Super-resolution Microscopy with DNA Molecules: Towards Localizomics

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Super-resolution fluorescence microscopy is a powerful tool for biological research. We use the transient binding of short fluorescently labeled oligonucleotides (DNA-PAINT) for easy-to-implement multiplexed super-resolution imaging that technically achieves sub-5-nm spatial resolution[1].

To translate this resolution to cellular imaging, we introduce Slow Off-rate Modified Aptamers (SOMAmers) as efficient and quantitative labeling reagents. We demonstrate the achievable image resolution and specificity by labeling and imaging of transmembrane as well as intracellular targets (**Figure 1**) in fixed and live cell-specimen[2].

Apart from ever increasing spatial resolution, efficient multiplexing strategies for the simultaneous detection of hundreds of molecular species are still elusive. We introduce a new approach to multiplexed super-resolution microscopy by designing the blinking behavior of targets with engineered binding frequency and duration. We assay this kinetic barcoding approach in silico and in vitro using DNA origami structures, show the applicability for multiplexed RNA and protein detection in cells and finally experimentally demonstrate 124-plex super-resolution imaging within minutes[3].

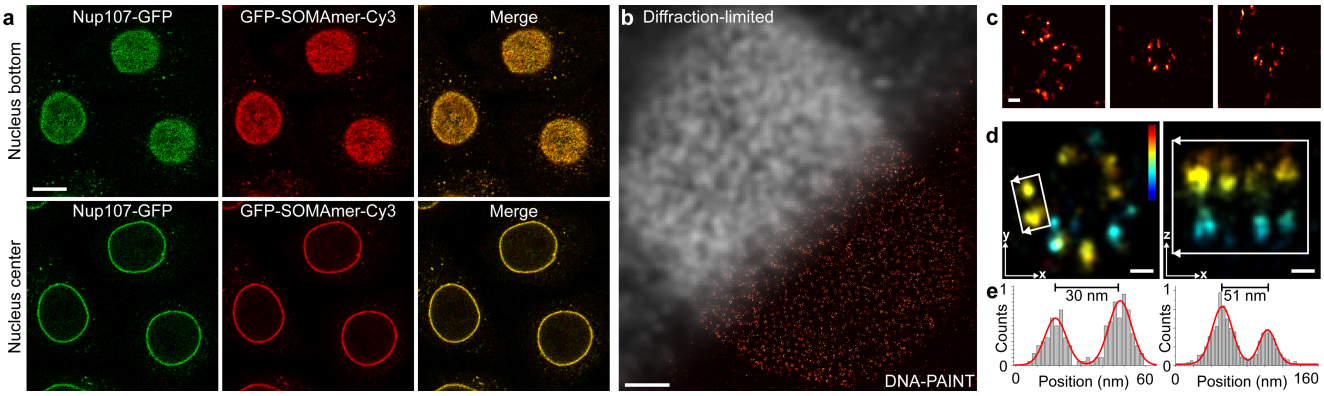

Figure 1: Intracellular labeling of GFP-tagged Nup107 for DNA-PAINT imaging using GFP–SOMAmers.

References

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