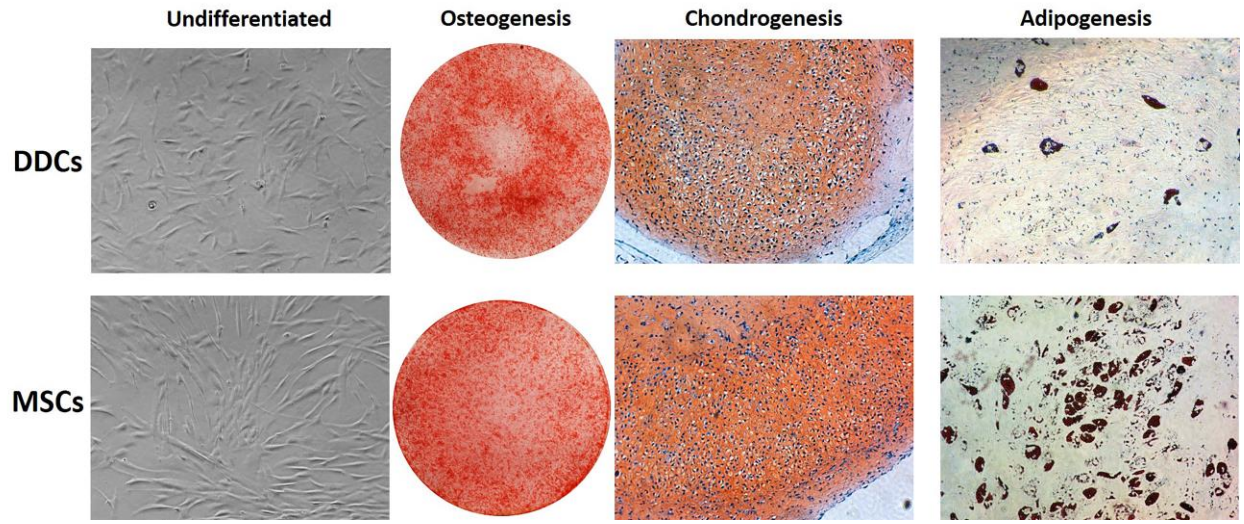
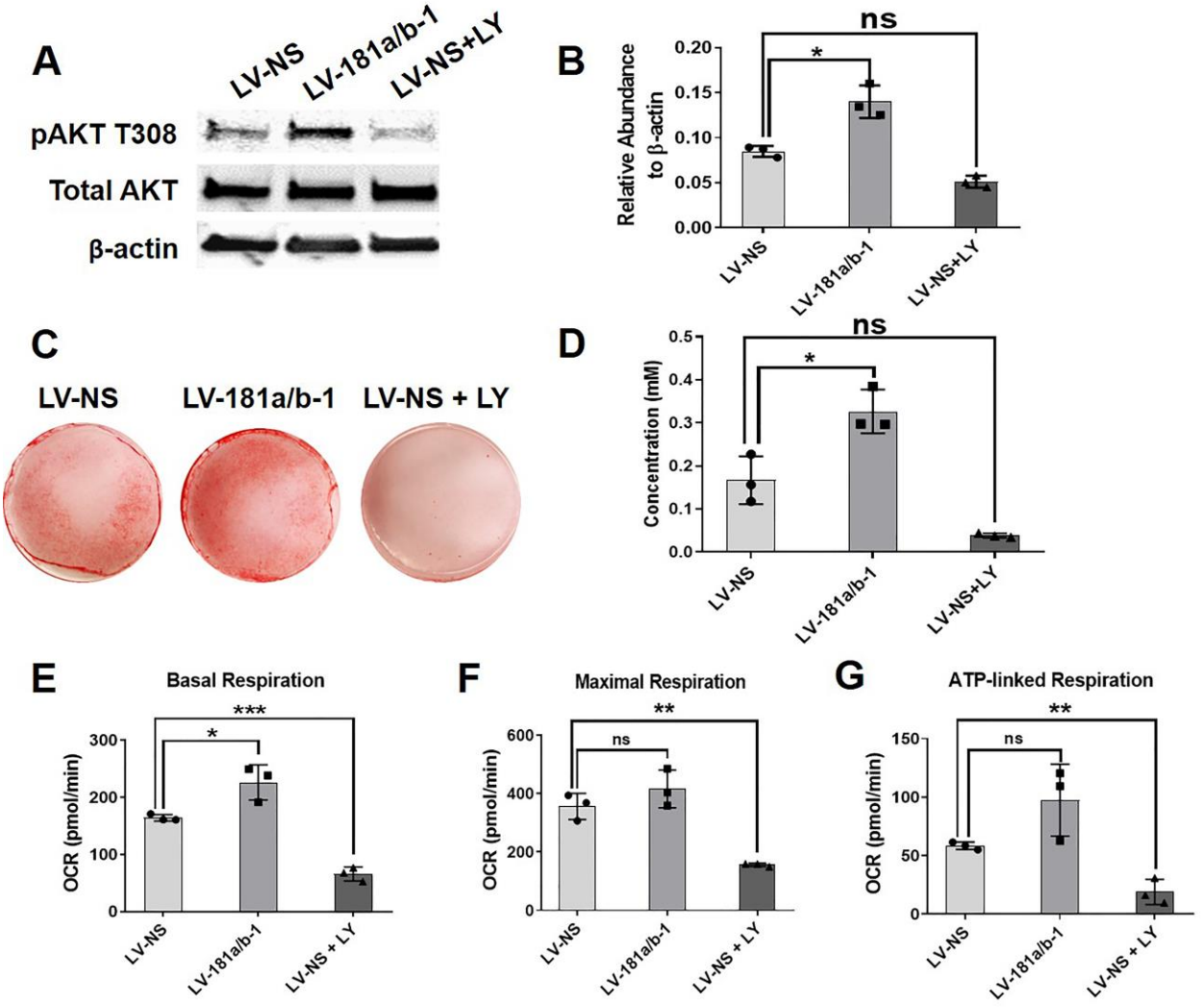


Supplemental Fig. 1: Tri-lineage potential of human primary de-differentiated DDCs and bone marrow-derived MSCs. Left panel shows light microscopy images of DDCs and MSCs. Using standardized induction medium and procedures, osteogenic, chondrogenic and adipogenic differentiation was achieved with both cell types as shown by Alizarin Red staining (day 14), Safranin O staining (day 21) and Oil Red O staining (day 14), respectively. Images are representative of assays carried out in our laboratory using cells from many independent sources.



Supplemental Fig. 2: **Effect of PI3K inhibitor, LY294002, on osteogenesis and mitochondrial metabolism during osteogenic induction.** DDCs were cultured in osteogenic induction medium with or without 5 μM of LY294002 (Cell Signaling Technology #9901). The effects of LY294002 (LY) on PI3K/AKT signaling was confirmed 16 h later by Western blotting using the anti-pAKT-T308 antibody (A, B). Addition of the inhibitor significantly suppressed osteogenesis as shown by the decrease in Alizarin Red staining at day 20 (C, D). During 4 days of osteogenic induction, addition of the PI3K inhibitor also suppressed basal and maximal respiration as well as ATP-linked respiration as measured by using the Seahorse XF Mito Stress Test kit (E-G). Data expressed as ± SD; $n = 3$; *$p < 0.05$; ** $p < 0.01$; *** $p < 0.001$