**Supplementary Figure legends**

## Supplementary Figure 1

**(A)** Detection of ctDNA in pre-operative plasma samples according to stage. ctDNA can be detected in pre-operative plasma samples at all stages of CRC. The fraction of plasma samples positive for ctDNA increases with increasing disease stage. **(B)** Boxplot of the levels of cfDNA analyzed per SSV in ctDNA-positive and -negative pre-operative plasma samples. **(C)** Elevated levels of CEA in pre-operative plasma sample according to stage. Elevated levels of CEA can be detected at all stages of CRC. However, no association between CEA level and disease stage was observed. **(D)** Boxplot of the number of GE analyzed per SSV in patients with and without relapse of disease.

## Supplementary Figure 2

**(A)** Comparison of the time to relapse detection using CEA and standard-of-care CT imaging for fourteen relapse patients. The analysis showed that the average time to relapse was 12.3 months for CEA and 16.9 months for CT-imaging. Notice: In two cases, CEA detected relapse after standard-of-care CT-imaging and for three other patients CEA was not detected above threshold in any serum sample, hence CEA did not detect relapse in these cases. **(B)** Comparison of lead time using ctDNA and CEA in fourteen relapse patients. (Left panel) Lead times obtained using ctDNA and CEA in individual patients. (Right panel) Boxplots of lead time obtained when using ctDNA and CEA. *P*-values,Wilcoxon signed rank test.

## Supplementary Figure 3

Changes in ctDNA levels after local or systemic interventions such as surgery or chemotherapy divided into response and non-response groups.

## Supplementary Figure 4

Comparison of serial ctDNA analysis performed using SSV and SPM ddPCR assays.