Super-resolution Imaging by Peptide-PAINT and Multivalent LCD-LCD Interaction in Regulating PAX3FOXO1 Transcription in Rhabdomyosarcoma

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Point Accumulation and Imaging in Nanoscale Topography (PAINT) is a single-molecule technique for super-resolution microscopy that uses exchangeable single-stranded DNA oligos or peptide-pair (docker and imager strand/peptide) to create fluorescence blinking. This characteristic distinguishes PAINT from other widely employed techniques such as Stochastic Optical Reconstruction Microscopy (STORM) and Photo-Activated Localization Microscopy (PALM). PAINT exhibits various potential advantages when compared to STORM and PALM, such as improved localization precision and increased multiplexing capability. Furthermore, Peptide-PAINT has several other advantages. The introduction of the docker peptide into the protein of interest, as opposed to the normal procedure of externally introducing it in DNA-PAINT, enables the attainment of comparable spatial resolution while streamlining experimental protocols and facilitating its utilization in living cellular systems. Deciphering the ultrastructure details of various cellular organelles in fixed mammalian cells using Peptide-PAINT will be discussed.

Rhabdomyosarcoma (RMS) is classified as a group of malignant neoplasms originating from soft tissues and is recognized as one of the prevalent malignancies affecting the pediatric and young adult populations. The aggressive subtype known as alveolar rhabdomyosarcoma (aRMS) has been observed to exhibit a correlation with the presence of a fusion gene called PAX3-FOXO1 or PAX7-FOXO, with PAX3-FOXO1 being more prevalent. Both PAX3 and FOXO1 are transcription factors (TFs) that play crucial roles in various biological processes. Nevertheless, PAX3-FOXO1 also functions as a transcription factor (TF); however, it leads to abnormal control of transcription, hence promoting the development of cancer. The role of multivalent interaction between the low complexity domains (LCDs) of PAX3FOXO1 in forming transcriptional hubs, and the underlying mechanism for transcription dysregulation will be discussed.