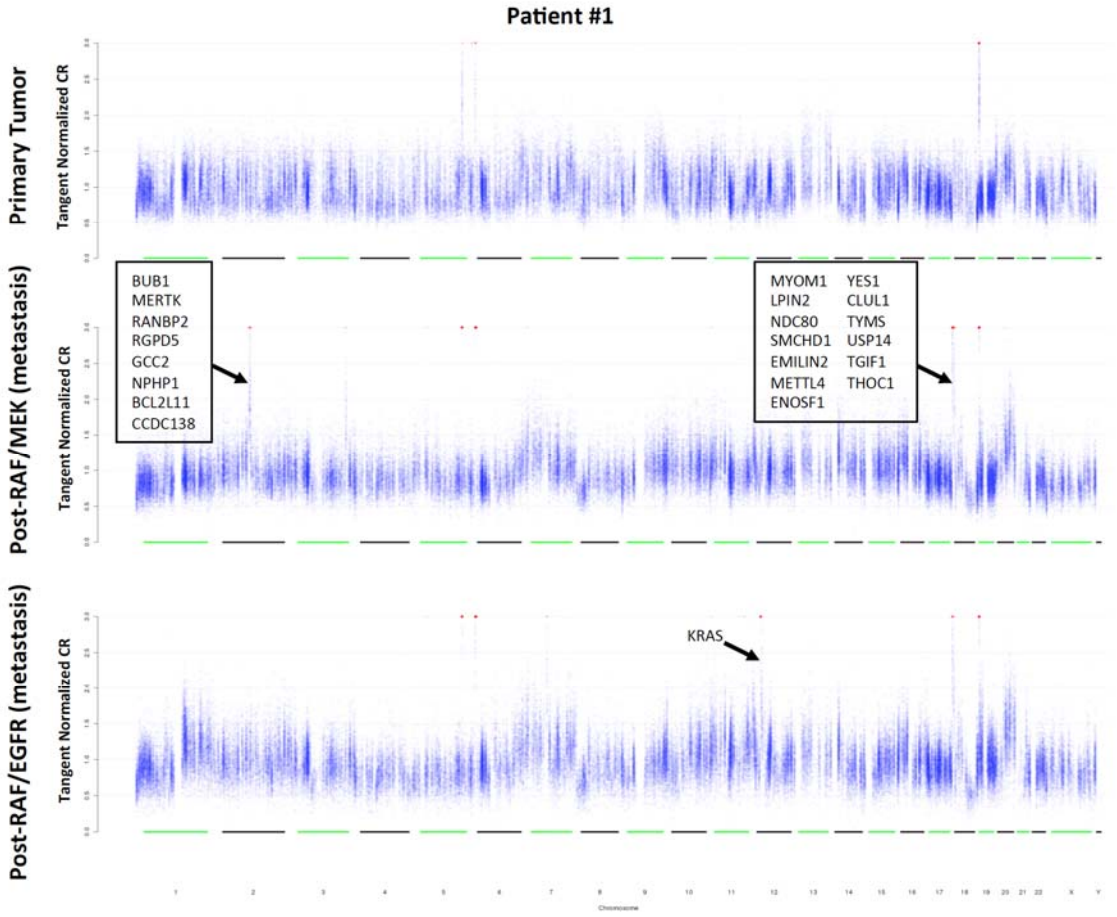

Fig. S3: Copy number alterations for Patient #1. DNA copy number traces for Patient #1 are shown for the primary tumor, a biopsy of a metastatic lesion taken upon progression on combined RAF/MEK inhibitor therapy, and a biopsy of a different metastatic lesion taken upon progression on combined RAF/EGFR inhibitor therapy. As shown in Fig. 2, *KRAS* amplification on chromosome 12 was identified in the post-RAF/EGFR biopsy from this patient. By contrast, no clear resistance mechanism was identified in the post-RAF/MEK biopsy. A chromosome 2 amplicon present only in the post-RAF/MEK biopsy that may be involved in resistance was identified, and the genes contained within that chromosome are shown. A chromosome 18 amplicon was also identified, and the genes contained within that amplicon are also shown. While it is possible that the chromosome 18 amplicon might be involved in resistance, the same amplicon is present in the post-RAF/MEK and post-RAF/EGFR biopsies that were taken from distinct metastatic lesions. Thus, it is perhaps more likely that this amplicon was present in a common founding metastatic clone from which each lesion was derived, though no definitive conclusions can be made.