In silico association of mutation profiles with drug sensitivity in consensus molecular subtypes of colorectal cancer

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INTRODUCTION

CMS1 MSI immune	CMS2 Canonical	CMS3 Metabolic	CMS4 Mesenchymal
14%	37%	13%	23%
MSI, CIMP high, hypermutation	SCNA high	Mixed MSI status, SCNA low, CIMP low	SCNA high
BRAF mutations		*KRAS* mutations	
Immune infiltration and activation	WNT and MYC activation	Metabolic deregulation	Stromal infiltration, TGF-β activation, angiogenesis
Worse survival after relapse			Worse relapse-free and overall survival

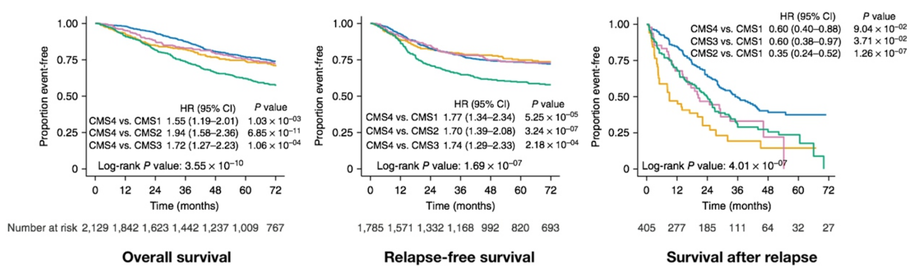
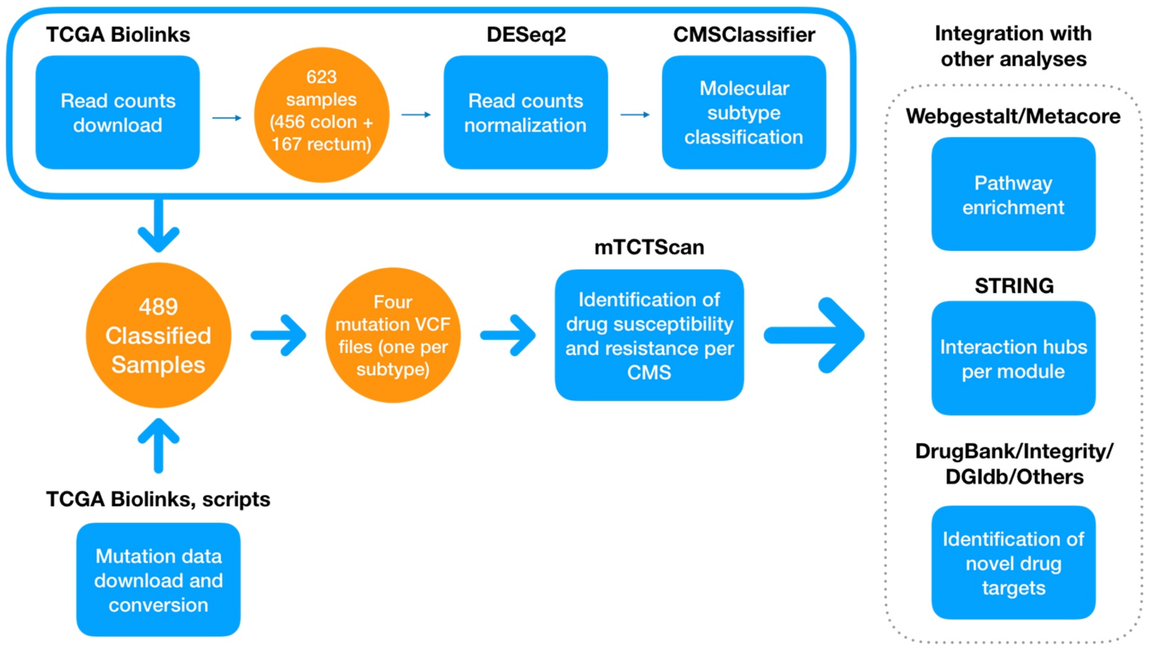


Figure 1 – Consensus molecular subtypes (CMS) characteristics and survival rates for each of them. Adapted from Guinney et al. (2015)[1].

METHODOLOGY



RESULTS

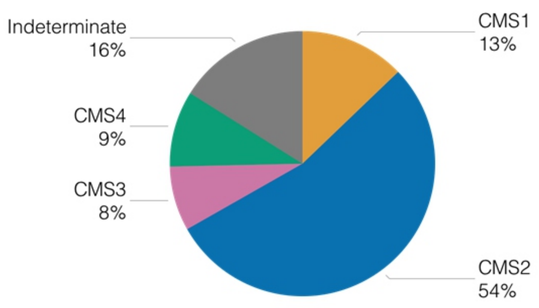


Figure 2 – CMS classification for TCGA primary tumor samples.

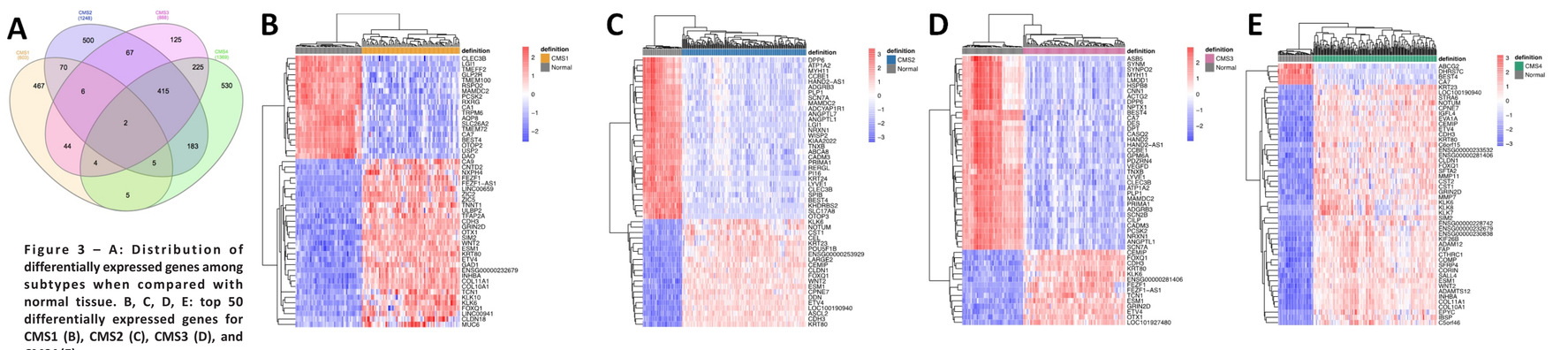


Figure 3 – A: Distribution of differentially expressed genes among subtypes when compared with normal tissue. B, C, D, E: top 50 differentially expressed genes for CMS1 (B), CMS2 (C), CMS3 (D), and CMS4 (E).

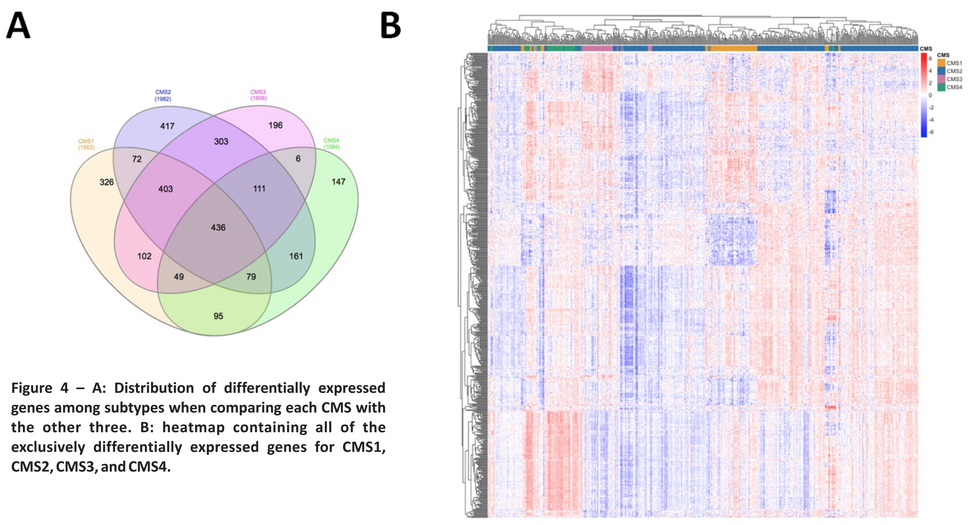


Figure 4 – A: Distribution of differentially expressed genes among subtypes when comparing each CMS with the other three. B: heatmap containing all of the exclusively differentially expressed genes for CMS1, CMS2, CMS3, and CMS4.

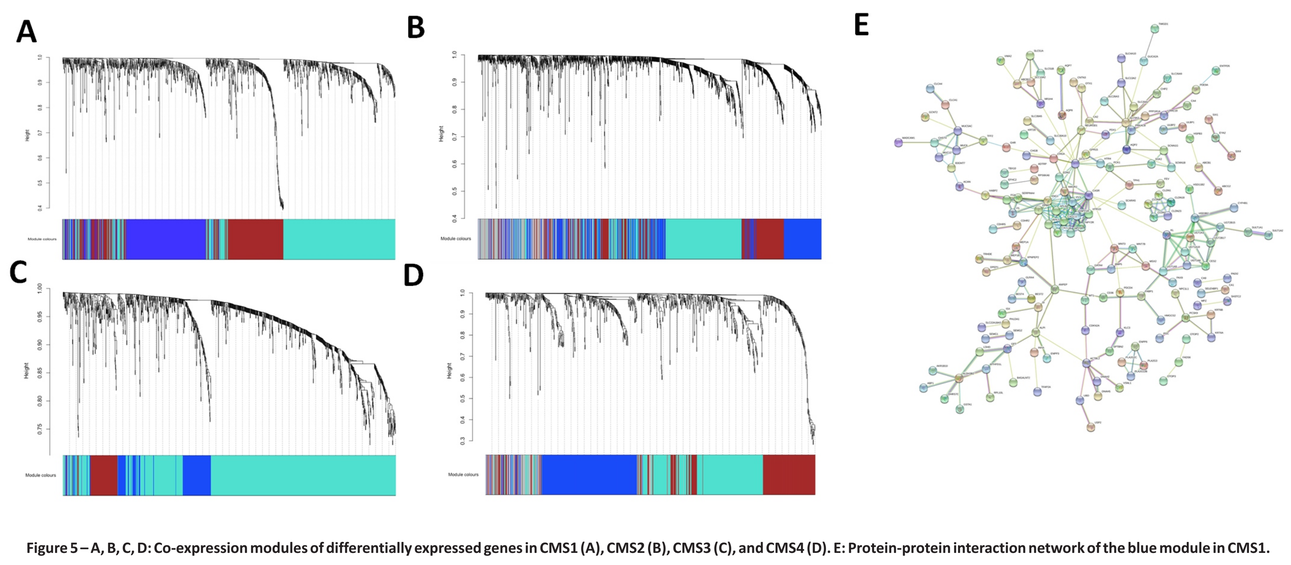


Figure 5 – A, B, C, D: Co-expression modules of differentially expressed genes in CMS1 (A), CMS2 (B), CMS3 (C), and CMS4 (D). E: Protein-protein interaction network of the blue module in CMS1.

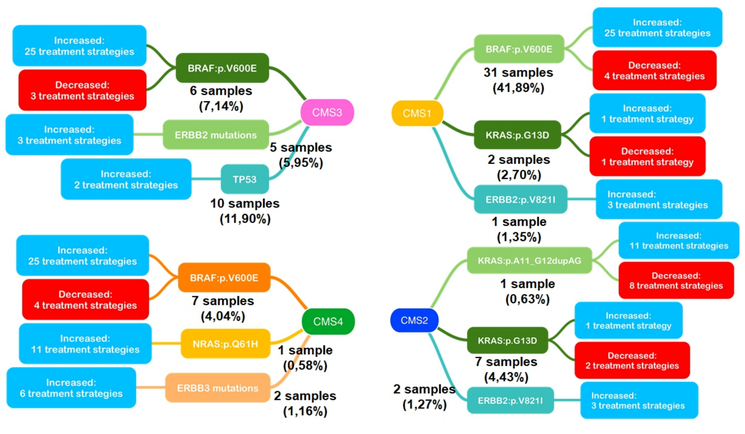


Figure 6 – High score mutations and associated drug sensitivities in each of the subtypes.

Table 1 – Number of drugs identified in each of the subtypes using DGIdb.

	CMS1	CMS2	CMS3	CMS4
Exclusive DEGs	326	417	196	147
Number of drugs identified	27	1266	306	216
Exclusive drugs identified	5	943	209	139

NEXT STEPS

Mutation data is an important asset in the identification of viable subtype-specific treatment options. This information can help us identify treatment strategies not currently in use in colorectal cancer and lead us to the validation of new drugs currently in pre-clinical phase.

1 – GUINNEY, J. et al. The consensus molecular subtypes of colorectal cancer. Nature Medicine, v. 21, n. 11, p. 1350–1356, 2015.

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