

## ■ ASSOCIATED CONTENT

### SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.jproteome.1c00403>.

Peptide/proteome coverage at different processing volumes by two different searching software tools; boosting effects of “MBR” on peptide and protein identification; Venn diagrams showing the number of protein groups identified from each of three biological replicates at different numbers of cells; pairwise correlation of protein LFQ intensities between any two replicates for different numbers of cells; schematic diagram for dissociation of mouse colon tissues, the locations of five crypt cell subpopulations, and their isolation by FACS; volcano plots showing the proteome differences among different colon crypt cell types; protein identification and LFQ quantification in 50–1000 MCF10A cells using SOPs-MS; protein identification and LFQ quantification in colon crypt cell types using SOPs-MS; and comparison of SOPs-MS with existing nanoproteomics approaches for the analysis of small numbers of cells ([PDF](#))

Protein identification and LFQ quantification in 50-1000 MCF10A cells using SOPs-MS ([XLSX](#))

Protein identification and LFQ quantification in colon crypt cell types using SOPs-MS ([XLSX](#))

Comparison of SOPs-MS with existing nanoproteomics approaches for the analysis of small numbers of cells ([XLSX](#))