

Latency and interval therapy affect the evolution in metastatic colorectal cancer

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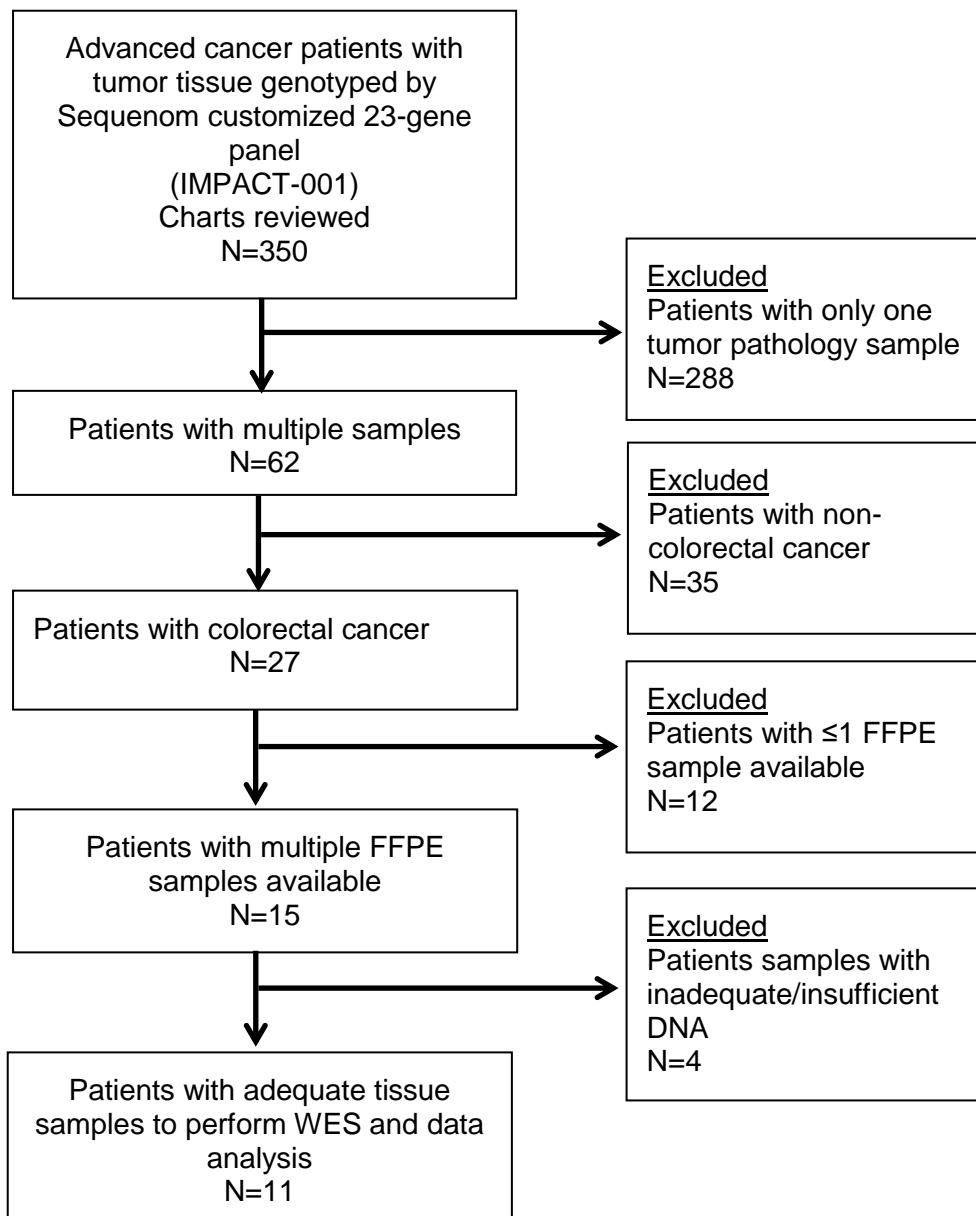
Yasser Riazalhosseini

Department of Human Genetics,

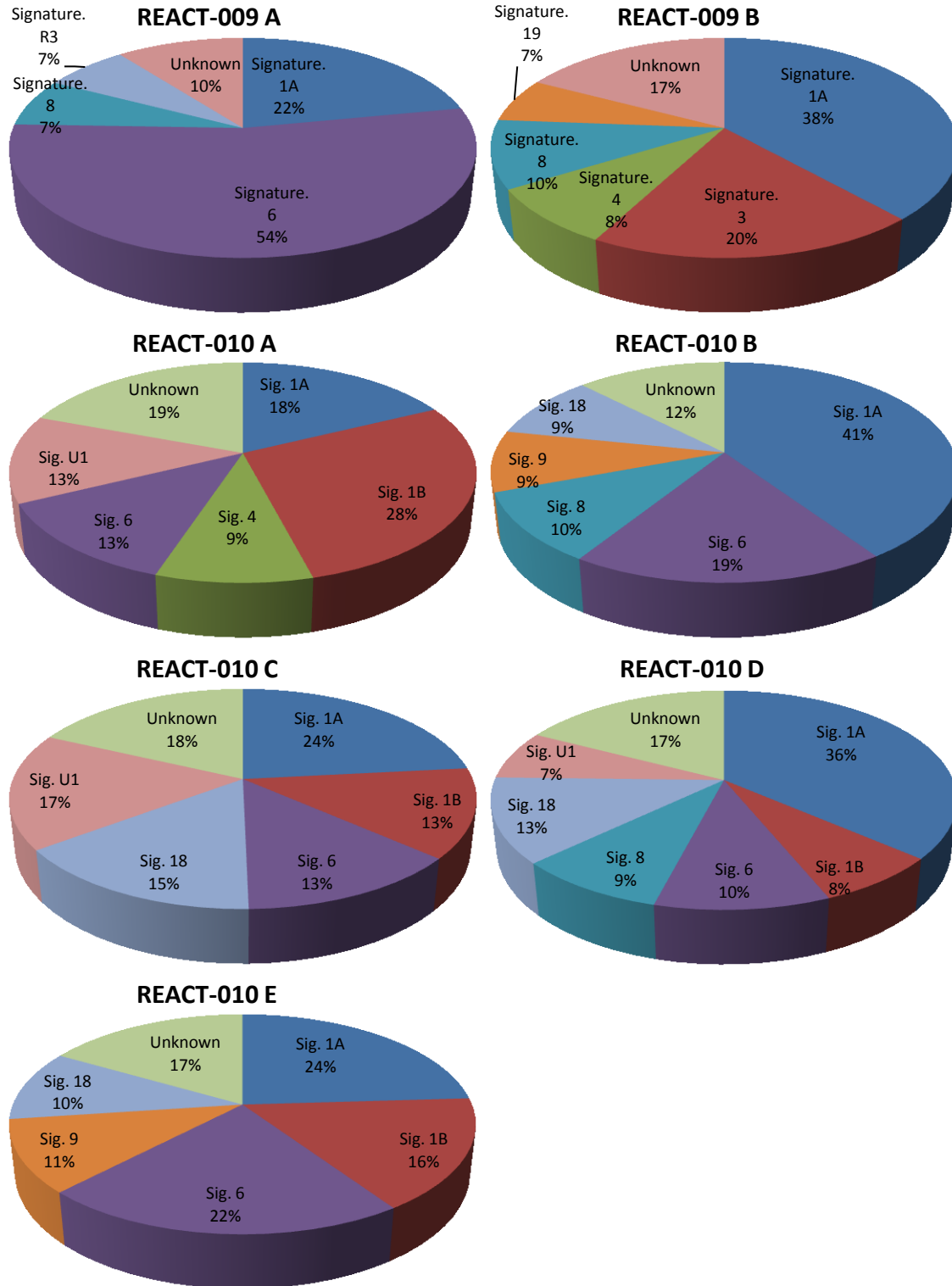
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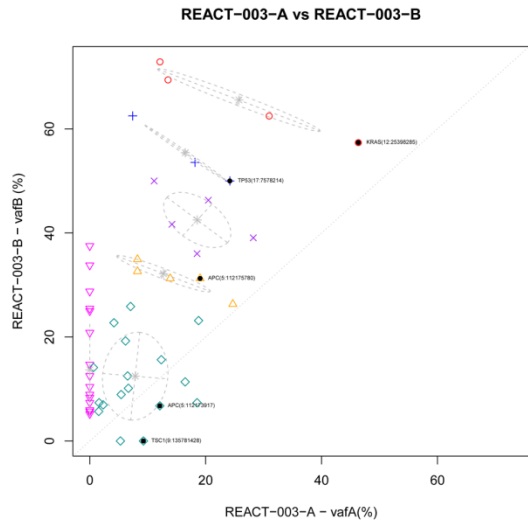
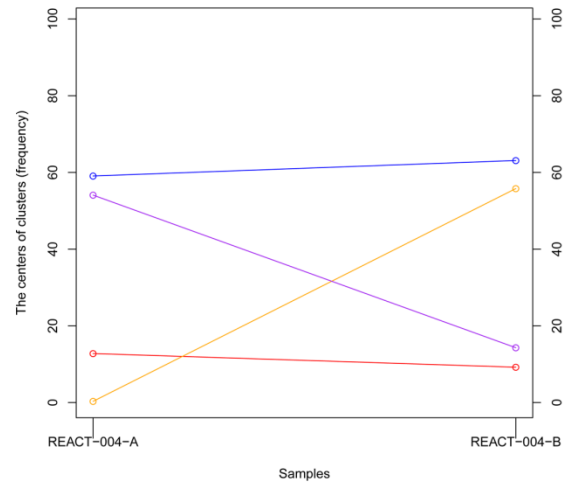
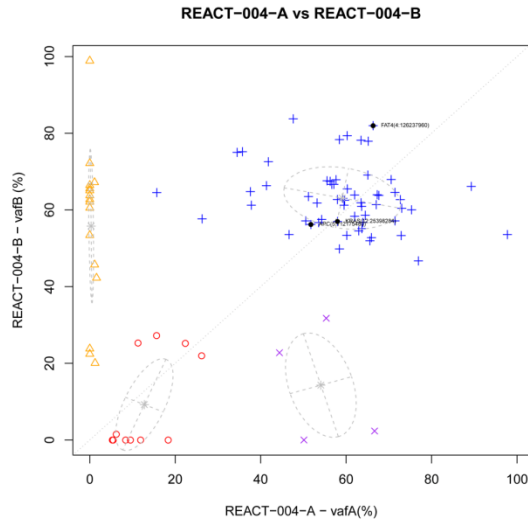
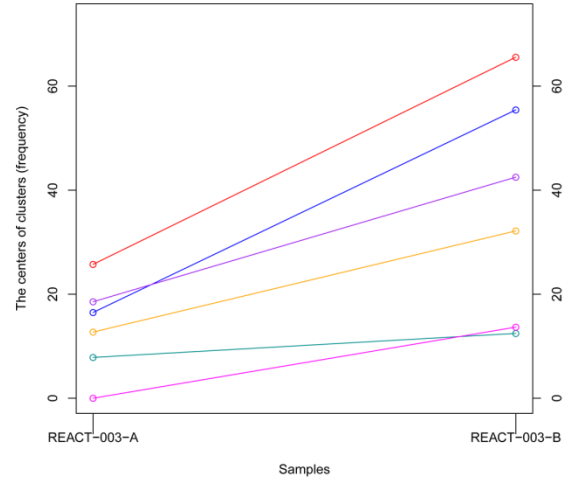
Supplementary Figure 1. CONSORT diagram showing patient selection.



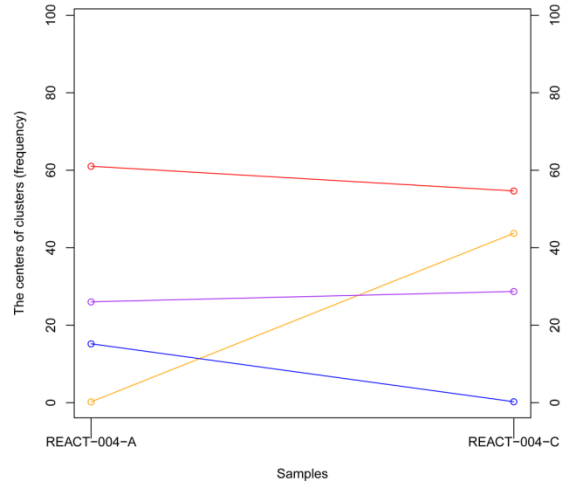
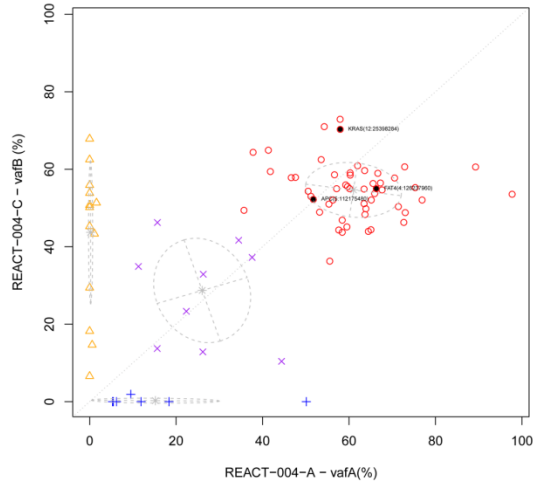
FFPE = formalin-fixed paraffin-embedded; WES = Whole exome sequencing



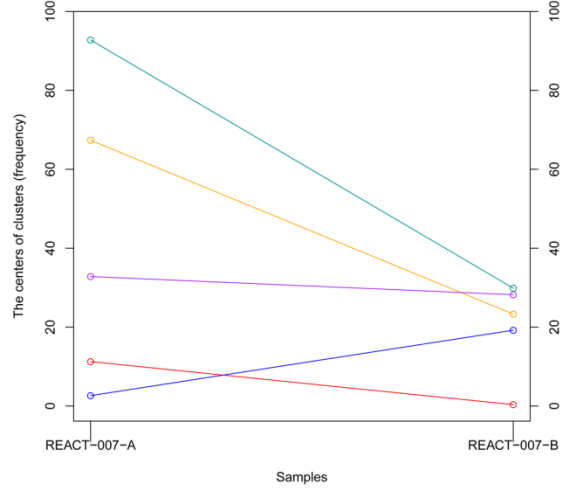
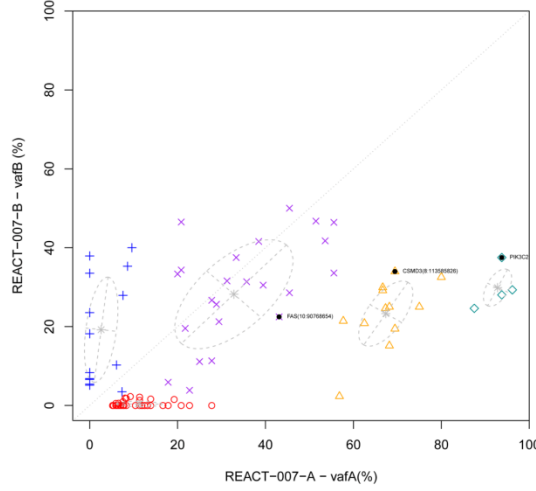
Supplementary Figure 2) Mutation signature in two patients REACT009 and REACT010 and their metastatic lesions

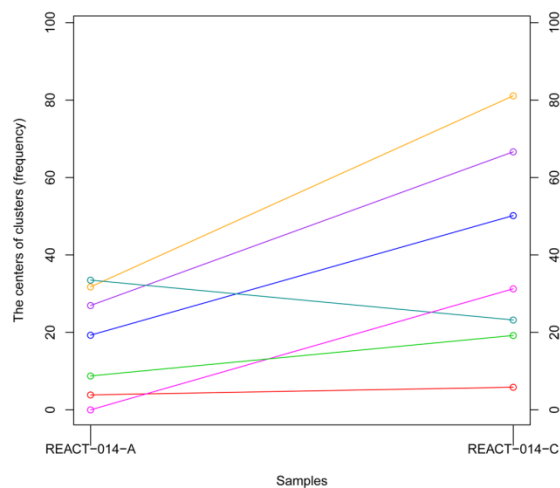
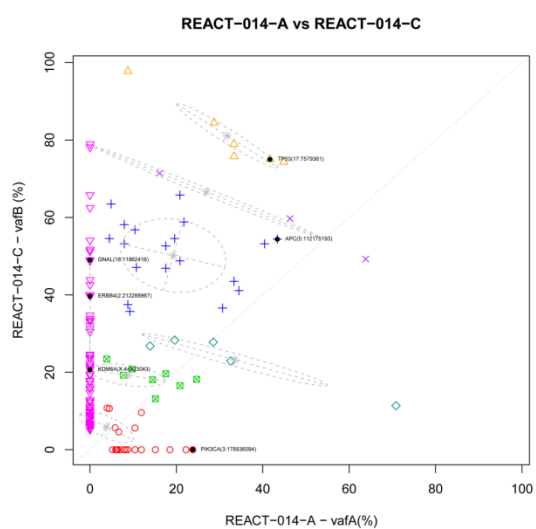
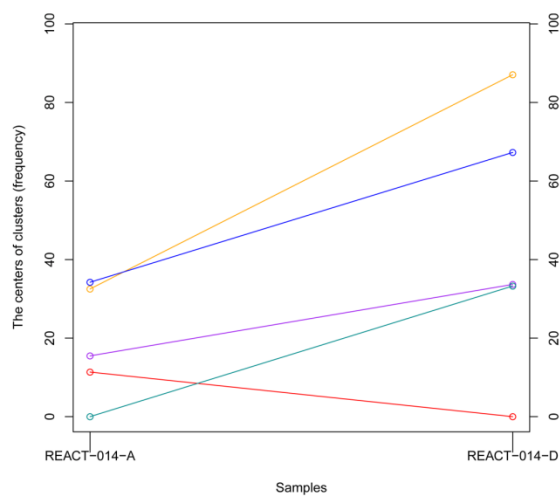
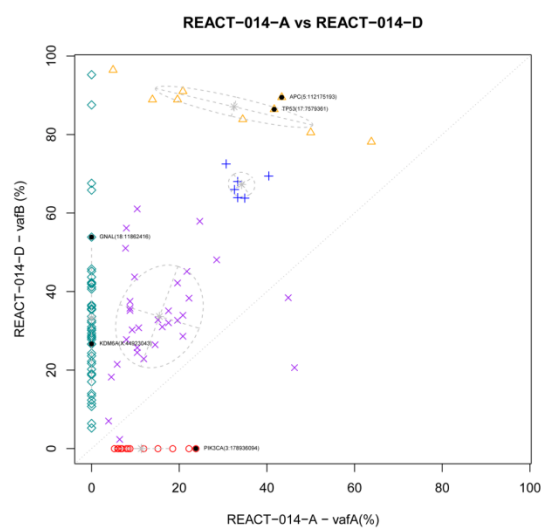
A)**B)**

REACT-004-A vs REACT-004-C



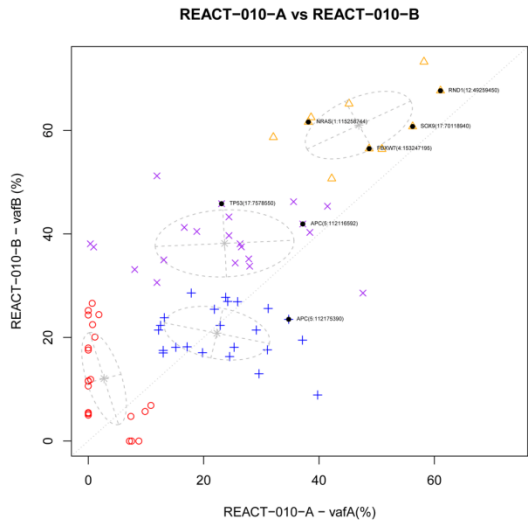
REACT-007-A vs REACT-007-B



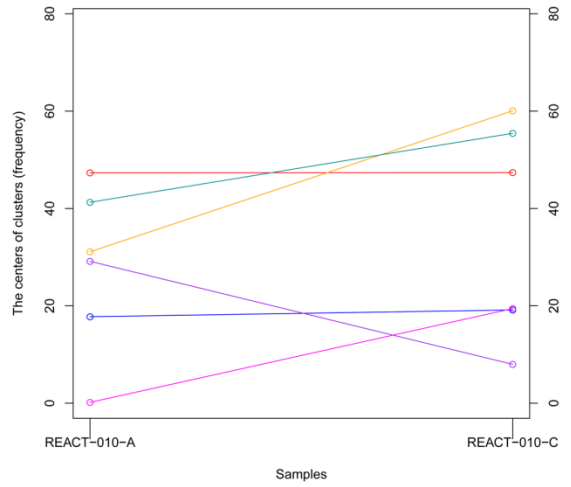
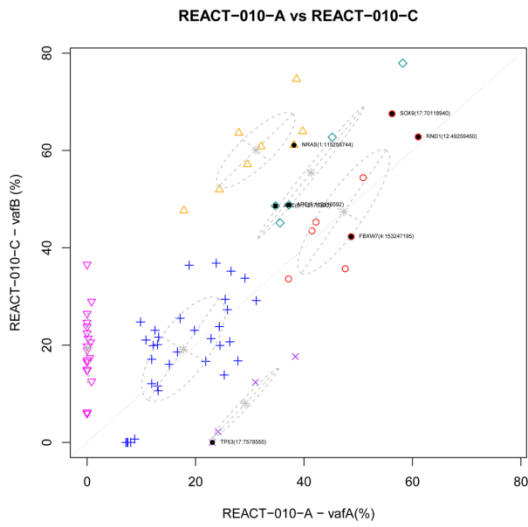
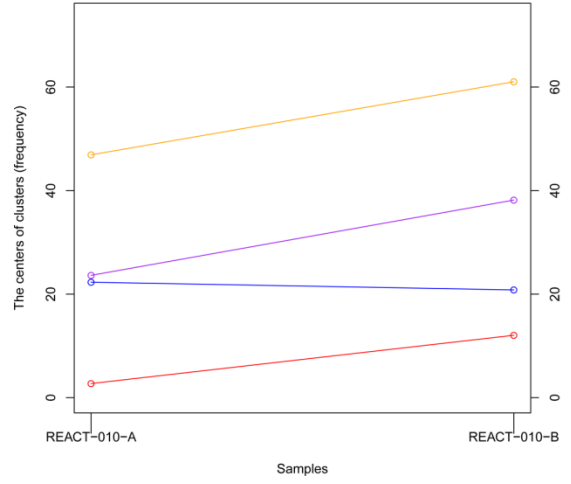


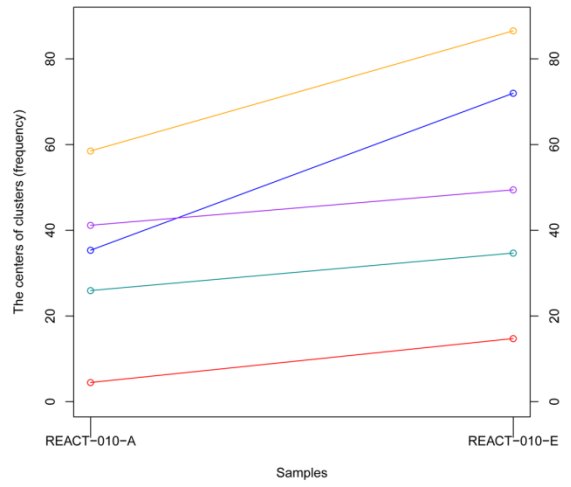
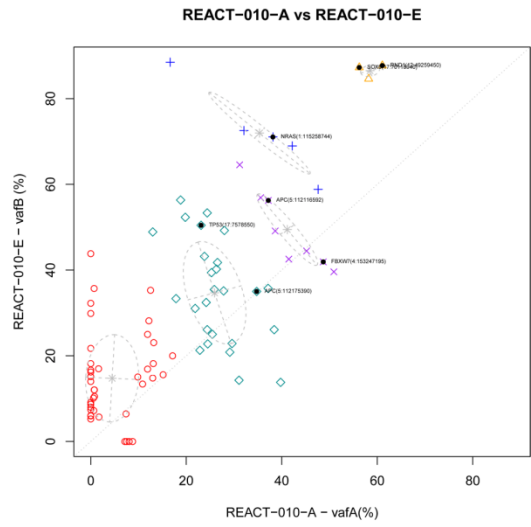
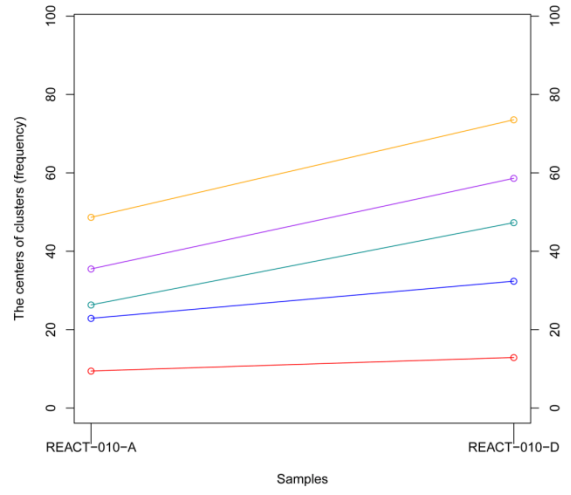
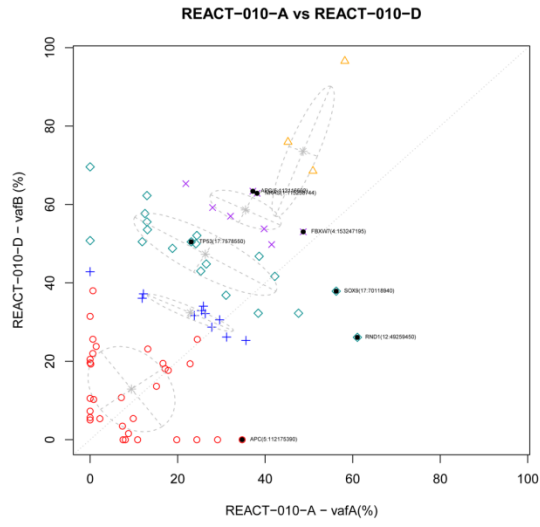
Supplementary Figure 3) A) Clustering of the mutations between the primary and different metastatic lesions in other patients with primary tumor **B)** Changes in the cell population proportions in different clusters between primary and different metastasis in these patient

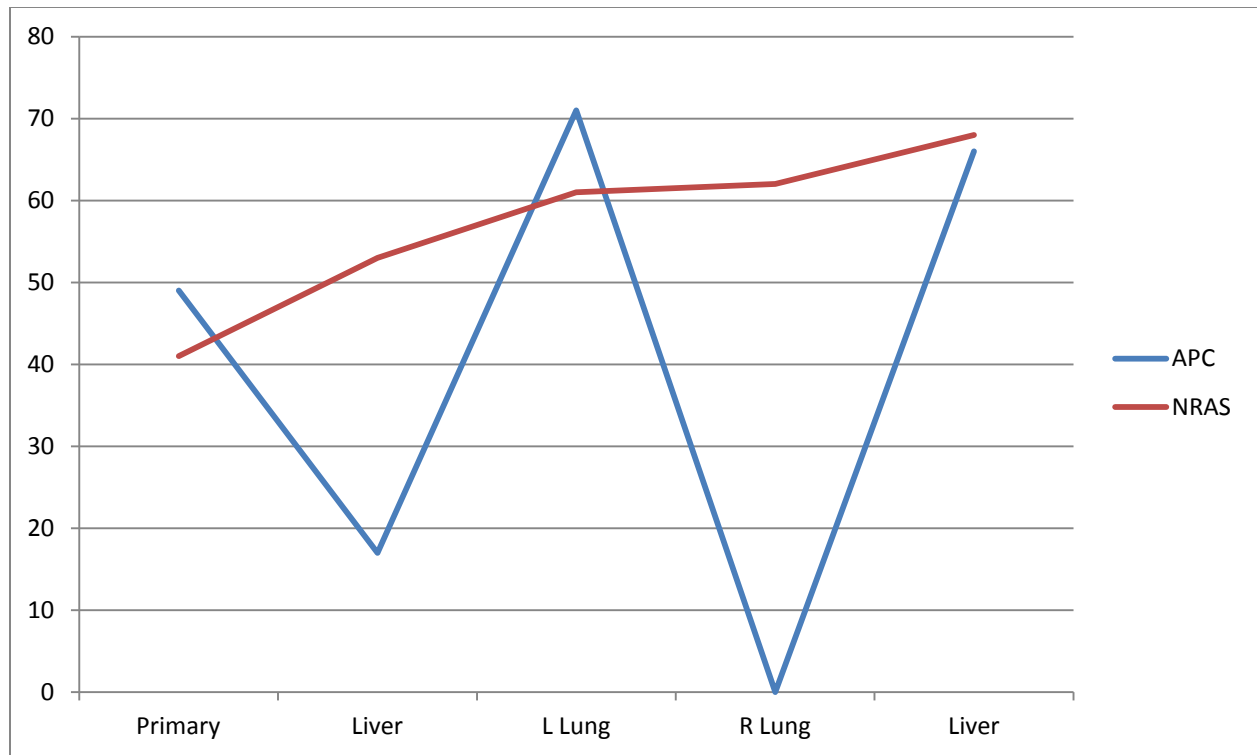
A)



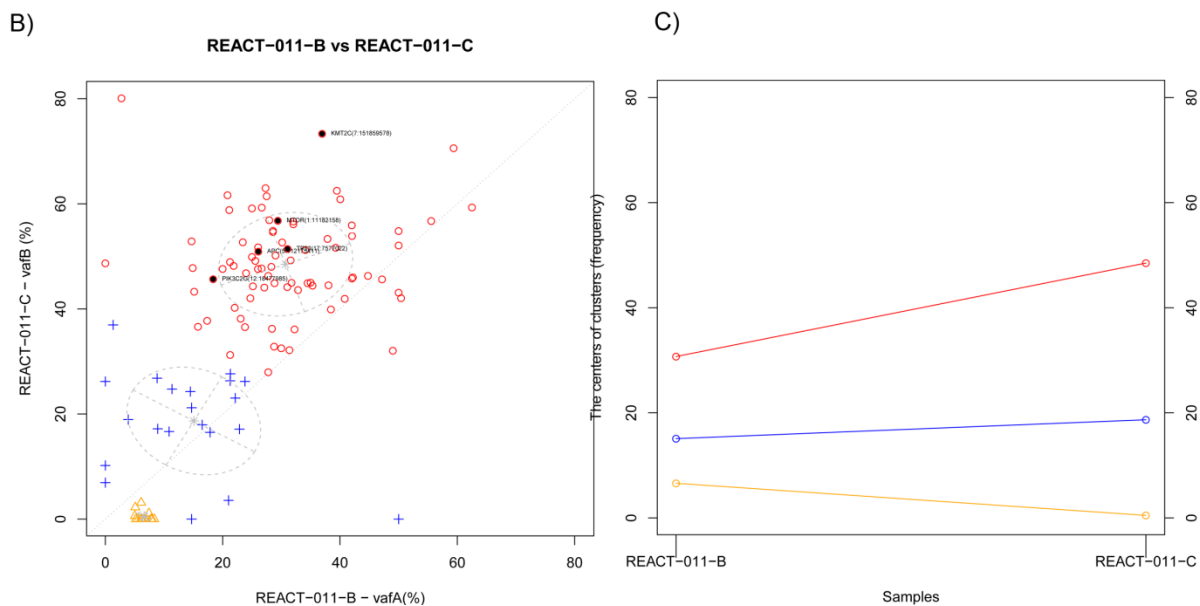
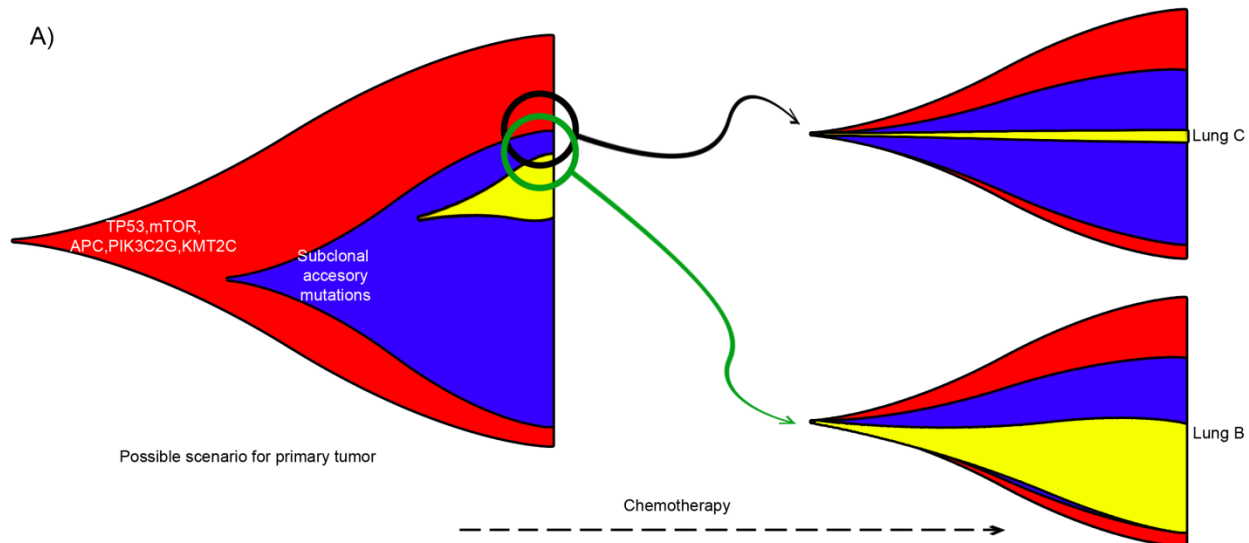
B)







Supplementary Figure 4) A) Clustering of the mutations between the primary and different metastatic lesions in patient REACT-010 B) Changes in the cell population proportions in different clusters between primary and different metastasis in this patient. C) Deep sequencing results shows an enrichment of NRAS codon 13 mutated cells emerging in metastatic disease following administration of interval systemic chemotherapy. Interestingly between left Lung and right Lung that there were no chemotherapy administration, the rate of the increase has slowed down.



Supplementary Figure 5) A) Proposed scenario for the evolution within the primary and metastatic lesion in patient REACT-011 B) Clustering of the mutations between the primary and metastatic lesions C) Changes in the cell population proportions in different clusters between primary and metastasis