**Supplementary Legends:**

**Supplementary Figure 1. Gating strategy for lymphoid cell identification and quantification in tumor tissue.**

After CT26 tumor tissue dissociation, cells were stained with viability dye (eFluor 780) and anti-CD45, anti-CD3, anti-CD4, anti-CD8, anti-CD25, and anti-Foxp3 antibodies and analyzed by flow cytometry. The frequency among CD45+ TILs of CD8+ T cells (CD45+ CD3+ CD8+), CD4+ T cells (CD45+ CD3+ CD4+), and Treg (CD25high Foxp3+) were analyzed.

**Supplementary Figure 2. Gating strategy for myeloid and tumor cell identification, quantification, and phenotype (PD-L1 expression) in tumor tissue.**

After CT26 tumor tissue dissociation, cells were stained with viability dye (eFluor 780) and anti-CD45, anti-CD11b, anti-Ly6G, anti-Ly6C, anti-F4/80, anti-MHC-II, anti-CD206, and anti-PD-L1 antibodies and analyzed by flow cytometry. The frequency among CD45+ TILs of total TAM (CD45+ CD11b+ Ly6G- Ly6Clow F4/80+), TAM2 (CD45+ CD11b+ Ly6G- Ly6Clow F4/80+ MHC-II- CD206+), TAM1 (CD45+ CD11b+ Ly6G- Ly6Clow F4/80+ MHC-II- CD206+), PNN-MDSC (CD45+ CD11b+ Ly6G+), and Mo-MDSC (CD45+ CD11b+ Ly6G- Ly6C+ F4/80- ) were analyzed. PD-L1 expression was analyzed for each myeloid population and for CD45- cells, considered to be mostly tumor cells.

**Supplementary Figure 3. Gating strategy for the quantification of functional lymphoid cells in tumor tissue.**

After CT26 tumor tissue dissociation and stimulation with PMA/ionomycin for 4 h, cells were stained with viability dye (eFluor 780) and anti-CD45, anti-CD3, anti-CD8, anti-IFNγ, and anti-TNFα antibodies and analyzed by flow cytometry. The frequency of IFNγ+ and TNFα+ CD8+ TILs (CD45+ CD3+ CD8+) were analyzed.

**Supplementary Figure 4. FTD/TPI synergizes with oxaliplatin to induce immunogenic cell death *in vitro*.**

**A.** CT26 cells were treated with various doses of OxPt (5, 10, 25, 50 or 100 µM), FTD/TPI (5, 10, 25, 50 or 100 µM), or a combination of these two drugs for 24 h and viability assessed by crystal violet assay (left). A heat map corresponding to the crystal violet results, showing the percentage of adherent cells as a function of dose, is shown on the right.

**B.** CT26 cells were treated with various doses of OxPt (5, 10, 25, 50 or 100 µM), FTD/TPI (5, 10, 25, 50 or 100 µM), or a combination of these two drugs for 24 h and cell death analyzed by flow cytometry following Annexin-V/7-AAD staining (above). Representative contour plots are shown on the left. A plot showing the percentage of cell death (AV+ 7AAD+ and AV+ 7AAD- cells) is shown on the right.

Representative data from three independent experiments are shown (mean and SD).

n.s, not significant; \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001, £££p < 0.001 (*versus* untreated cells). Data sets were compared using an unpaired Mann-Whitney Wilcoxon test.

**Supplementary Figure 5. FTD/TPI synergizes with oxaliplatin to induce immunogenic cell death *in vitro*.**

**A.** Mutational status of three human MSS colorectal cancer cell lines: Caco-2, Colo-320, and SW620.

**B.** Caco-2, Colo-320, and SW620 cells were treated with various doses of OxPt (5, 10, 25, 50 or 100 µM), FTD/TPI (5, 10, 25, 50 or 100 µM), or a combination of these two drugs for 48 h and viability assessed by crystal violet assay (above). Heat maps corresponding to the crystal violet results, showing the percentage of adherent cells as a function of dose, are shown below.

**C.** Caco-2, Colo-320, and SW620 cells were treated with various doses of OxPt (5, 10, 25, 50 or 100 µM), FTD/TPI (5, 10, 25, 50 or 100 µM), or a combination of these two drugs for 48 h and cell death analyzed by flow cytometry following Annexin-V/7-AAD staining (above). Plots showing the percentage of cell death (AV+ 7AAD+ and AV+ 7AAD- cells) are presented below.

Representative data from three independent experiments are shown (mean and SD).

n.s, not significant; \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001, £££p < 0.001 (*versus* untreated cells). Data sets were compared using an unpaired Mann-Whitney Wilcoxon test.

**Supplementary Figure 6. The FTD/TPI and oxaliplatin combination induces a CD8+ T-cell immune response.**

CT26-tumor bearing mice (n = 5/group) were treated with 0.5% HPMC solution (control), Ox-Pt (5mg/kg), FTD/TPI (150 mg/kg/day), or a combination of Ox-Pt and FTD/TPI and tumors are harvested eight days after treatment.

The frequency of CD8+ cells analyzed by immunohistochemistry at the invasive margin and tumor core for each tumor group and representative images of CD8 staining and representative phenotype maps for each group are presented.

**Supplementary Figure 7. The FTD/TPI and oxaliplatin combination induces a CD8+ T-cell immune response.**

CT26-tumor bearing mice (n = 5/group) were treated with 0.5% HPMC solution (control), Ox-Pt (5mg/kg), FTD/TPI (150 mg/kg/day), or a combination of Ox-Pt and FTD/TPI and tumors are harvested eight days after treatment.

Pathologist view of Inform program converted CD8/DAPI staining as an “H-DAB” staining. Co-localization of CD8 positive T cells stained in brown and with small nuclei and tumor cells detecting with large and heterogeneous nuclei morphology can be highlighted.

**Supplementary Figure 8. Comparison of the FTD/TPI or 5-FU with oxaliplatin combination on myeloid cell tumor infiltration.**

CT26-tumor bearing mice (n = 5/group) were treated with 0.5% HPMC solution (control), Ox-Pt (5mg/kg) and FTD/TPI (150 mg/kg/day) or Ox-Pt (5mg/kg) and 5-FU (50 mg/kg) and tumors are harvested eight days after treatment.

Frequency of PNN-MDSC, Mo-MDSC, total TAM, TAM1 and TAM2 among CD45+ TILs was measured by flow cytometry in each control or treated group of mice.

**Supplementary Figure 9. The FTD/TPI and oxaliplatin combination induces a CD8+ T-cell immune response.**

Correlation analysis between the functional parameters of CD8+ TILs and immunosuppressive populations. The Spearman R factor (heat map on the left) is associated with the corresponding p-value (heat map on the right).

**Supplementary Figure 10. TAM depletion with liposome clodronate induces a CD8+ T-cell immune response.**

CT26-tumor bearing mice (n = 5/group) were treated with a liposome control or liposome clodronate (5 mg/kg/day) and tumors are harvested eight days after treatment.

**A.** Bar graph comparing tumor size at the time of tumor recovery.

**B.** Frequency of total TAM, TAM1, and TAM2 among CD45+ cells measured by flow cytometry in control and treated groups of mice.

**C.** Frequency of CD8+ TILs among CD45+ cells measured by flow cytometry in control and treated groups of mice.

**D.** Frequency of IFNγ+ and TNFα+ CD8+ cells measured by flow cytometry in each control and treated group of mice.

n.s, not significant; \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001. Data sets were compared using an unpaired Mann-Whitney Wilcoxon test.

**Supplementary Figure 11. Toxicity evaluation of chemo immunotherapy association in CT26 model.**

Mice weight is shown and each line represents an individual mouse during CT26 tumor growth monitoring under control (0.5% HPMC solution), OxPt (5mg/kg) + FTD/TPI (150 mg/kg/day), or Ox-Pt + FTD/TPI + anti-PD-1 treatment.

**Supplementary Table 1. List of mouse primers used for mRNA relative expression**

**Supplementary Table 2. List of antibodies used for identification of myeloid and lymphoid cells and for the study of lymphoid function**