**Frontiers in Experimental Methodologies in Single-cell Analyses**

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All cells are different. Starting from the same genetic information, every cell functions differently but harmoniously, together in place via cell-cell interactions. In diseases, such functions are disrupted and cells behave abnormally with high heterogeneity. To understand diseases such as cancers that possess highly diverse genetic features, it is important to investigate their heterogeneity at the single cell level. Recent advances in single cell analyses by next-generation sequencing and tissue clearing technologies have broaden our understanding about how complex biological systems work. Yet, current single cell methods are unable to detect isoforms or post-translation modifications of proteins, which play significant roles in cell signaling pathways whose malfunctions often lead to the onset of many diseases. Also, to fully understand the biological status of the samples, investigating both mRNA and proteins in situ is critical. However, consolidated tissue clearing/expansion methodologies for the simultaneous preservation of various tissue features including tissue architectures, fluorescent proteins, antigenicity of proteins and nucleic acids have not been reported. I will present my recent works in development of novel single cell analysis platforms to address the challenges described above and discuss the future directions toward their applications for spatial multi-omics in various biological systems.