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Mutational Landscaping of Liver Metastases with Desmoplastic and Replacement Growth Patterns

Pieter-Jan van Dam[1], Boris Galjart[3], Pascale De Paepe[4], Tom Feryn[5], Valerie Duwel[6], Luc Dirix[1], Sigrid Stroobants[7], Peter Vermeulen[1, 2], Steven Van Laere[1, 2]

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7 Department of Nuclear Medicine, UZA, Edegem, Belgium

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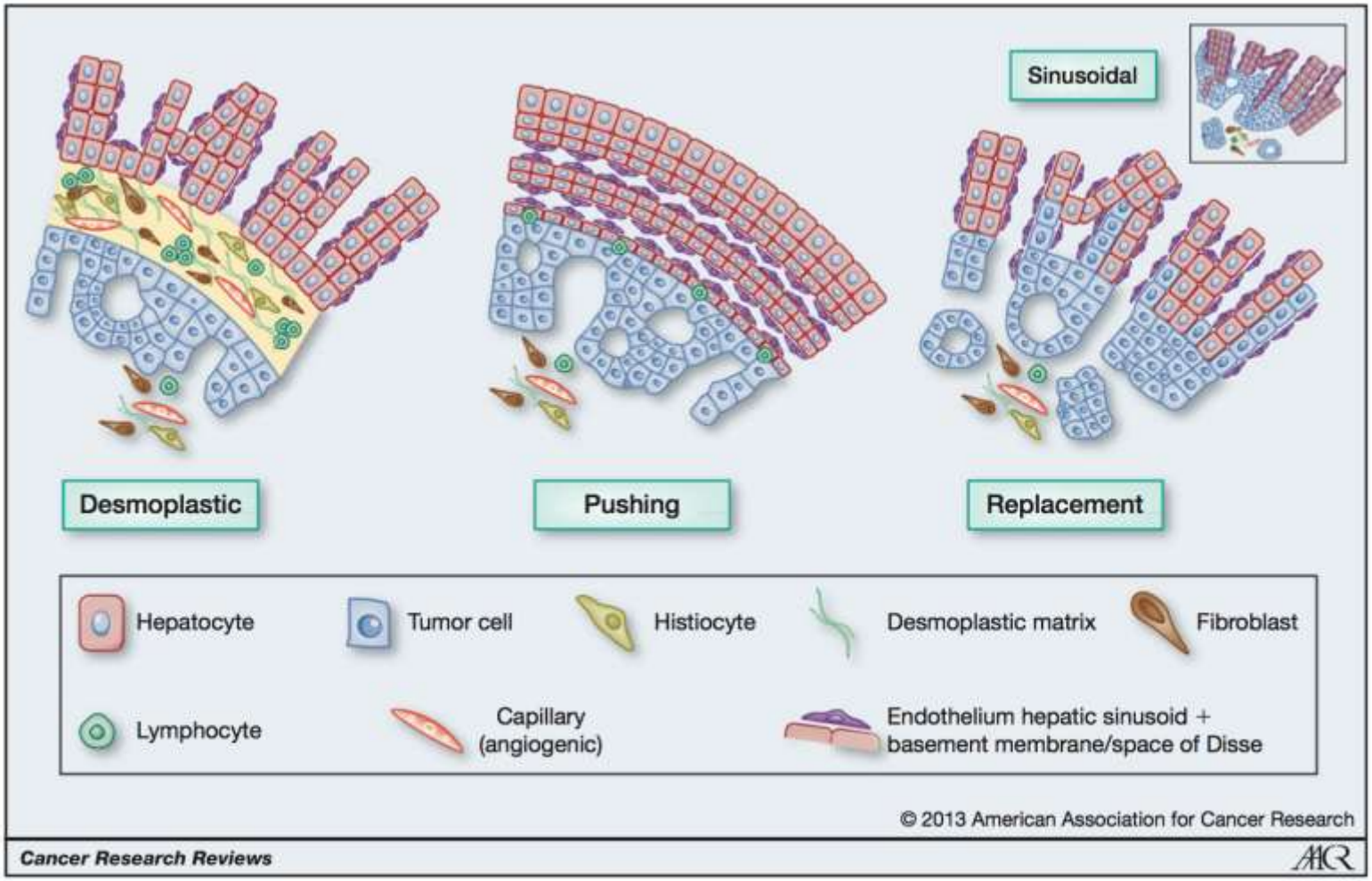
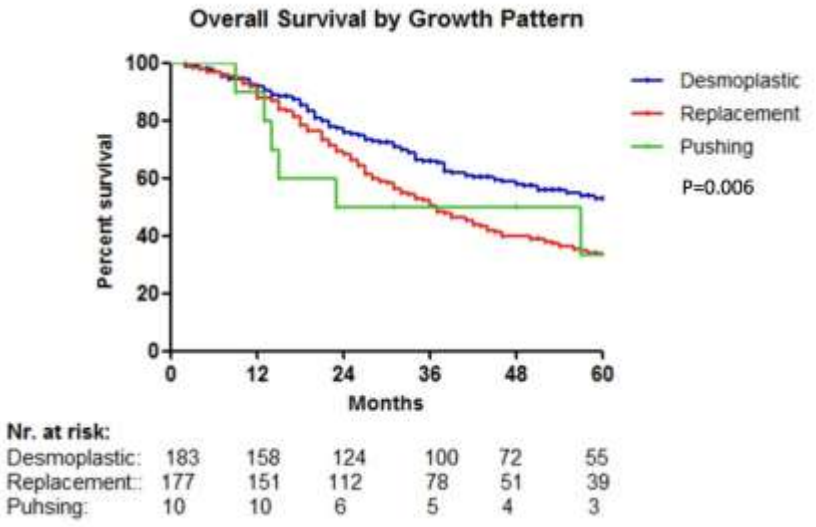
Introduction



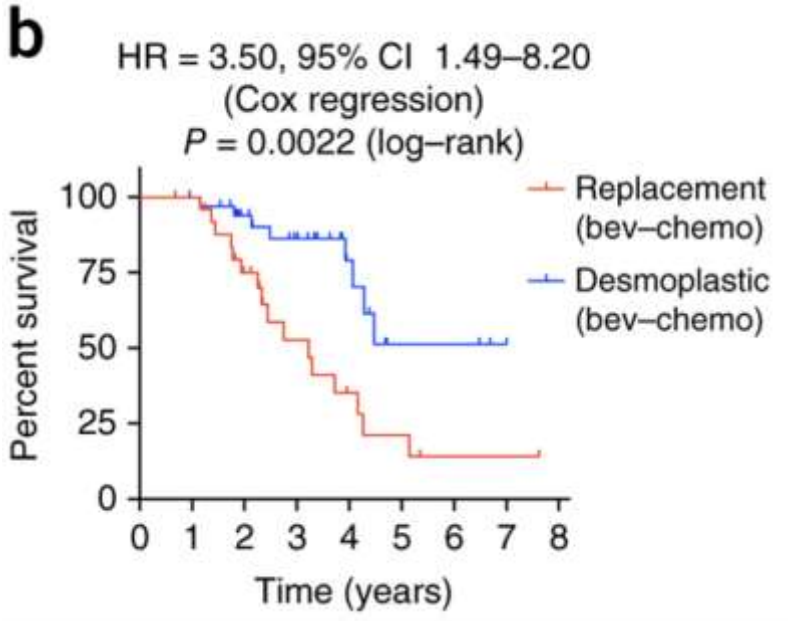
Van den Eynden G et al. *Cancer Res* 2013;73:2031-2043

Importance of Growth Patterns

Prognostic



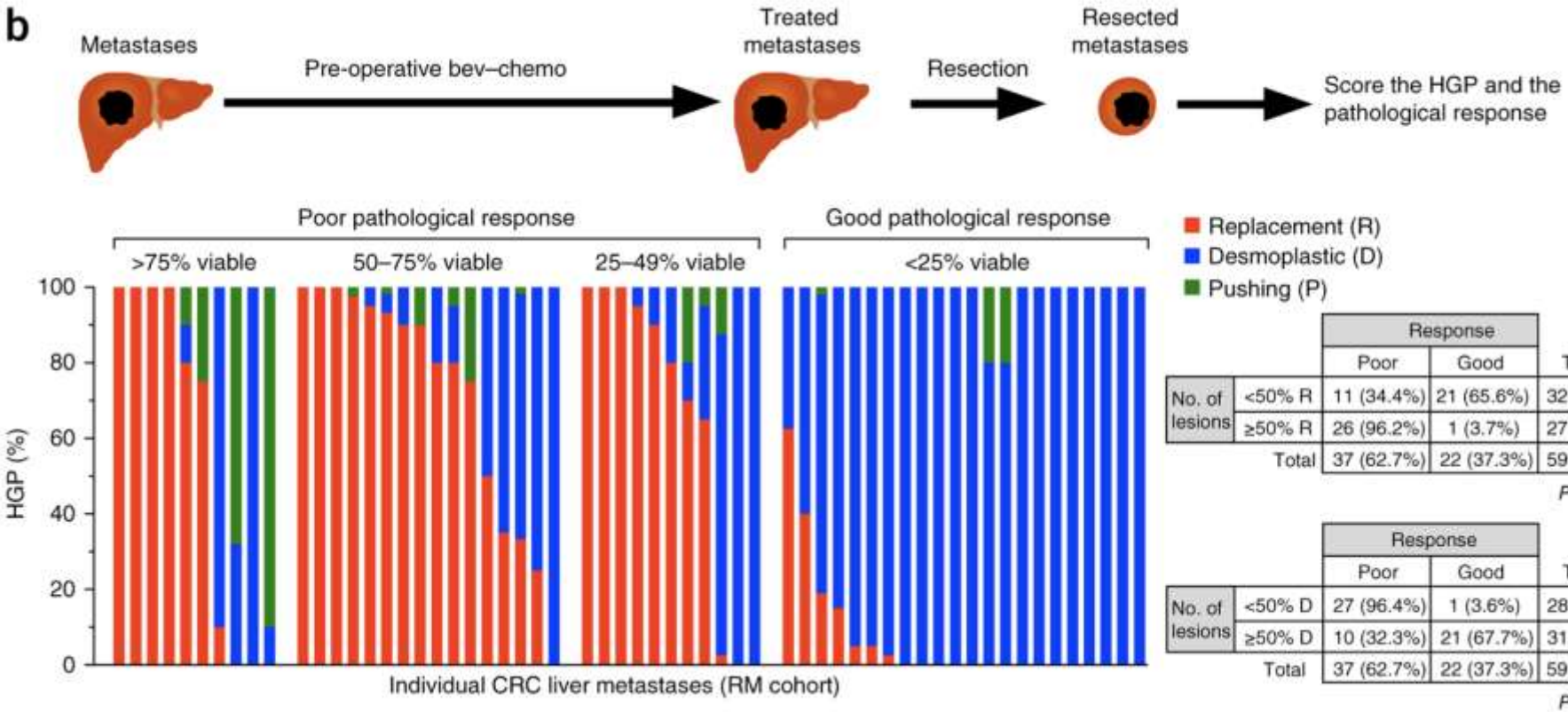
van Dam et al. Submitted



Frentzas et al. Nat Med 2016

Importance of Growth Patterns

Predictive



		Response		
		Poor	Good	Total
No. of lesions	<50% R	11 (34.4%)	21 (65.6%)	32 (100%)
	≥50% R	26 (96.2%)	1 (3.7%)	27 (100%)
	Total	37 (62.7%)	22 (37.3%)	59 (100%)

$P < 0.001$

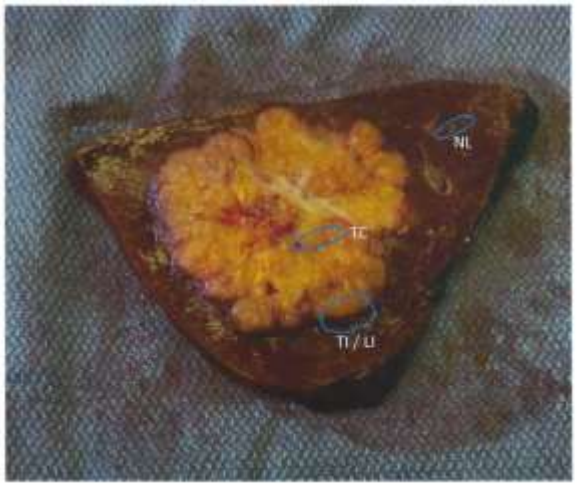
		Response		
		Poor	Good	Total
No. of lesions	<50% D	27 (96.4%)	1 (3.6%)	28 (100%)
	≥50% D	10 (32.3%)	21 (67.7%)	31 (100%)
	Total	37 (62.7%)	22 (37.3%)	59 (100%)

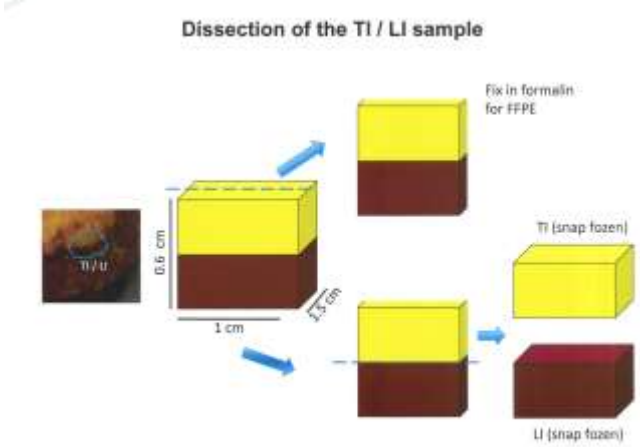
$P < 0.001$

Frentzas et al. Nat Med 2016

Materials and Methods

- Multi-centric prospective study
- Standardized Sampling





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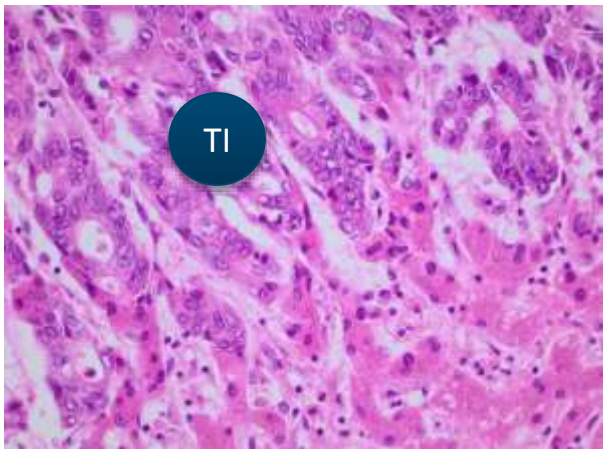
Materials and Methods

- Multi-centric prospective study
- Standardized Sampling
- RNA-sequencing of Liver Metastases

Tumor-Liver Interfase Sampling



RNA extraction and cDNA sequencing

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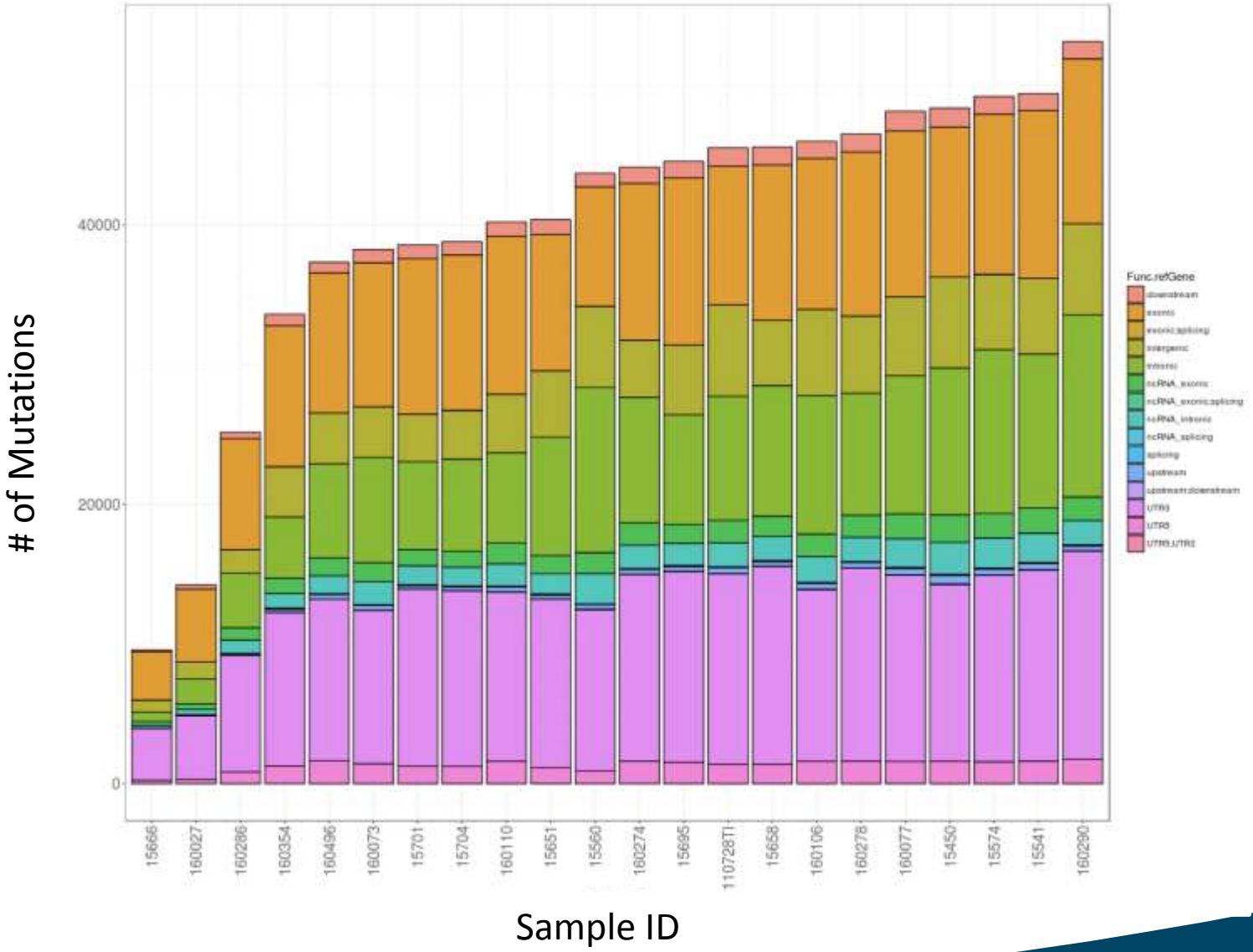
Materials and Methods

- Multi-centric prospective study
- Standardized Sampling
- RNA-sequencing of Liver Metastases
- Bio-informatics pipelines:
  - Differential Gene Expression
  - Mutations
  - Alternative Splicing
  - Fusions

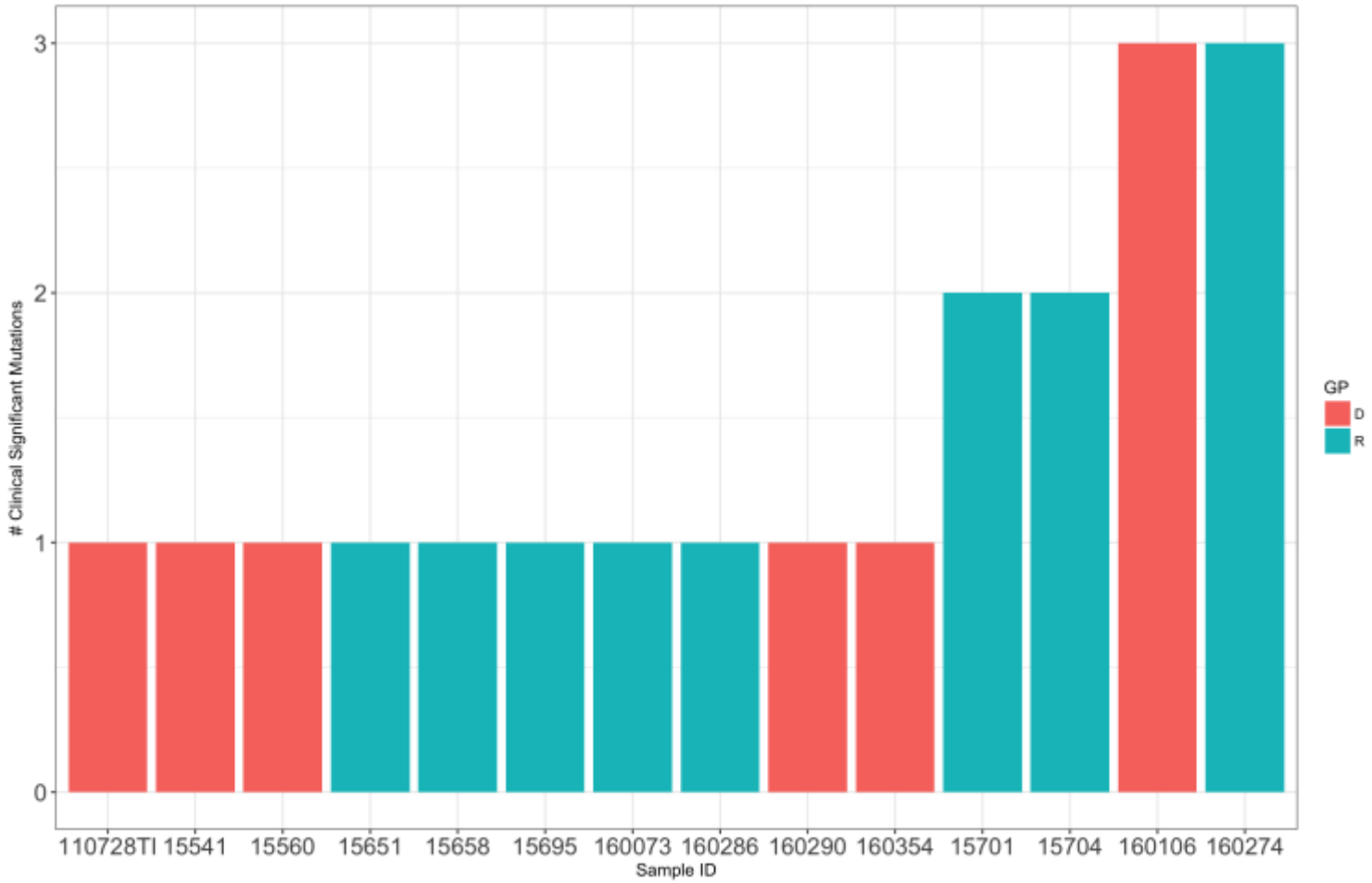
Materials and Methods

- Multi-centric prospective study
- Standardized Sampling
- RNA-sequencing of Liver Metastases
- Bio-informatics pipelines:
  - Differential Gene Expression
  - **Mutations of 22 Tumor Interfase samples**
  - Alternative Splicing
  - Fusions

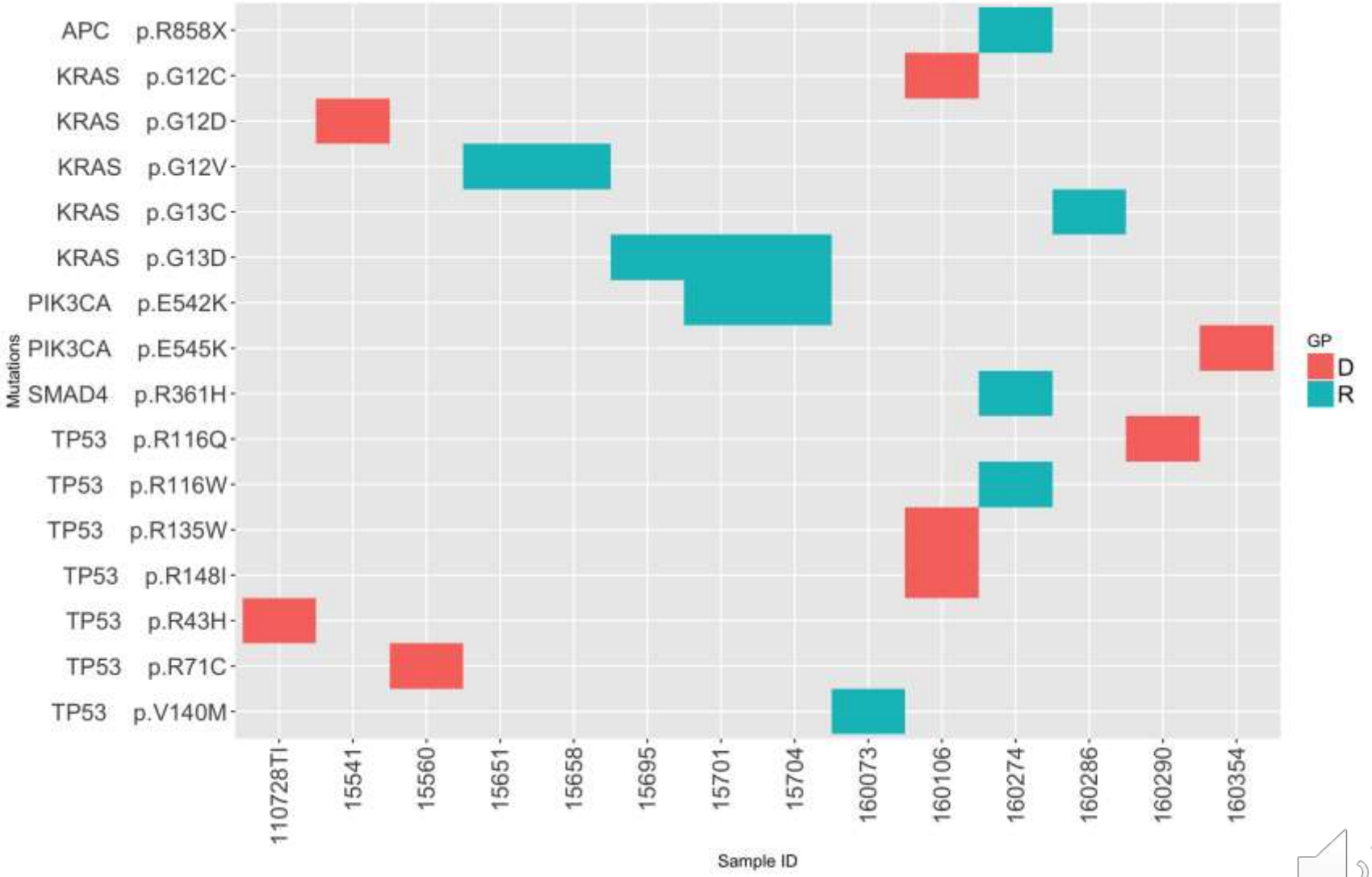
Results: Number of total mutations



Results: Clinical Significant Mutations

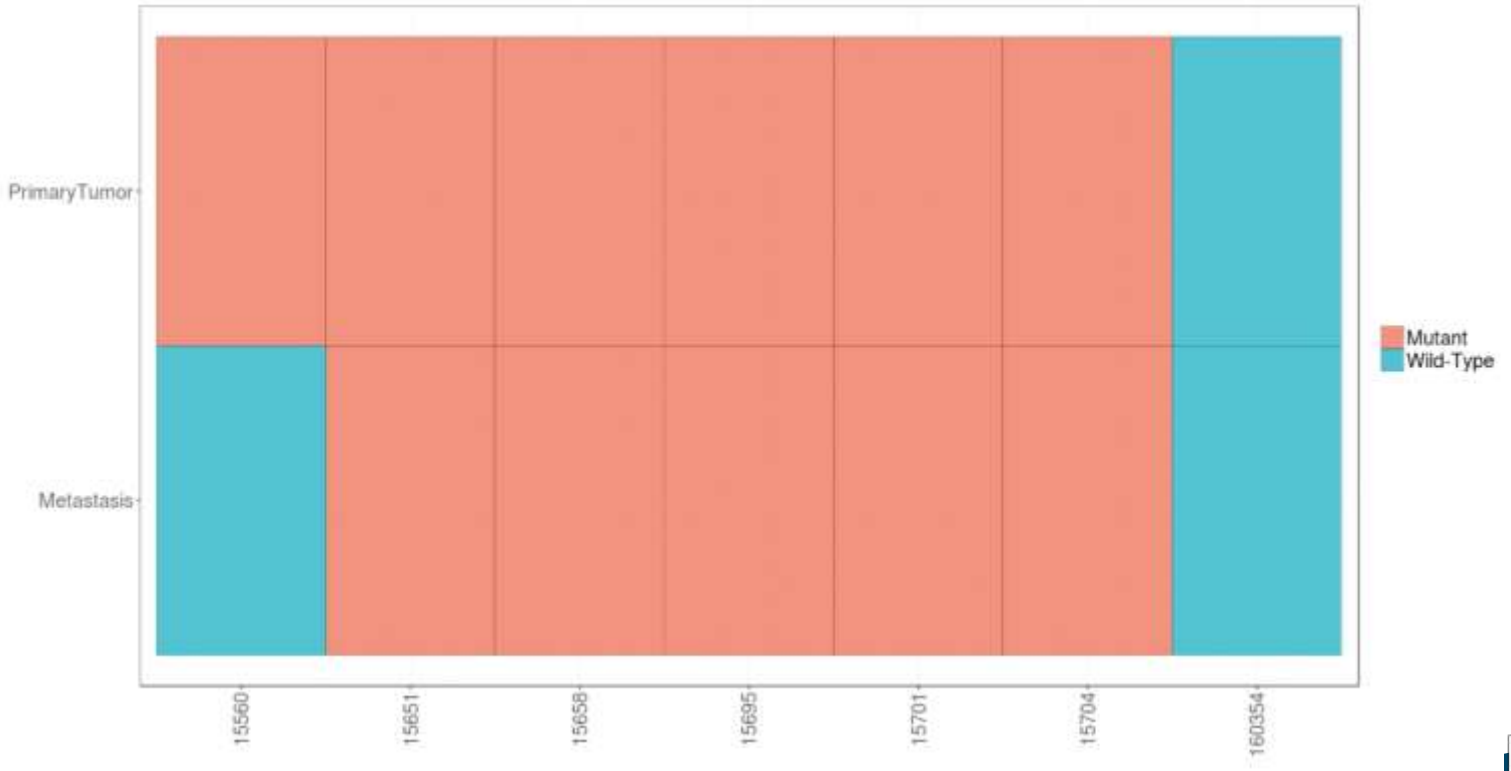


Results


APC p.R858X
KRAS p.G12C
KRAS p.G12D
KRAS p.G12V
KRAS p.G13C
KRAS p.G13D
PIK3CA p.E542K
PIK3CA p.E545K
SMAD4 p.R361H
TP53 p.R116Q
TP53 p.R116W
TP53 p.R135W
TP53 p.R148I
TP53 p.R43H
TP53 p.R71C
TP53 p.V140M
Mutations
110728TI
15541
15560
15651
15658
15695
15701
15704
160073
160106
160274
160286
160290
160354
Sample ID
GP
D
R

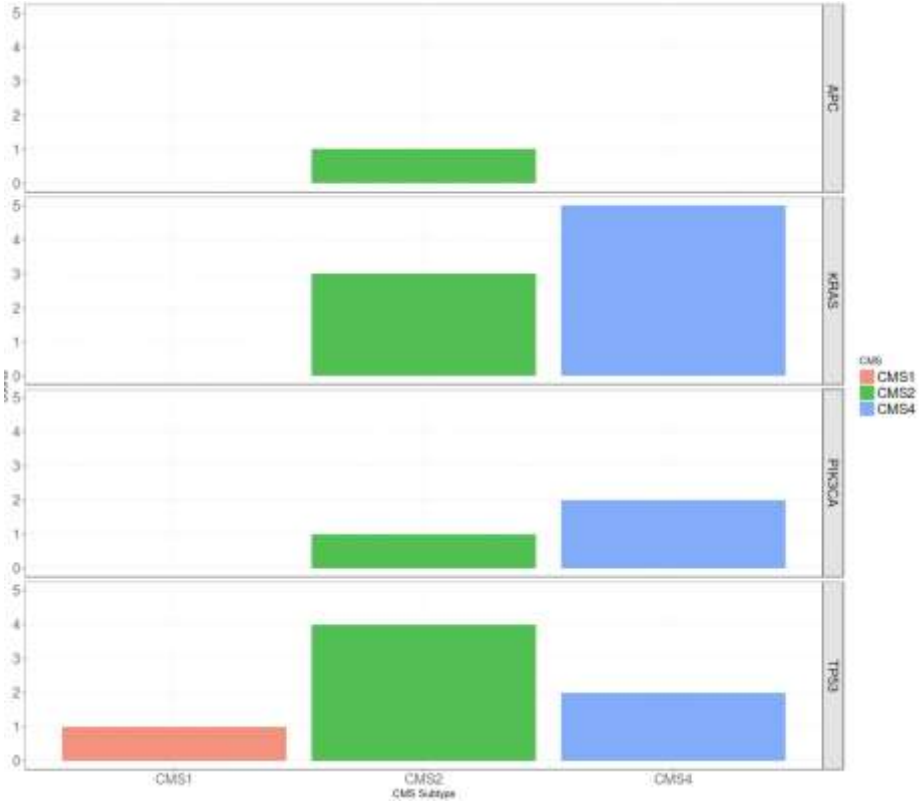
Results

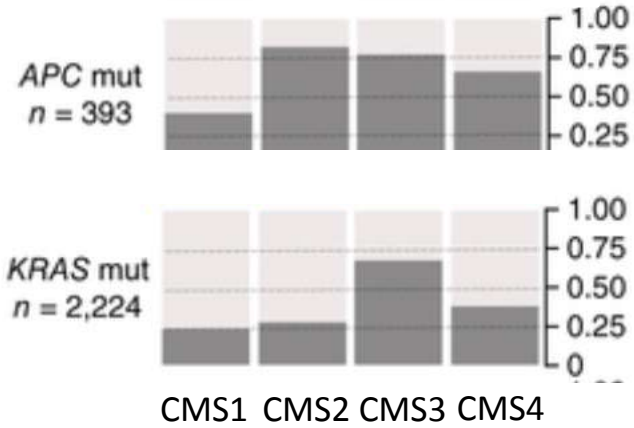
- 7 liver metastases had previously known KRAS status from Primary Tumor
- 6/7 concordance

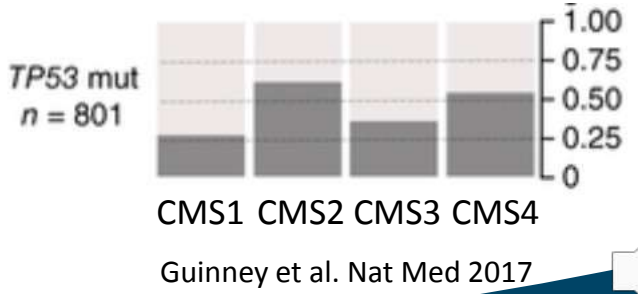


Results

- Consensus Molecular Subtypes (CMS) were inferred from differential gene expression data







Guinney et al. Nat Med 2017

Conclusions

- We present mutational profiling results of a prospective RNA-seq study of liver metastases with different HGPs.
- Current results are concordant with both current literature and known KRAS mutational status.
- Our study accentuates the feasibility of variant calling on RNA-seq samples.
- Current results will be extended by integrating DGE results and extending the cohort.

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We would like to thank all patients for participating in this study.

Thank you for your attention.

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