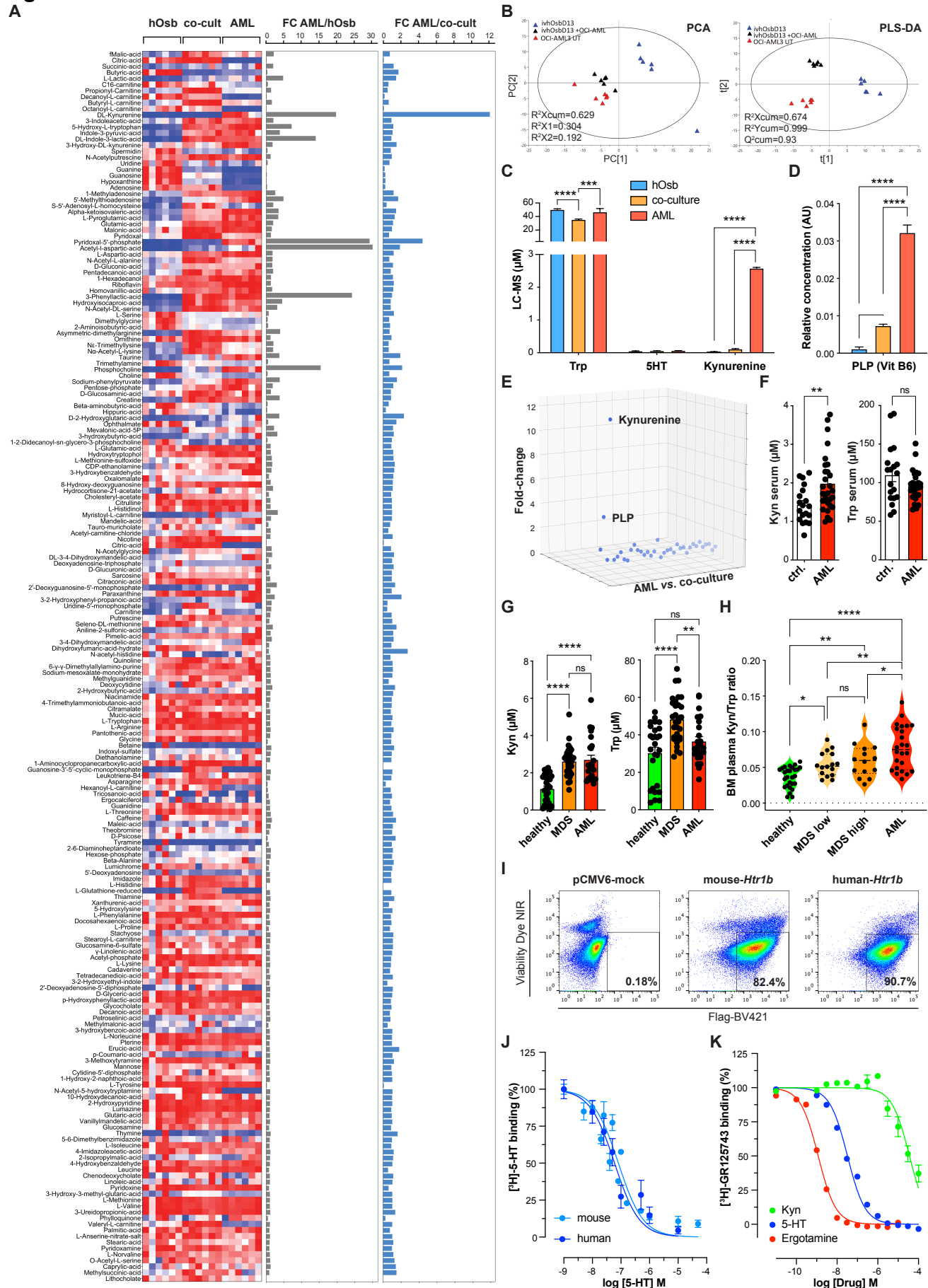


**Figure S2**



**Supplementary Figure S2. Kynurenine is an oncometabolite increased in AML and MDS patients that binds to HTR1B. Related to Figure 2.** (A) Heat-map of metabolites with CV <30%. Left to right columns: supernatants from human osteoblasts (hOsb) untreated, co-culture of hOsb with OCI-AML3 cell line (co-cult; 24h) and AML untreated (AML); n=6 for all. Grey bar-graph represents the fold change (FC) of AML vs. hOsb and blue bar-graph represents the FC of AML vs co-culture. (B) Unsupervised principal component analysis (PCA) and partial least squares-discriminant analysis (PLS-DA) scores plots for metabolites with CV <30%, and three or four components respectively with the indicated values. (C) Liquid chromatography-mass spectrometry (LC-MS) quantification of indicated metabolites (n=3/group); multiple unpaired t-test. (D) Relative abundance of PLP in each supernatant compared within the metabolomic analysis (n=6). (E) 3D representation of the FC of AML vs. co-culture of metabolites with CV <15%, x axis shows the metabolites, y axis the fold change (FC) and z is the axial plane which gives the 3D perspective. (F) Kyn and Trp circulating absolute levels ( $\mu\text{M}$ ) in serum of vehicle (ctrl., n=19) or MLL/AF9 (AML, n=28) injected mice; unpaired t test. (G) Kyn and Trp BM absolute levels ( $\mu\text{M}$ ) in plasma of healthy (n=27), MDS (n=30) or AML (n=24) human patient samples. (H) Kyn/Trp levels in BM plasma of healthy (n=27), MDS -stratified in low- (n=16) and high-risk (n=14) groups based on the Revised International Prognostic Scoring System (IPSS-R)- and AML (n=24) patients. (I) Representative flow plots of HEK293T cells transfected with mock vector, mouse or human *Htr1b-MycDkk*, pCMV6-Entry vector. (J) Radioligand competitive-binding assay with the indicated concentrations of test compounds, [ $^3\text{H}$ ]-5-HT (25nM), and HEK-293T membranes overexpressing either the mouse or the human HTR1b receptors (n=2 experiments). (K) Radioligand competitive-binding assay with the indicated concentrations of test compounds (0.3nM to 300 $\mu\text{M}$ ), [ $^3\text{H}$ ]-GR125743 (1.38nM), and HEK-293T-HTR1B membranes (n=3 experiments). All data are represented as mean  $\pm$  SEM; Statistical analysis performed with one-way ANOVA unless otherwise indicated.