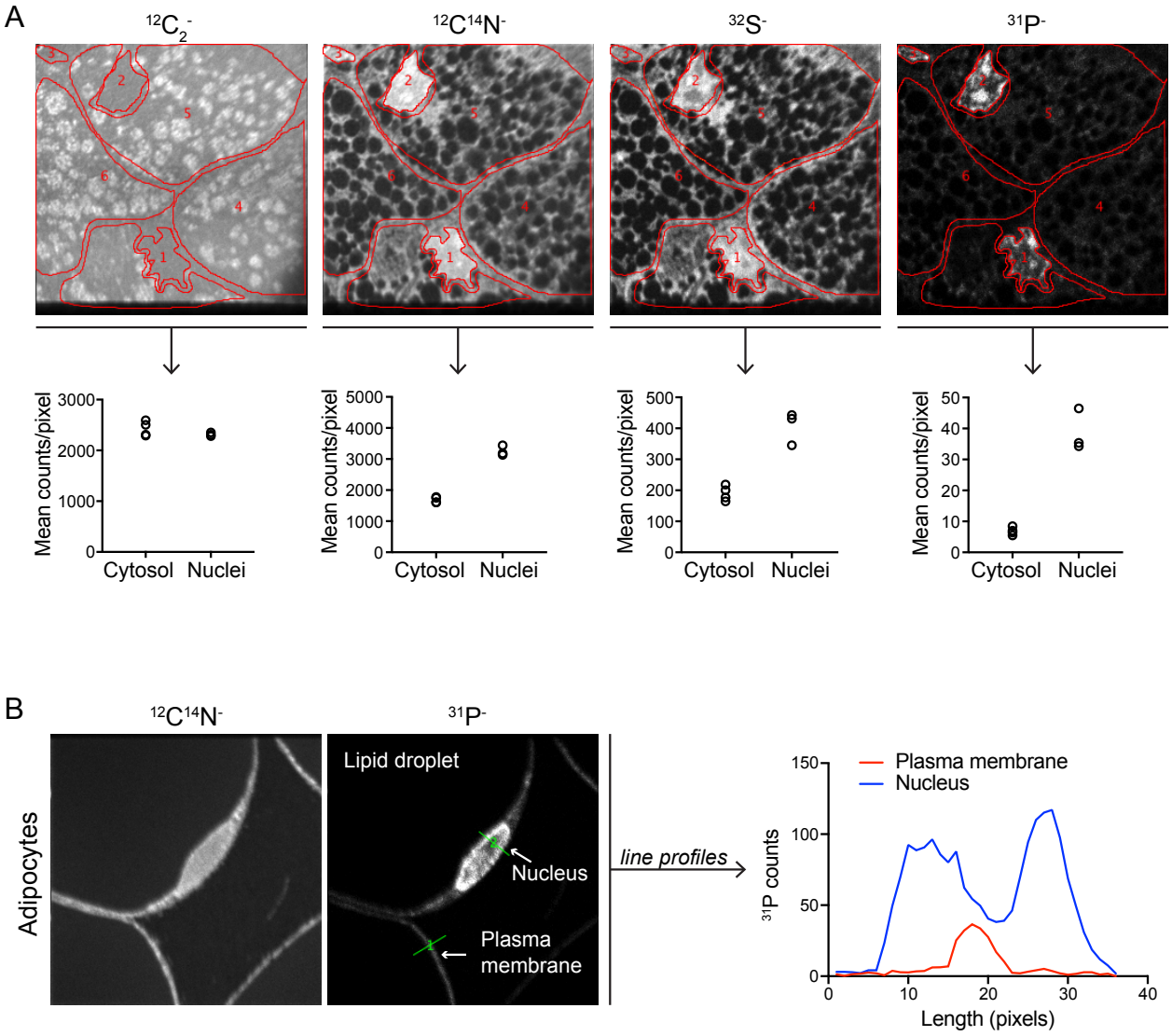


Figure S1. Quantitative mass images reveal characteristic histological features.

(A) Mass images (top row) demonstrating foam cells in the intimal core of atherosclerotic plaque. The intensity of the signal in any given pixel is related to underlying ion counts. The ion counts for each region of interest outlined in red are graphed below each image. Note that the y-axis scale of each specific ion is different due to the underlying differences in elemental abundance and species-specific differences in ionization efficiency. Phosphorus is particularly good at revealing nuclei because its abundance in the condensed chromatin is higher than the phosphorus content of the cytosol; however, the lower count rate for phosphorus translates into a higher requisite acquisition time in order to obtain sufficient counts.
(B) Adipocytes in an adipose tissue section further demonstrate the intensity of phosphorus signal in the nucleus. Because the defining central lipid droplet in the adipocyte is comprised of triglycerides that do not contain phosphorus, the signal in the plasma membrane (phospholipids) is easily discriminated from the cytosolic contents, albeit at a lower intensity than the nucleus. The qualitative difference in signal that is evident in the phosphorus ($^{31}P^-$) image is shown quantitatively by line profiles corresponding to the green lines.

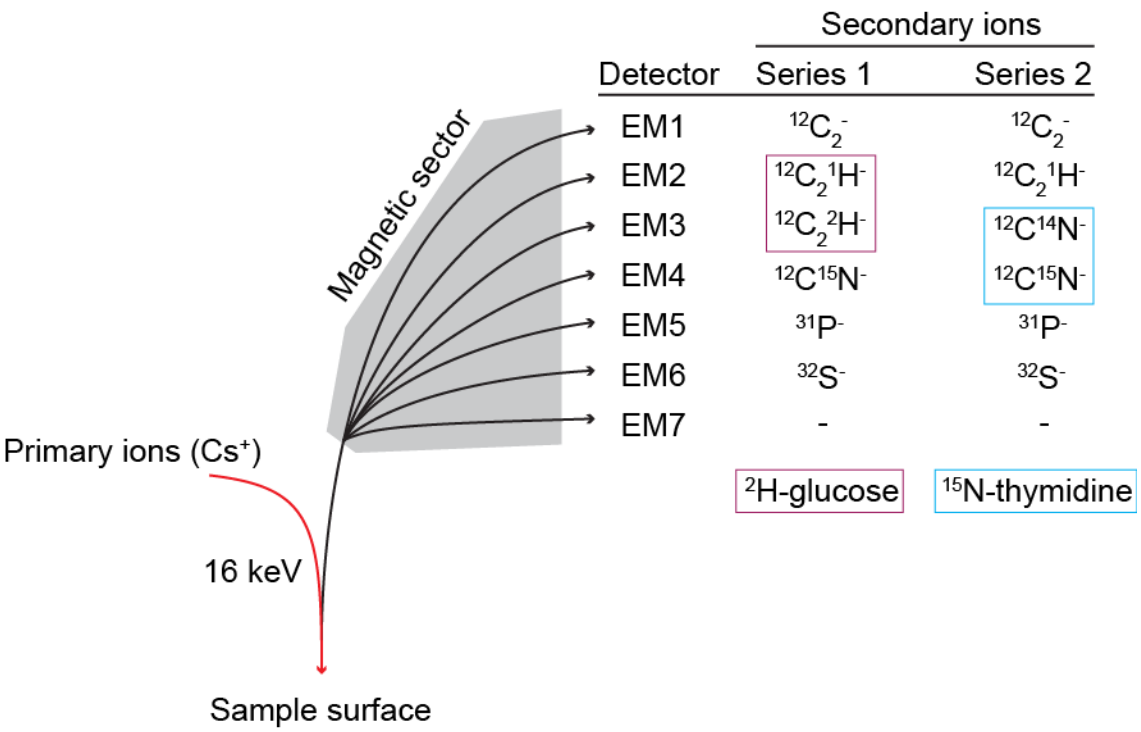


Figure S2. Analytical configuration of the NanoSIMS instrument.

This schematic depicts key aspects of the NanoSIMS 50L and analytical parameters used in this study, similar to prior descriptions(12, 23). The sample surface (*e.g.* 0.5 micron section of aortic root) is sputtered with a beam of primary ions emitted from a cesium (Cs^+) source. The sputtering process at the sample surface results in the removal of the uppermost layer of atoms and small polyatomic fragments, and therefore the quantitative imaging plane represents a fraction of the depth of the 0.5 micron section. A fraction of the sputtered atoms and small polyatomic fragments are ionized. The negatively charged ions are shaped into a beam of secondary ions and transmitted to a magnetic sector mass spectrometer. A trolley containing 7 moveable electron multiplier (EM) detectors is aligned along the focal plane of the magnetic sector. In this study, we performed peak switching where successive planes were acquired in an alternating fashion, thereby generating two different series of images. Although in this study we quantified two labels with this approach, note that the 7th dectector (EM7) was not utilized. With this same configuration, two additional labels could be quantified in multiplexed fashion. For example, halogenated labels (*e.g.* BrdU) could be directly quantified using EM7; whereas, introduction of a peak switch on EM2 from $^{12}C_2{}^1H^-$ to $^{12}C^{13}C^-$ would enable the quantification of ^{13}C-tagged labels.