Single molecule imaging of gene fusion transcripts and RNA Trafficking

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ABSTRACT:
Sufficient RNA plays a central role in mediating gene expression. We study the intracellular distribution and trafficking of messenger RNAs and long non-coding RNAs by utilizing a single molecule florescent in situ hybridization (smFISH) method. In smFISH, we deposit a large number of probes on the same mRNA target to visualize single RNA molecules them in fixed cells. We have used this technique, to reveal the mechanism by which mRNAs are transported from the cell body to active synapses in dendrites of the hippocampal neurons. The same technique allowed us to image the sites of alternative splicing in the nucleus at single molecule resolution. Recently, we adapted this technique to detect gene fusions events resulting from chromosomal translocations. The resulting “Fusion-FISH” method provides a very sensitive and early diagnosis of cancers caused by translocations such as those associated with Ewing’s Sarcoma. We are currently using Fusion-FISH to detect gene fusion transcripts in solid tumors and developing the use of this assay for imaging tumor specific RNAs in exosomes. We are also exploring the molecular basis of cancers by analyzing RNA levels, distribution and interactions to potentially discover foundations for meaningful therapeutic intervention.