ICOS is an inducible T-cell co-stimulator that is structurally and functionally related to CD28/B7-1. ICOS is not expressed on naive T cells but is induced upon T-cell activation.

ICOS regulates both pro- and anti-inflammatory cytokine production by effector and regulatory T cells (Tregs), as well as T-cell proliferation and survival. ICOS is involved in the interaction between T- and B-cells (e.g., class switching), and it mediates responses to T-cell-dependent antigens.

ICOS is differentially expressed on T cell subsets in PBMC and in the tumour microenvironment.

**Figure 1:** (A) ICOS expression in 15 different T cell subsets from NSCLC patients PBMC and tumour samples. (B) The highest incidence of ICOS expression is observed in intratumoral TRegs. (C) MRNA expression of both ICOS and FOXP3 in 15 different tumour types. (D) Correlation between ICOS expression and Foxp3 expression in various tumour types.

**Figure 2:** (A) Tumours with high ICOS expression have different phenotypic characteristics (e.g., increased proliferation and decreased apoptosis). (B) Representative IHC pictures of tumours stained with ICOS (purple staining) and Foxp3 (brown nuclear staining, clone 236A/E7) showing two distinct phenotypes. (C) Tumours with high ICOS expression are typically associated with poor survival in several cancer types such as head and neck, ovarian, hepatocellular carcinoma, and gynecologic cancer (1-4). The preferential high expression of ICOS in intratumoral TRegs makes this protein a strong candidate for a depotting antibody strategy.

We identified and characterized an IgG3 anti-ICOS antibody called KY1044 by demonstrating its capacity to deplete TRegs in vitro and in vivo. We have confirmed that KY1044 improves the TEFF cells to TReg cell ratio by increasing the percentage of ICOS-positive cells. (A) KY1044 treatment of the tumour microenvironment leads to an increase in ICOS-expressing effector CD8+ T-cells and a decrease in ICOS-expressing TRegs.

**Figure 3:** (A) Representative IHC pictures of tumours stained with ICOS (purple staining) and Foxp3 (brown nuclear staining, clone 236A/E7) showing two distinct phenotypes. (B) Tumours with high ICOS expression are typically associated with poor survival in several cancer types such as head and neck, ovarian, hepatocellular carcinoma, and gynecologic cancer. (C) The preferential high expression of ICOS in intratumoral TRegs makes this protein a strong candidate for a depotting antibody strategy.

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**Figure 4:** (A) Representative IHC pictures of tumours stained with ICOS (purple staining) and Foxp3 (brown nuclear staining, clone 236A/E7) showing two distinct phenotypes. (B) Tumours with high ICOS expression are typically associated with poor survival in several cancer types such as head and neck, ovarian, hepatocellular carcinoma, and gynecologic cancer. (C) The preferential high expression of ICOS in intratumoral TRegs makes this protein a strong candidate for a depotting antibody strategy.