**Supplementary figure legends**

**Supplementary figure 1:** Characterization of the cSCC immune infiltrate demonstrates the presence of tumoral Tregs. (A) Haematoxylin and eosin stain and (B) CD3 immunostain of sequential cSCC sections. Boxes show areas which are magnified in figure 1, i.e. (i) = intratumoral, corresponding to figure 1A, (ii) = peritumoral, corresponding to figure 1B. (C) Cells expressing CD4, CD8, CD25 and FOXP3 were present in the tumoral immune infiltrate and (D) Tregs expressed both CD25 (red, membranous) and FOXP3 (brown, nuclear). (E) Flow cytometric quantification of FOXP3+ Treg frequencies in blood and skin lesions in subjects with cSCC, KA and BCC. Scale bars = 50 µm

**Supplementary figure 2:** CLA is expressed by tumoral T cells and Tregs in cSCCs. (A + B) cSCCs from a different subset of patients in a separate institution (Duke University) were analysed for expression of CLA. (A) Representative flow cytometry contour plot showing CLA+ T cells in cSCC. (B) Data demonstrating CLA+ frequency in T cells from normal skin (n=6) and cSCCs (n=12). Horizontal bars = mean. (C) Confocal microscopy of cSCC showing CLA-expressing FOXP3+ tumoral Tregs, scale bars = 50 µm

**Supplementary figure 3:** Blood vessels are located in the peritumoral areas of cSCCs. (A + B) Serial immunofluorescence microscopy sections of 2 different cSCCs showing CD31+ blood vessels located in stroma around islands of tumor keratinocytes as indicated by cytokeratin (CK) 16 positivity, scale bars = 50 µm.

**Supplementary figure 4:** cSCC blood vessels express e-selectin. Immunofluorescence microscopy of sequential cSCC sections demonstrating CD31+ blood vessels expressing e-selectin in peritumoral/stromal areas of cSCC. Arrows denote the same vascular structures on sequential sections, scale bars = 50 µm.

**Supplementary figure 5:** Tumoral Treg suppression of anti-CD3 induced tumoral effector T cell proliferation can be inhibited by anti-OX40. (A) Expression of CD25 and CD127 in sorted tumoral Tregs, showing 99% purity of sorted CD25highCD127low Tregs. (B-C) Tumoral effector T cells were co-cultured in the presence of autologous irradiated PBMCs and 1µg/ml anti-CD3 with/without the addition of tumoral Tregs. Tritiated thymidine uptake was used to assess (B) tumoral CD4+ T cell proliferation, n=4 tumors, (C) tumoral CD8+ T cell proliferation, n=4 tumors, values expressed as normalized to 100% for effector T cells alone. (D) Flow cytometry plots demonstrating OX40 and FOXP3 expression in CD3+CD4+CD25highCD127low gated tumoral lymphocytes from 3 representative cSCCs. (E) Results for experiments shown in figure 5E expressed in cpms. Dots/circles = median values for each tumor with circles for isotype control, squares for anti-OX40, horizontal bar = median for all tumors, error bars = IQR, n=4 tumors. (F) Tumoral CD4+ effector T cells were cultured ± tumoral Tregs ± agonistic anti-OX40 antibody in the presence of anti-CD3, median cpms from triplicate wells shown, n=4 tumors.

**Supplementary figure 6:** Comparison of FOXP3+ Treg frequencies between well differentiated cSCCs (G1) and moderately or poorly differentiated cSCCs (G2-3). (A) Immunohistochemistry of all FFPE cSCCs used in this study. Grey dots indicate cSCCs where metastatic outcome is not known, black dots where metastatic outcome is known. (B) Flow cytometry from fresh cSCCs, in these cases, the 5 year outcome of whether the cSCC has metastasized is currently not known due to insufficient duration of follow up post-operatively. Dots = mean values from 5 HPFs per tumor, horizontal bars = means.