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Metabolomics at the Single-cell Level

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Characterization of metabolites in single cells raises the potential to determine basic molecular processes that are responsible for the establishment and maintenance of important functional cell heterogeneity. For example, in the 1- to 4-cell embryo of *Xenopus laevis* (frog), coordinated cell divisions set up cell heterogeneity along the left-right, dorsal-ventral, and animal vegetal axes of the body plan. However, there is little knowledge about how small molecules contribute to the formation of cell-to-cell differences and how these molecules participate in early cell fate decisions. In this presentation, we discuss recent developments in mass spectrometry that enable the characterization of metabolites in single cells. We highlight metabolic studies under denaturing as well as native(-like) experimental conditions. Next, we focus on a single-cell mass spectrometry approach that we have developed on the basis of microsampling, capillary electrophoresis, and electrospray ionization tandem mass spectrometry. This technology has allowed us to detect hundreds of metabolite signals, including ~70 identified metabolites, between single cells in the 8- and 16-cell *Xenopus laevis* embryo. Furthermore, we have used single-cell CE-ESI-MS to quantify previously unknown metabolic differences between identified cells that develop into dorsal and ventral structures, including neural, epidermal, and gut tissues. These quantitative data also revealed reorganization of the metabolome in the temporal dimension. The ability to measure broad diversity of small molecules in cells in the complex body of the live vertebrate embryo using microcapillary-sampling single-cell mass spectrometry now raises an opportunity to help better understand molecular processes underlying cell differentiation and development.