

“CLEAR” technology can revolutionize protein imaging & facilitate detection of Cancer and Neurobiological Diseases

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A novel imaging platform called Cleavable Light-Erased Antibody Reporter (CLEAR) could help researchers visualize an unprecedented number of proteins within the same biological sample using just a single fluorescent marker.

This could unveil new possibilities for high-resolution, multiplexed imaging across cells and tissues, with important implications for disease diagnosis and biological research.

Proteins are the primary orchestrators of biological function and remain the principal targets for therapeutic intervention, as well as key markers for disease diagnosis. A comprehensive proteomic map of a tissue sample—capturing the identity and precise spatial organisation of every protein within its native context could help pathologists in diagnosing cancers or understanding complex neurological disorders. However, mapping a large number of proteins within their native spatial context has remained a major challenge.

In order to overcome this challenge, researchers at the Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR), Bengaluru, an autonomous institute of the Department of Science and Technology (DST) developed the imaging platform CLEAR that can enable scientists to visualize a large number of proteins within the same biological sample using a single fluorophore.

It could make comprehensive protein mapping possible at high resolution with the potential of transforming diagnosis in areas such as cancer biology, immunology, and neurological disorders, where understanding spatial protein organization is critical.

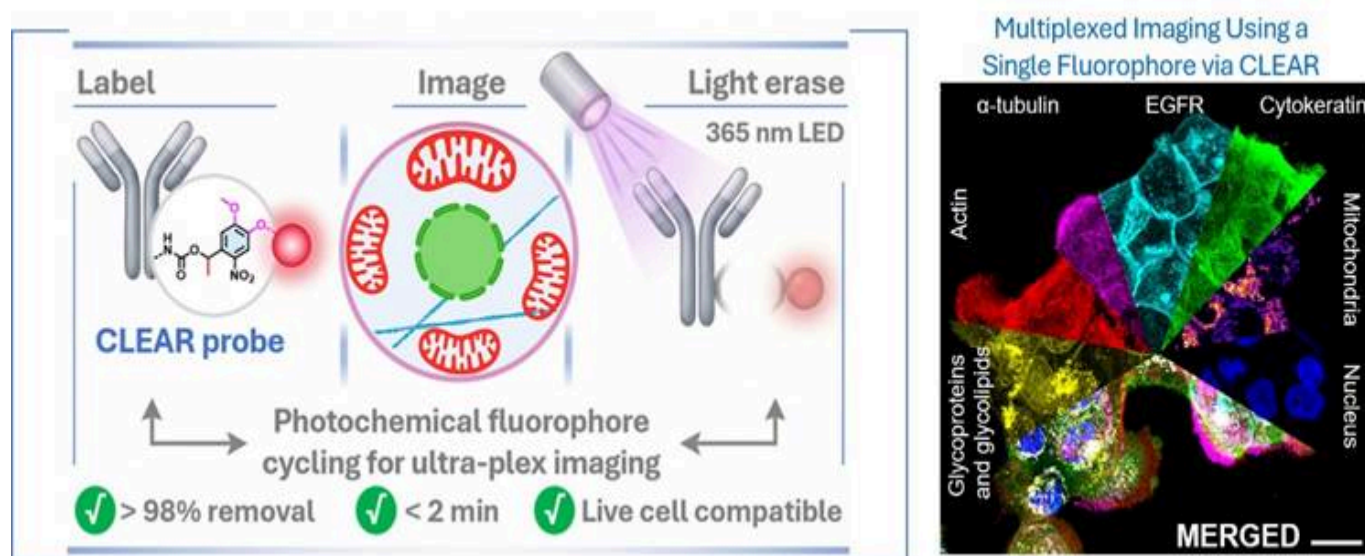


Fig: Illustration of the CLEAR imaging workflow and resulting high-plex images generated using a single fluorophore

The team led by Prof. Sarit S. Agasti designed and synthesized the CLEAR probes, developed the imaging workflow, and validated the platform across different biological systems. Experimental design, probe chemistry, and imaging analysis were carried out within the group. Collaborative efforts with researchers at the Indian Institute of Science (IISc) helped demonstration of the platform in complex biological settings, particularly in immune cell systems.

They introduced a light-cleavable probe system that enables repeated cycles of labelling and imaging within the same spectral window. Unlike existing multiplexing techniques, CLEAR combines high multiplexing capability with speed, high spatial resolution, and compatibility with delicate biological samples, including live cells. This approach fundamentally redefines multiplexed imaging by enabling virtually unlimited protein visualization without requiring multiple fluorophores.

The newly developed method published in the journal Chemical Science (Royal Society of Chemistry), works like a chalkboard – the things written can be erased to make room for new writing. The method, enables scientists to label proteins of interest within cells using cleavable fluorescent tags. After acquiring the images of a set of proteins under a microscope, a gentle pulse of 365 nm LED light is applied to erase the fluorescent signal, allowing a new set of proteins to be labelled in the same cell and to be imaged in the same optical window. By iteratively repeating this cycle, increasingly detailed and information-rich maps of multiple proteins can be generated across specimens, ranging from single cells to complex tissue sections.

CLEAR has the potential to transform biomedical research and clinical diagnostics by enabling detailed mapping of proteins in cells and tissues. This can improve early disease detection, especially in cancer and neurological disorders, and aid in understanding immune responses.

In the long term, the technology could contribute to precision medicine by providing comprehensive molecular insights that guide targeted therapies. The technology aligns with global efforts toward spatial proteomics and precision medicine.

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