LOCALIZING ALS ASSOCIATED PROTEIN FUS WITHIN SYNAPTIC COMPARTMENT USING SUPER-RESOLUTION MICROSCOPY TECHNIQUES

Dhruva K. Deshpande, Maria Demestre, Tobias Bockers and Jens Michaelis

Department of Biophysics,

University of Ulm,

Albert-Einstein-Allee 11, 89081 Ulm, Germany

E-mail: dhruva.deshpande@uni-ulm.de

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ABSTRACT:

Fused in Sarcoma (FUS) is a DNA-/RNA-binding protein associated with amyotrophic lateral sclerosis (ALS), a neurological disorder characterized by motor neuron degeneration. As abnormal accumulation of mutated FUS is indicated in ALS disease pathogenesis, it is of interest to understand its subcellular and synaptic distribution in normal phenotype of motor neurons [1].

We utilize super-resolution fluorescence microscopy techniques like direct Stochastic Optical Resolution Microscopy (STORM) and Stimulated emission depletion microscopy (STED) which allows a sub-diffraction imaging along with specific labeling of multiple proteins, making it the perfect tool for analyzing synaptic compartment which have distances below the diffraction limit.

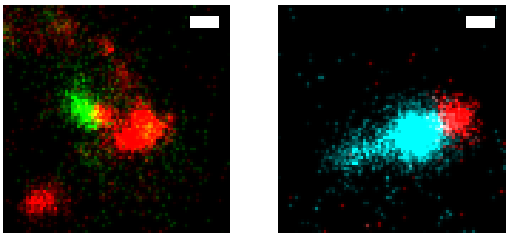

Figure 1: Reconstructed super-resolved single molecule localization microscopy (SMLM) images of co-localizing proteins FUS (red), Bassoon (green), HOMER (cyan). Scale bar = 100 nm

To determine FUS localization we image human induced pluripotent stemcells (hiPS) derived motor neurons [2]. In our experiments FUS is labelled simultaneously (Fig. 1) with known synaptic markers and their relative distances are measured in super-resolution images to determine their relative localizations.

REFERENCES:

[1] Schoen, Michael et al., "Super-Resolution Microscopy Reveals Presynaptic Localization of the ALS/FTD Related Protein FUS in Hippocampal Neurons". *Frontiers in Cellular Neuroscience* (9) 465 (2016).

[2] Stockmann, Marianne et al., "Developmental and Functional Nature of Human iPSC Derived Motoneurons" *Stem Cell Reviews and Reports* 9 (4): 475–492 (2013).