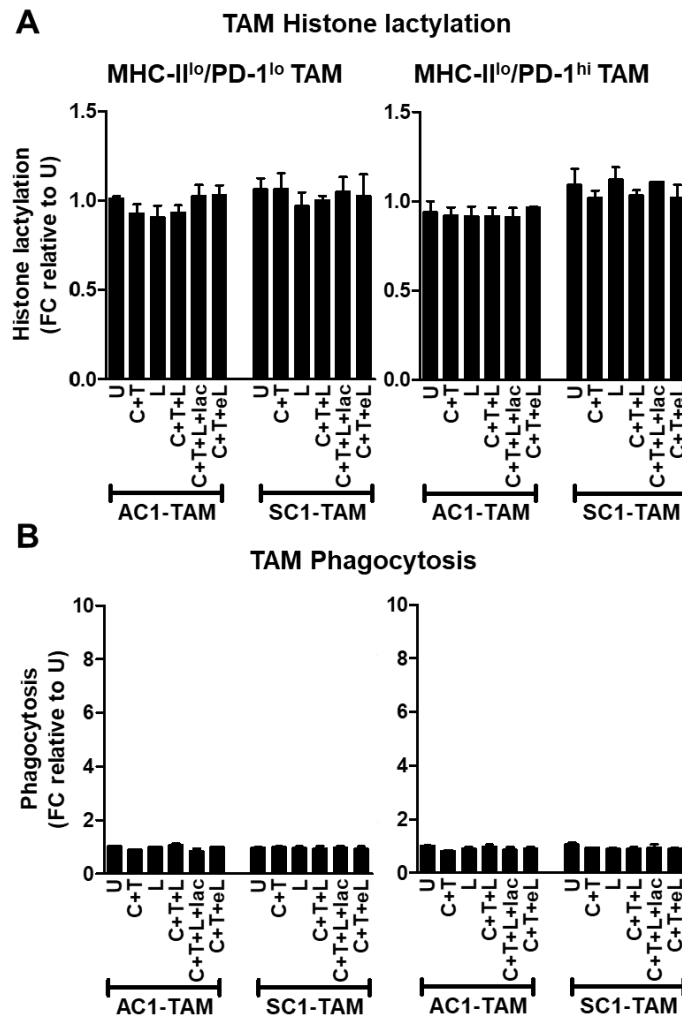


Supplementary Figure S12



Supplementary Figure S12. Conditioned media from PI3Ki + MEKi + PORCNI treated PTEN/p53-deficient tumor derived cells does not alter histone lactylation and phagocytic activity of MHC-II<sup>lo</sup> TAM. (A-B) AC1/SC1 cells were treated with copanlisib (C, 100 nM), trametinib (T, 5 nM), LGK'974 (L, 50 nM) or their combination for 72 hours. For mechanistic dissection, lactate (lac, 100 nmol/ $\mu$ L) and LGK'974 (eL, 50nM) were added to the CM collected after C+T+L and C+T treatments of AC1/SC1 cells, respectively. FACS-sorted TAM were incubated with the indicated CM for 24 hours followed by co-culture with CTV dye stained-

AC1/SC1 cells for 2 hours. Bar graphs demonstrate fold change (FC) in (A) histone lactylation and (B) phagocytosis of MHC-II<sup>lo</sup>/PD-1<sup>hi/lo</sup> expressing TAM relative to untreated group. n=2 independent biological experiments. Significances/p-values were calculated by one-way ANOVA and indicated as follows, \*\*\*p<0.001.