Immune and tumor cell 'tug-of-war' controls anti-cancer activity, study finds

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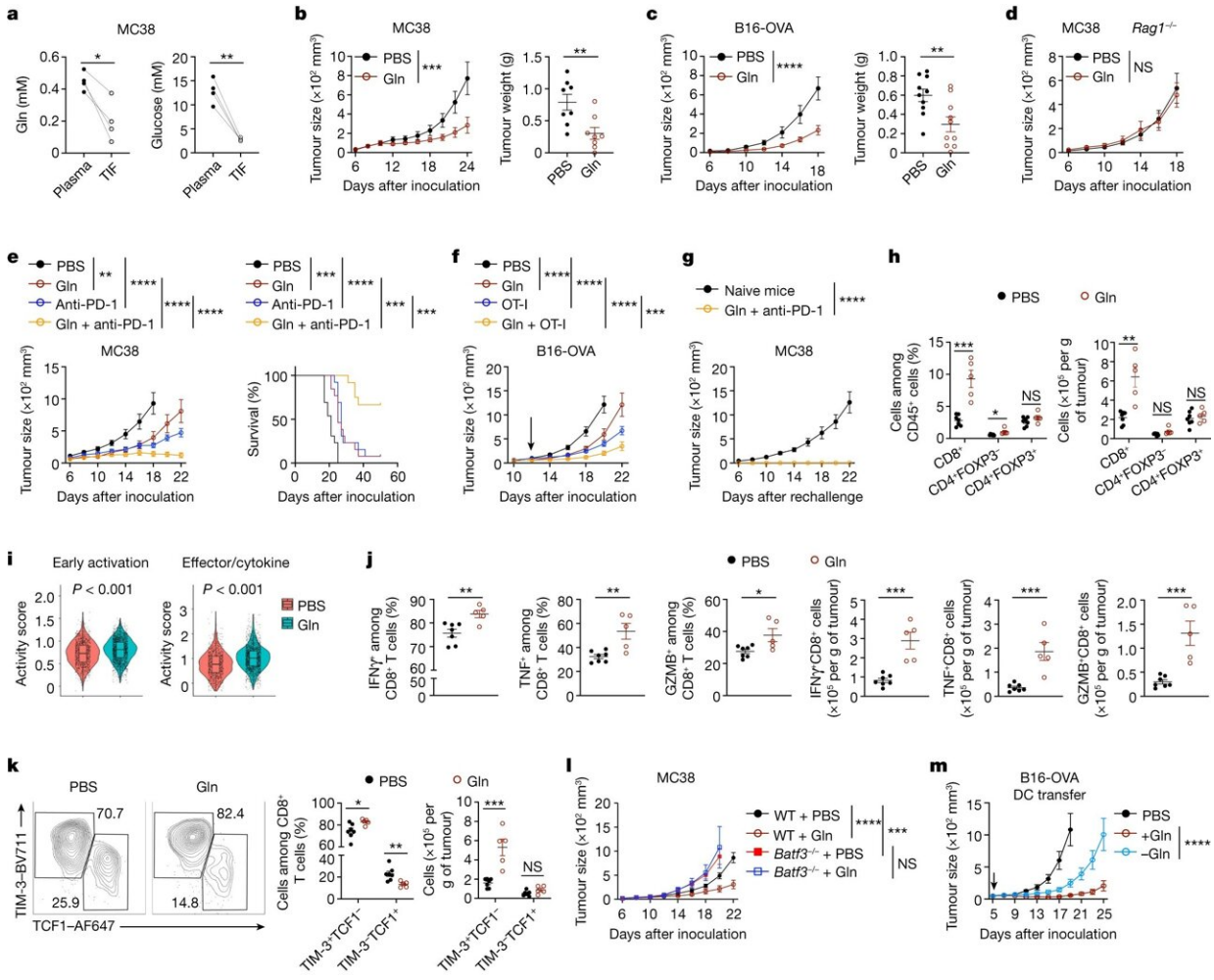

Intratumoral glutamine supplementation promotes cDC1-mediated anti-tumor immunity. **a**, Levels of glutamine and glucose in plasma and TIF of mice bearing MC38 tumors at day 15 ($n = 4$ per group). **b**,**c**, Growth and endpoint weight of MC38 (**b**; $n = 8$ per group) and B16-OVA (**c**; $n = 10$ per group) tumors (day 24

and 18, respectively) after intratumoral PBS or glutamine supplementation. **d**, MC38 tumor growth in *Rag1*$^{-/-}$ mice after PBS or glutamine treatment (n = 7 per group). **e**, MC38 tumor growth and mouse survival after indicated treatments (n = 12 for Gln + anti-PD-1, n = 13 for all other groups). **f**, Growth of B16-OVA tumors in mice receiving intratumoral PBS or glutamine with activated OT-I cells (indicated by arrow) (n = 10 per group). **g**, MC38 tumor growth in tumor-free (having received prior glutamine + anti-PD-1 treatment; n = 8) or naive mice (n = 5) upon challenge with MC38 cells. **h**, Indicated T cell populations at day 15 in MC38 tumors treated with PBS (n = 7) or glutamine (n = 5). **i**, DCs, CD45$^+$ non-macrophage immune cells, macrophages and CD45$^-$ cells were sorted from PBS- and glutamine-treated MC38 tumors and mixed for scRNA-seq analysis. Violin plots show activity scores of early activation and effector/cytokine signaling signatures in intratumoral CD8$^+$ T cells from MC38 tumors treated with PBS (n = 1,113 cells) or glutamine (n = 2,031 cells). Box plots show the median (center line) with interquartile range of 25% to 75%. **j**,**k**, IFNγ$^+$, TNF$^+$ and granzyme B$^+$ (GZMB$^+$) (**j**) or effector-like (TIM-3$^+$TCF1$^-$) and stem-like (TIM-3$^-$TCF1$^+$) (**k**) CD8$^+$ T cells at day 15 from MC38 tumors treated with PBS (n = 7) or glutamine (n = 5). **l**, MC38 tumor growth in indicated mice treated with PBS (n = 10 for wild-type, n = 8 for *Batf3*$^{-/-}$) or glutamine (n = 9 for wild-type, n = 8 for *Batf3*$^{-/-}$). WT, wild-type. **m**, Growth rate of B16-OVA tumors after transfer of OVA-pulsed cDC1s activated in the presence or absence of glutamine (n = 9 for DCs treated with glutamine, n = 8 for DCs treated without glutamine). Non-transfer control mice (n = 10) received PBS. Data are mean ± s.e.m., except in **i**. **a**, Two-tailed paired Student's t-test. **b**, **c**,**h**,**j**,**k**, Two-tailed unpaired Student's t-test (**b**,**c**, tumor weight). **b–g**,**l**,**m**, Two-way ANOVA for tumor size. **e**, Mantel–Cox test for survival. **i**, Two-tailed Wilcoxon rank sum test. Data are representative of two (**a**,**d–h**,**j**,**l**,**m**) or at least three (**b**,**c**,**k**) independent experiments. *P