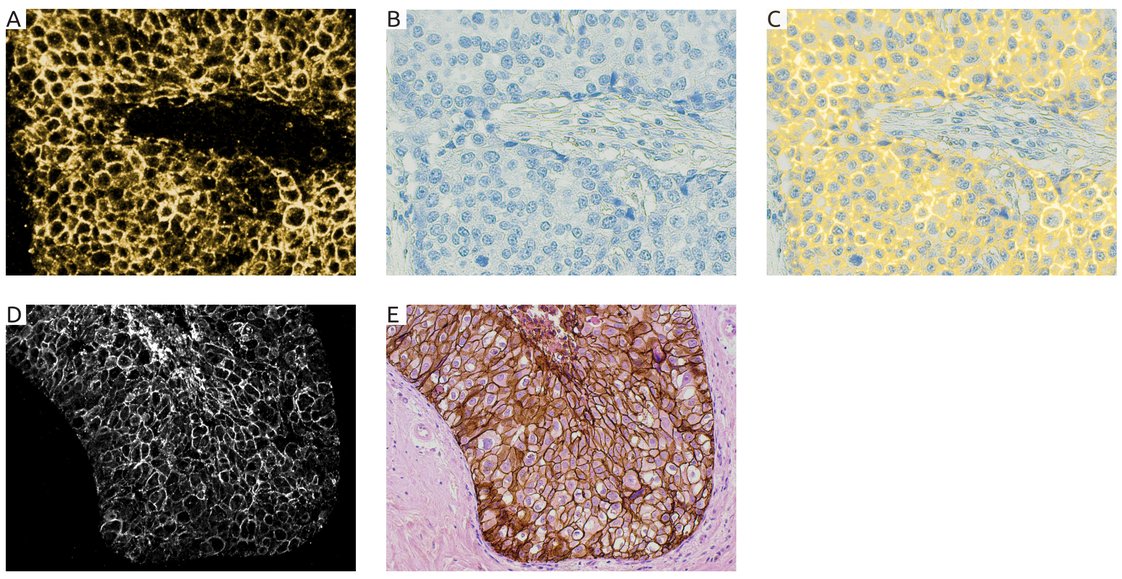


Figure 3. Examples of UCNP imaged tissues and cells. All images show formalin fixed paraffin embedded human breast cancer tissue samples. In A-C, samples were labelled with UCNP-Her2 conjugates and haematoxylin. The results can be presented in different ways, depending on the clinical need. UCNP signal (A) or hematoxylin (B) can be visualised alone, or in combination (C). D and E show a comparison between Her2 3+ breast cancer tissue labeled with UCNP-Her2 conjugate (D) or DAB (E).

Conclusions

The emerging field of UCNPs opens up new possibilities. Staining solutions and a novel device developed by us give hope for more accurate diagnosis by keeping the advantage of H&E staining and combining it, in one image, with luminescent data, ideal for generating ground truth for machine learning algorithms.

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Scan for high resolution