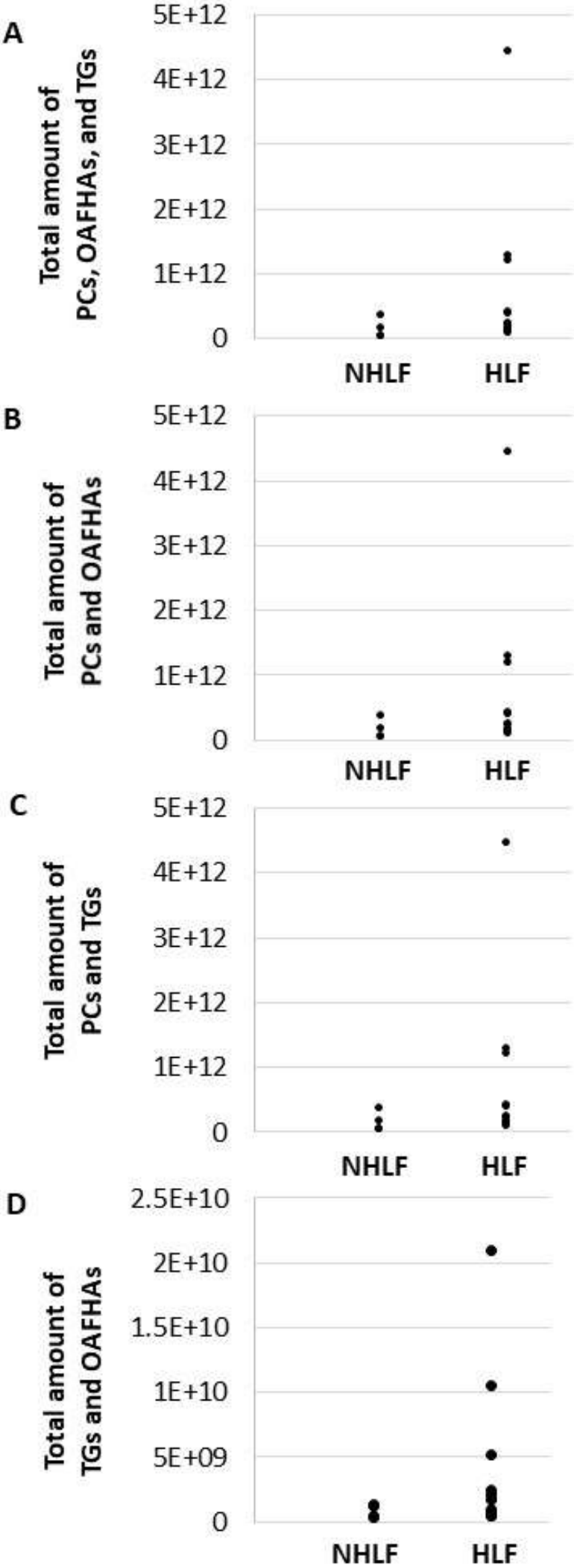Supplemental figure 3