RAPID MS-BASED SINGLE-CELL ANALYSIS ASSISTED BY PHOTOCHEMICAL DERIVATIZATION IN LIVING CELL MEMBRANES REVEALS LIPIDOMIC PATTERNS WITH LOCATED C=C BONDS

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Abstract - Traditional lipidomics methods are not well-suited for studying unsaturated lipids containing located C=C bonds in single cells. We proposed a single-cell mass spectrometry (MS) platform assisted by aphotochemical derivatization (PCD) method termed Visible-light-activated Ru $(bpy)_3^{2+}$-catalyzed Singlet Oxygen-mediated Hydroperoxidation(VRSOH), for the rapid and simultaneous detection of multiple lipid C=Clocation isomers in living cell membranes at the single-cell level. First, the VRSOH method combined with MS analysis achieved the localization of C=C bonds in mono- and polyunsaturated lipids and cellular lipid extracts. Then,based on the home-built rapid single-cell MS platform and Ru-L, a modified form of $Ru(bpy)_3^{2+}$ that allowed the VRSOH method to be applied to living cell membranes, 15 lipid C=C location isomers from the top-rankedphosphatidylcholines (PCs) in both primary and metastatic colorectal cancer(CRC) cells were quantified with a throughput of∼16cells/min. The results also revealed specific lipidomic patterns associated withCRC metastasis and the existence of subgroups with distinct migration potentials in metastatic CRC cells. In light of the lipidomic pattern discovery, stearoyl-CoA desaturase 1 (SCD1) may serve as a potential target for CRC metastasis prevention.

Keywords - Mass Spectrometry; Single Cell; Photochemical Derivatization; Lipidomic Analysis