**SUPPLEMENTARY LEGENDS**

**Supplementary Figure 1.** Flow cytometric analysis of purity of neutrophil isolation technique from bone marrow of mice.

**Supplementary Table 1.** Baseline characteristics of patients undergoing hepatectomy.

**Supplementary Figure 2. (A)** HIF-1α and cit-H3 levels were also measured using Western blot analysis in paired recurrent mCRC samples and their non-tumor counterparts. Similar to the findings in the mice model, in human also there is increased NET formation within the hypoxic tumors (N, nontumor liver; T, Tumor). Selected samples ae representative of 15 unique paired samples. **(B)** CFSE-labelled Hepa1-6 murine hepatocellular cancer cell line demonstrated increased adhesion to neutrophil monolayers stimulated with PMA (100nM) compared with unstimulated neutrophils. Addition of DNAse results in adhesion levels comparable to control. P<0.001 versus control, DNAse. **(C)** MTT assay show increased tumor proliferation at 48 hours after culturing Hepa1-6 cells with media from PMA-stimulated neutrophils (NM). Addition of DNAse results in proliferation levels similar to control. \*P<0.001 versus control, DNAse groups. **(D)** Hepa1-6 cell migration through 8-µm PET membranes and invasion through Matrigel was significantly increased in the presence of media from PMA-stimulated neutrophils (NM) compared with MC38 alone. This was reversed back to control values with the addition of DNAse to the stimulated media. **(E)** Messenger RNA levels of IL-6, a protumorigenic downstream product of MAP kinase activation, was significantly elevated in the MC38 cells cultured in NM and decreased in the groups treated with DNAse or knocked down of TLR9. **(D)** Detection of serum HMGB1 levels in mCRC patients undergoing major (n=35) or minor liver surgery (n=15). Box plots show higher HMGB1 levels in mCRC patients undergoing major resection. \*P<0.001 versus control and NM+DNAse. Data are presented as mean±SEM from n=3 separate experiments.

**Supplementary Figure 3.** Schematic diagrams of the proposed role of NETs in the progression of metastatic disease after surgical stress. **(A)** Acute and chronic ischemic conditions induce neutrophils to form NETs that play an important role in the establishment and growth of metastases **(B)** NETs increase tumor progression by activation TLR9 dependent growth signaling pathways inside tumor cells.