

560 **Figure S1. Haematoxylin and eosin stainings of tumor organoids and original mismatch repair**
561 **deficient colorectal cancers**, related to Figure 1.

562 Excised tumor pieces or tumor organoids derived thereof were fixed, paraffin-embedded and stained with
563 haematoxylin and eosin. Inserts show higher magnification images of boxed area. Scale bar = 50 μ m.

564

565 **Figure S2. MHC-I expression of mismatch repair deficient colorectal cancer organoids and original**
566 **tumors**, related to Figure 1.

567 (A) Cell surface MHC-I expression of mismatch repair deficient colorectal cancer organoids as
568 determined by flow cytometry. Organoids were stimulated with 200 ng/mL IFN γ for 24 hours or left
569 unstimulated. Histograms indicate fluorescence intensity of anti-HLA-A,B,C-PE or isotype control
570 antibodies.

571 (B) Excised tumor pieces were fixed and paraffin-embedded, and sequential slides were stained with
572 HCA2 and HC10 antibodies against MHC-I. Representative staining of MHC-I proficient (CRC-6M) and
573 deficient (CRC-4) tumors. CRC-4 shows positive MHC-I staining in stroma but absence of signal in the
574 tumor mass. CRC-6M contains MHC-I positive tumor cells grouped in islands. Scale bar = 100 μ m.

575

576 **Figure S3. Haematoxylin and eosin stainings of tumor organoids and original non-small cell lung**
577 **cancers**, related to Figure 3.

578 Excised tumor pieces or tumor organoids derived thereof were fixed, paraffin-embedded and stained with
579 haematoxylin and eosin. Inserts show higher magnification images of boxed area. Scale bar = 50 μ m.

580

581 **Figure S4. CD4⁺ reactivity against Geltrex**, related to Figure 5.

582

583 Quantification of CD137⁺ CD4⁺ T cells after stimulation of T cells with organoids cultured under
584 standard conditions (with Geltrex), cultured for 3 days without Geltrex, or cultured for 3 days without
585 Geltrex with Geltrex re-introduced 1 day before T cell challenge. T cells were obtained by two week co-
586 culture with autologous tumor organoids and where indicated (lower case e) further expanded using a
587 rapid expansion protocol (Dudley et al. 2013), in some cases preceded by CD137-based enrichment of
588 tumor-reactive cells (indicated by upper case E). Error bars indicate s.e.m. of at least 2 biological
589 replicates.

590 **Figure S5. Time course imaging of NSCLC-3 organoids targeted by tumor-reactive T cells**, related
591 to Figure 6.

592 Microphotograph images of NSCLC-3 organoids at indicated time points of culture with or without T
593 cells in the presence of a green-fluorescent caspase 3/7 probe. Where indicated, MHC-I and MHC-II were
594 blocked with W6/32 and Tü39 antibodies, respectively. T cells are obtained by two weeks of co-culture
595 with autologous tumor organoids followed by rapid expansion (indicated by upper case e).

596

597

Figure S1

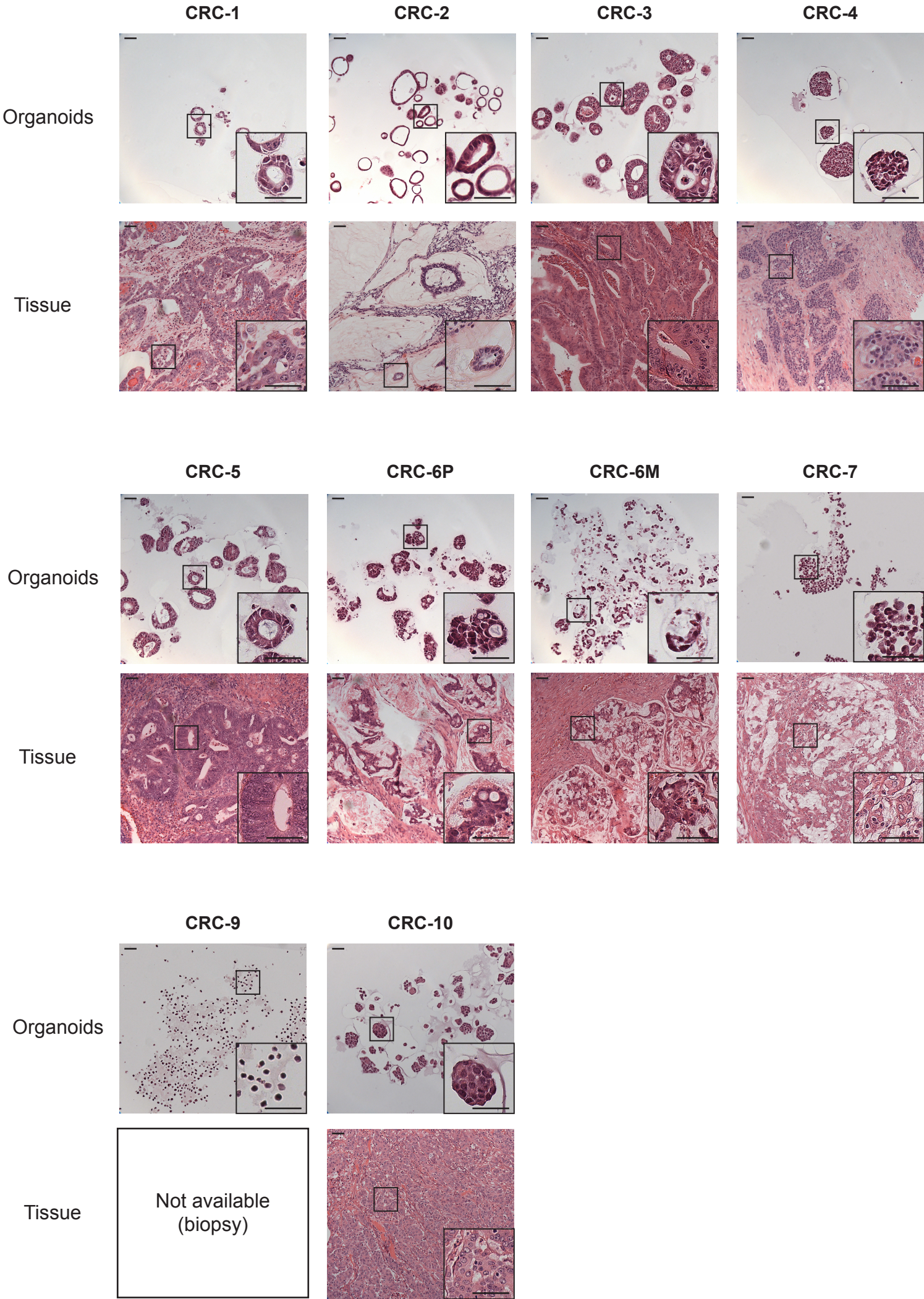
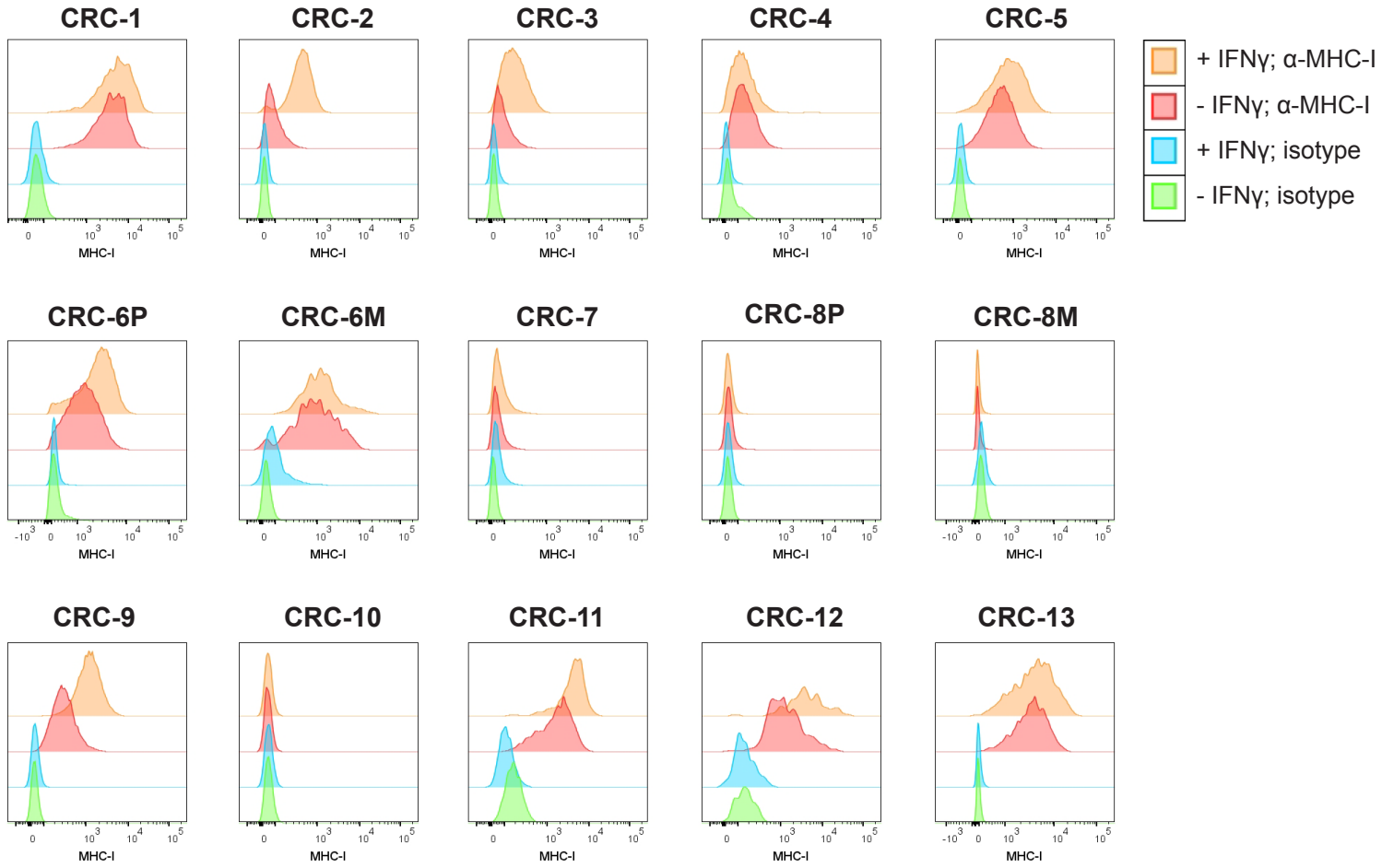


Figure S2

A



B

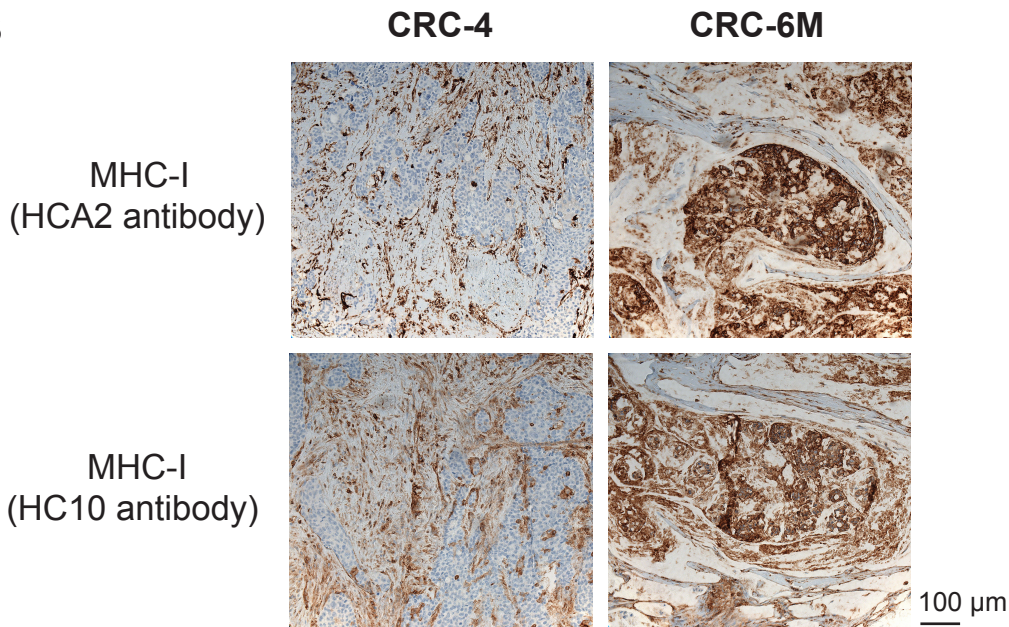


Figure S3

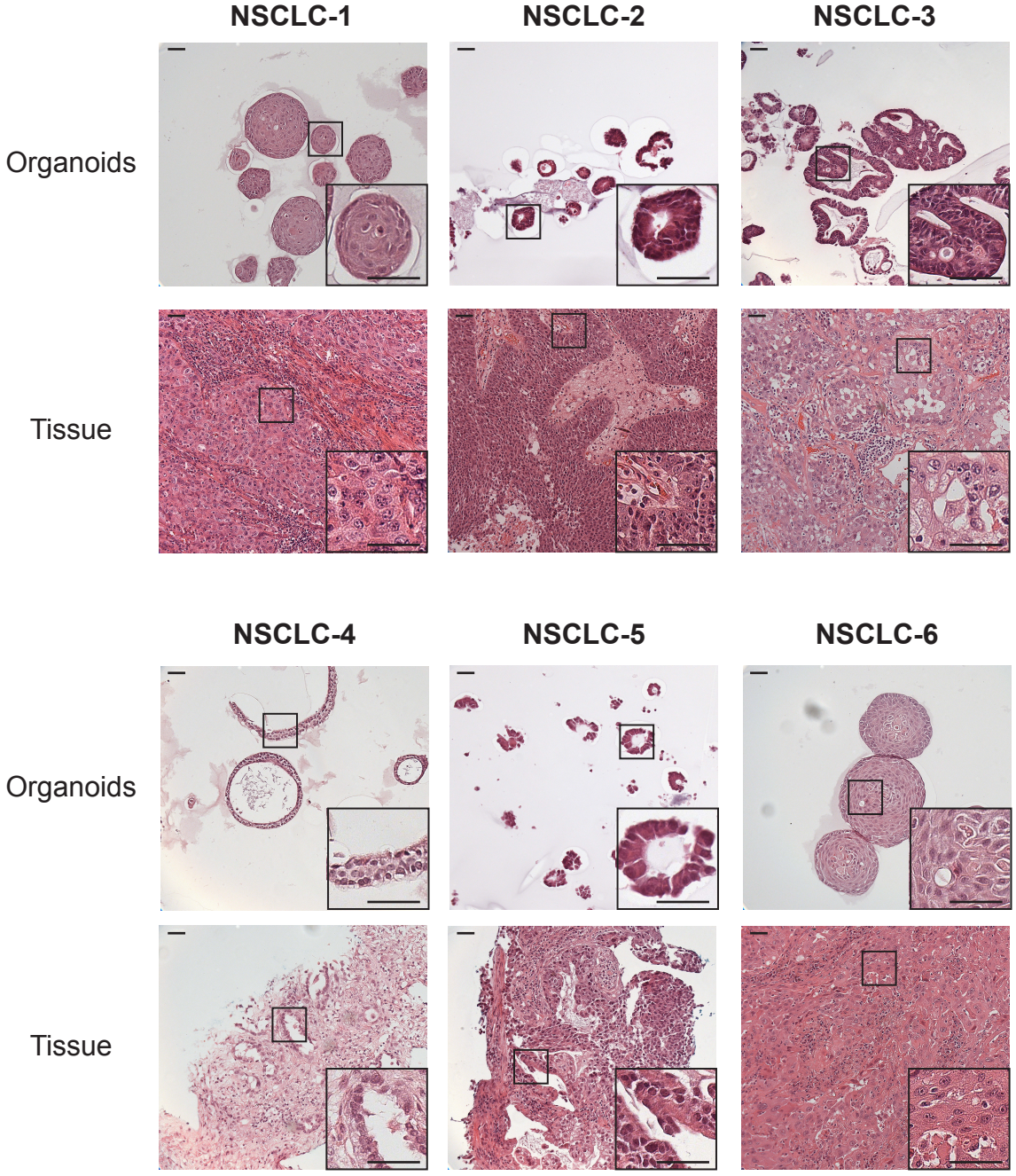


Figure S4

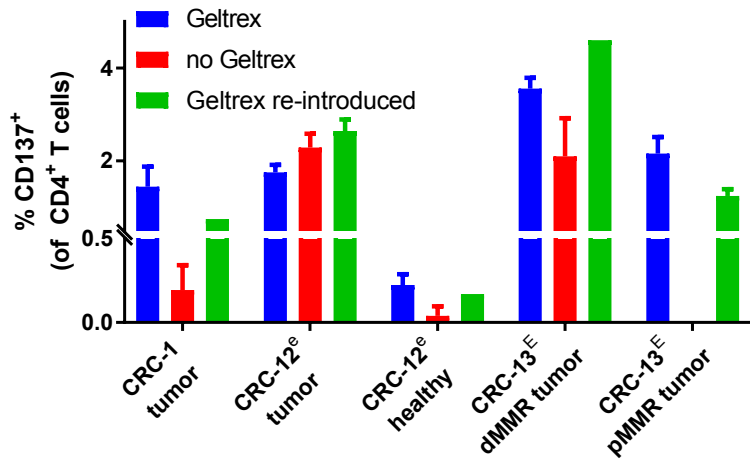


Figure S5

