**Introduction:** Bowel cancer is the second biggest cancer killer in Australia with over 4000 death from the disease yearly. It is a heterogenous disease and subtyping cancer types into more homogenous subgroups is used to determine appropriate treatment for patients and associated with better survival rates. For bowel cancer a few molecular alterations have made it into clinical practice, however accurate subgrouping has not yet made it to clinical applicability for this cancer type. Around 40% of patients with bowel cancer have a mutation in the KRAS gene, which is a gene found in the MAPKinase pathway, a pathway commonly altered in many cancer types. These patients are not only excluded from receiving anti-EGFR therapy such as cetuximab in the metastatic setting but also have a markedly variable and unpredictable response to standard chemotherapy regimens. The purposes of this study was to identify whether KRAS mutant bowel cancer could be further subtyped in more homogenous groups.

**Methodology:** We analysed transcriptomic data of 481 KRAS mutant cancers from seven independent cohorts including a TCGA discovery cohort (n=162) and an Affymetrix U133 Plus 2.0 array validation cohort (n=319 samples). Data was normalized for batch artifacts using the COMBAT R package and gene expression (KM) subtypes identified by non-negative matrix factorization. Samples were CMS classified using the CMSCaller R package. We performed single sample gene set enrichment (ssGSEA) projections to assess pathway level differences. We also compared clinico-pathological and molecular correlates. We used the Limma R package for statistical analyses of ssGSEA data and X2 or students T-tests for clinical data.

**Results:** KRAS mutant colorectal cancers segregated based on transcriptional signatures into two subgroups which we have termed KRAS-mutant-cluster-1/KM1 and KRAS-mutant-cluster-2/KM2. We observed a significantly reduced 5 year overall survival rate for patients with KM2 cancer compared to those with a KM1 cancer (Cox proportional hazard P<0.03). Our single sample gene set enrichment analysis (ssGSEA) highlighted differences based on KM clusters such as EMT activation and TGF-beta activation.

**Conclusion:** Here we show striking segregation of KRAS mutant cancers into two subgroups, KM1 and KM2. This is a step towards more accurate bowel cancer subtyping with the intention to guide prognosis, aid prediction of treatment response to currently available agents, and provide novel targets for adjuvant therapy.