STED Super-Resolution Microscopy of Clinical Paraffin-Embedded Human Rectal Cancer and Mouse Epidermal Tissue

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The sub-cellular organization and function of cells cultivated in culture chambers may differ vastly from that in intact tissues. Still, currently, most super-resolution studies focus on the investigation of cultured cells. In this study we have established STED super-resolution microscopy on mouse epidermal and human rectal cancer tissues.

In clinical practice tissues resected during cancer surgery are fixed and then paraffin-embedded. These tissues are required for diagnosis, but they are also a vast and underexplored resource for research. We demonstrate that STED super-resolution microscopy can be used to visualize protein distributions below the diffraction barrier. Sections of well-annotated paraffin-embedded human rectal cancer tissue stored in a clinical repository, were used to study protein distributions at the nanoscale. Using antisera against several mitochondrial proteins, STED microscopy revealed distinct submitochondrial protein distributions, suggesting a high level of structural preservation. We show that even after up to 17 years of storage in a clinical repository, it is still possible to use paraffin-embedded human tissue for super-resolution microscopy. Furthermore, STED microscopy of HER2 positive rectal adenocarcinoma tissue revealed details concerning the cell-surface and intracellular distribution of HER2 which are unamenable by conventional light microscopy. These findings demonstrate the potential of super-resolution microscopy to explore the thus far largely untapped nanoscale regime in tissues stored in biorepositories.

In addition, we show that similar protocols for formalin fixation and paraffin embedment of tissue can readily be transferred to model organisms such as mouse. Using antisera against the outer mitochondrial membrane protein Tom20, we were able to visualize the nanoscale distribution of Tom20 in sections of mouse epidermis using STED microscopy. Taken together, we demonstrate the use of STED super-resolution microscopy to image protein distributions in formalin fixed and paraffin-embedded human and mouse tissues with nanoscale resolution.