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FROM DYNAMIC STRUCTURES TO FUNCTIONAL MATERIALS

Mass Spectrometry for Characterizing Bioresponsive Molecules in Biological Environments

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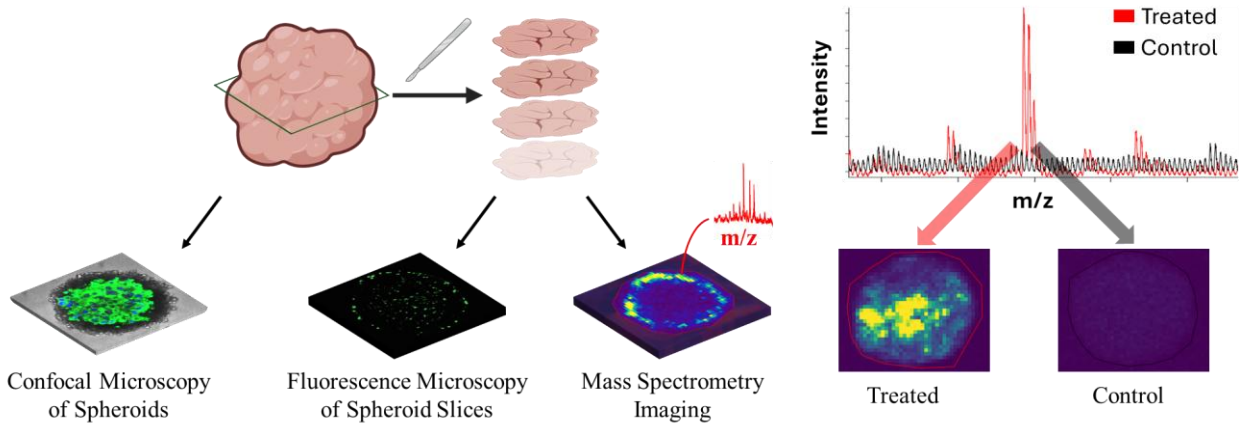
The rational design of bioresponsive molecules enables the spatiotemporal control over the molecular activation, which can be utilized for therapeutic applications as well as for biomaterials or biosensors. These molecules react to specific biological conditions, such as changes in pH, enzymes or the redox environment, thereby triggering the conversion from an inactive precursor into its active form.[1,2] Understanding the activation process in a complex biological environment or biologically relevant model systems is essential for the rational design of next-generation bioresponsive molecules. Current methods to study these processes often rely on labelling the bioresponsive precursors with fluorophores, allowing for high spatiotemporal resolution. However, incorporation of a fluorophore increases synthetic complexity and may alter the physicochemical properties, biodistribution, or activation behavior of the bioresponsive molecule. Mass spectrometry (MS) provides a label-free approach for characterizing homogenized cell lysates by detecting bioresponsive precursor molecules, their active forms, as well as intermediates and potential side products. While conventional MS methods lack spatial information, mass spectrometry imaging (MSI) combines molecular specificity and spatial resolution, thereby enabling the visualization of activation pathways and the detection of drugs, metabolites, biomolecules, and degradation products directly from 3D tumor spheroids.[3,4] Thus, MSI complements conventional methods, providing spatially resolved insights into the activation, distribution and stability of bioresponsive molecules in complex biological environments.[5]



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