

300 μL of H_2O was then added to the tube, and the cells were fully lysed by an ultrasonic cell disruptor (Bioruptor Pico, Diagenode, Belgium) for 10 min at 4°C . After mixing, 20 μL of suspension was collected for protein quantification and subsequent data normalization. Then, methanol (precooled to -80°C) was added into the tube to make 80% methanol solution (v/v). The tube was vortexed vigorously for 5 min and centrifuged at $14,000 \times g$ for 10 min at 4°C to remove the cell debris. Afterward, the metabolite-containing supernatant was transferred to a new tube on ice. The supernatant was evaporated to dryness in a vacuum concentrator and reconstituted in 100 μL of methanol: H_2O (1:1, v/v), which was centrifuged again at $14000 \times g$ for 15 min at 4°C to remove insoluble debris.