

The diagram illustrates the chemokine network involving CD8+ T cells, malignant cells, TAMs, and activated mDCs. The CD8+ T cell is shown on the left, expressing CXCR3 and CXCR5. The malignant cell is shown at the top right. The TAM is shown on the right. The activated mDC is shown at the bottom. Chemokines are represented by colored circles: CXCL11 (dark blue), CXCL10 (light blue), CXCL9 (green), CXCL13 (red), and XCL1 (yellow). Solid blue arrows indicate chemokine production by the malignant cell and TAM, and chemokine receptor expression by the CD8+ T cell. Solid red arrows indicate chemokine production by the activated mDC and chemokine receptor expression by the CD8+ T cell. Dashed blue arrows indicate chemokine production by the TAM and chemokine receptor expression by the CD8+ T cell. Dashed green arrows indicate chemokine production by the activated mDC and chemokine receptor expression by the TAM. Dashed red arrows indicate chemokine production by the activated mDC and chemokine receptor expression by the CD8+ T cell. Dashed orange arrows indicate chemokine production by the activated mDC and chemokine receptor expression by the CD8+ T cell.

CD8+ T cell in the RCC TME

secretion → IFN γ

IFN α → JAK/STAT signaling

IFN β → JAK/STAT signaling

JAK/STAT signaling → CXCL9/10/11

JAK/STAT signaling → PD-L1/2

CXCL9/10/11 → **recruitment** → CD8+ T cell

PD-L1/2 → **immunosuppression exhaustion** → CD8+ T cell

CD8+ T cell → **secretion** → IFN γ

IFN γ → CD8+ T cell

CD8+ T cell → **recruitment** → CXCL13 & XCL1

CD8+ T cell → **immunosuppression exhaustion** → CTLA4, TNFRSF9, ICOS, TIGIT, TIM3, LAG3

CD8+ T cell → **TRP depletion immunosuppressive TRP decay products** → IDO1

CD8+ T cell → **nutrient competition exhaustion?** → IDO1

IDO1 → **suppressed oxidative energy metabolism**

IDO1 → **immunosuppression exhaustion** → CD8+ T cell