

Biomedical Research Centre
at The Royal Marsden NHS Foundation Trust
and The Institute of Cancer Research, London

NHS
National Institute for
Health Research

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The ROYAL MARSDEN
NHS Foundation Trust

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cancer foundation

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Pan London Early Rectal Cancer Meeting

1st November 2018

**Avoiding major surgery and improving quality of
life in patients with early rectal cancer**

PRESERVE

The ROYAL MARSDEN
NHS Foundation Trust

ICR The Institute of
Cancer Research

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Early Rectal Cancer

Translational Research Opportunities

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The strength of this trial

- Distinctive cohort
- Untreated
- Close follow up
- Internal control: TME surgery arm vs local excision



Question to ask

Why are these tumours (still) early stage?

Which are high risk cancers at an early stage?



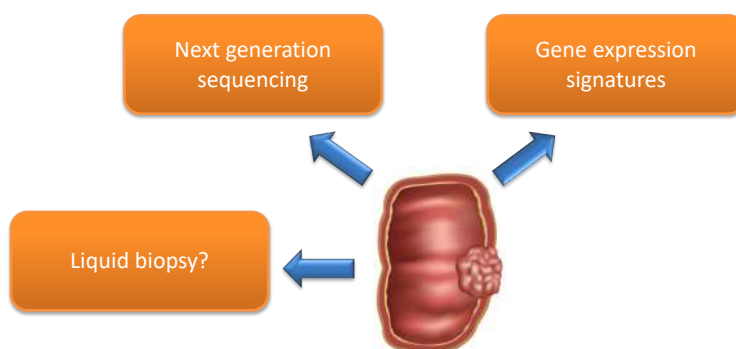
The consensus molecular subtypes of CRC

	CMS1 MSI immune	CMS2 Canonical	CMS3 Metabolic	CMS4 Mesenchymal
		37%	13%	23%
		SCNA high	Mixed MSI status, SCNA low, CIMP low	SCNA high
Right sided			KRAS mutations	More advanced stages EGFR activation, angiogenesis
	WNT and MYC activation		Metabolic deregulation	Worse relapse-free and overall survival



Guinney et al., Nature Medicine 2015

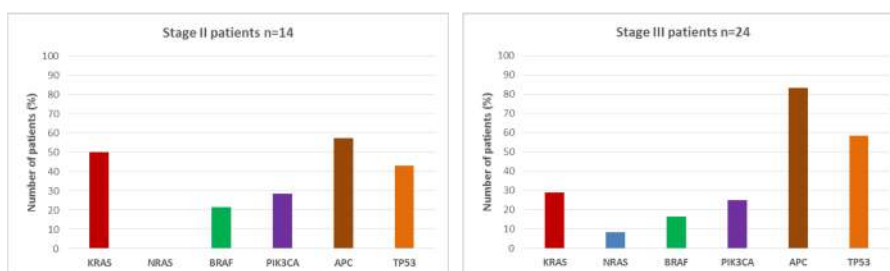
Translational approach to ERC



Results from TRACC study

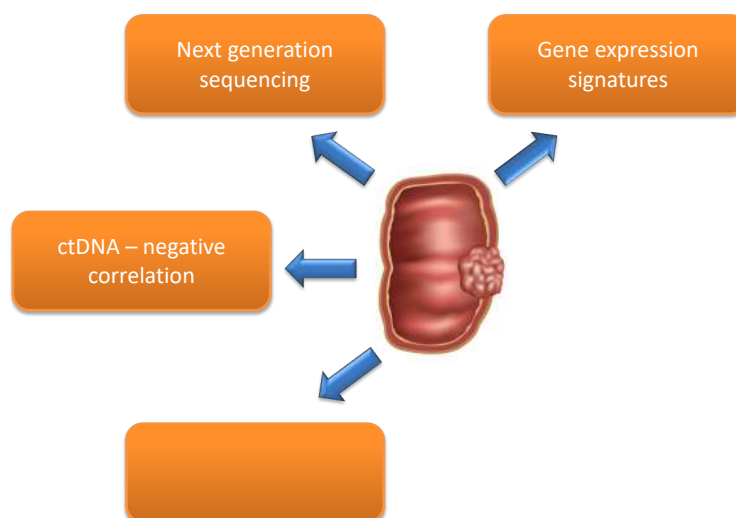
Tracking mutations in ctDNA to predict relapse in early CRC

- Assess whether ctDNA is detectable with ddPCR in patients with stage II/III CRC
- 37/38 (97%) patients have at least 1 mutation in one of the genes of interest in tissue



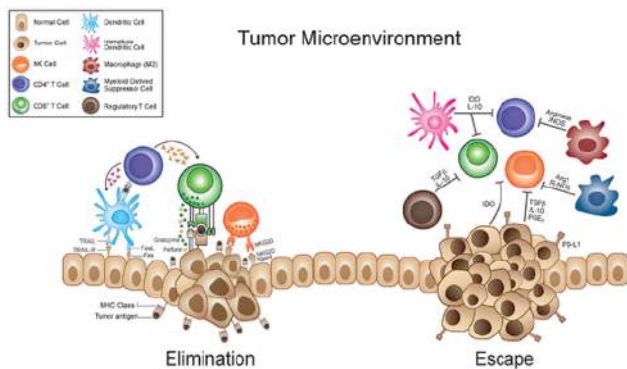
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Immunoprofiling

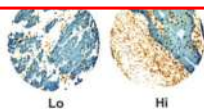


By Frontiers in Oncology
<https://commons.wikimedia.org/w/index.php?curid=33585764>

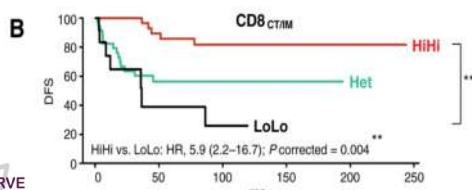
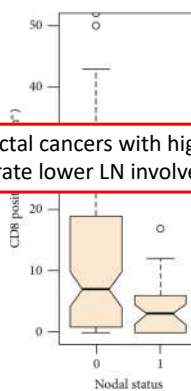
Immunoprofiling



Immunoscore as prognostic marker for rectal cancer



Early rectal cancers with higher CD8 infiltrate lower LN involvement



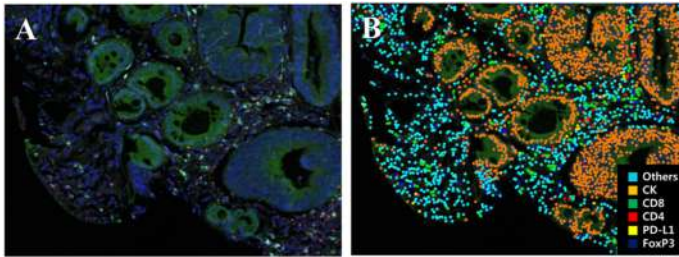
Anitei et al., Clin Cancer Research 2014
 Däster et al., Disease Markers 2014

Immunoprofiling

Immune infiltrate predictive?? for chemoradiotherapy in rectal cancer?

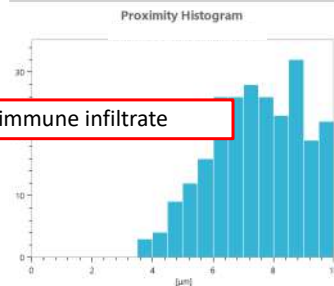
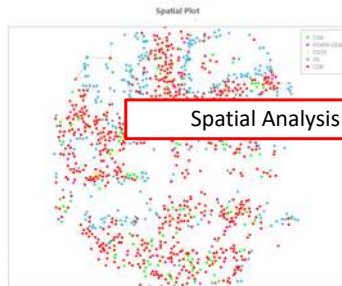
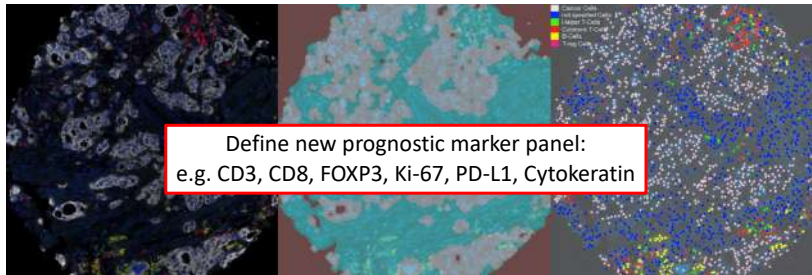
Lower ratios of $\frac{CD4}{PD-L1}$ $\frac{CD8}{PD-L1}$ $\frac{FOXP3}{PD-L1}$

in tumour regression than in residual disease group



Park et al., Oncotarget 2017

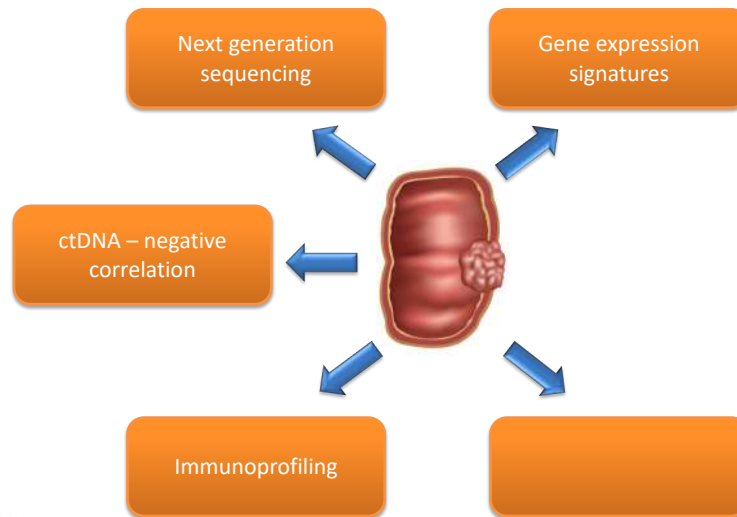
Immunoprofiling



Spatial Analysis of immune infiltrate

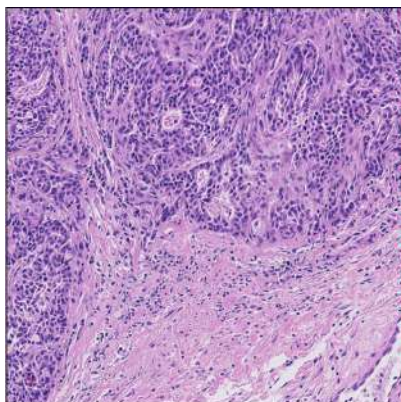


Translational approach to ERC



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Morphology and Microenvironment Analysis

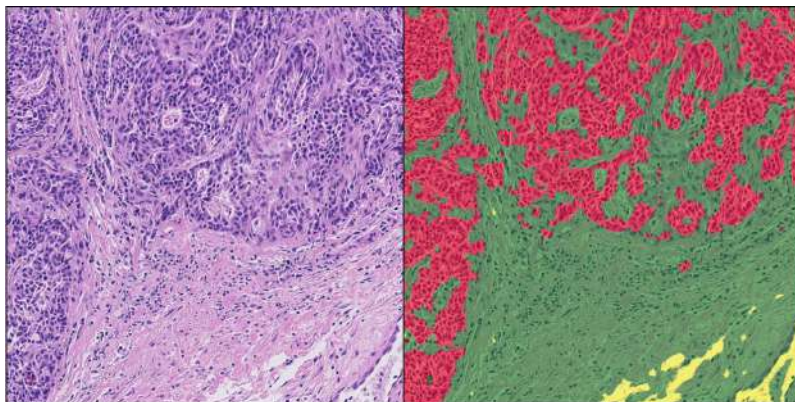


Correlation with Radiology

- Diameter
- Depth and width of invasion
- Gross morphology
- Lymph node involvement
- Further assessment
 - Tumour budding
 - Lymphovascular invasion
 - Grading
- Tumour/Stroma Ratio

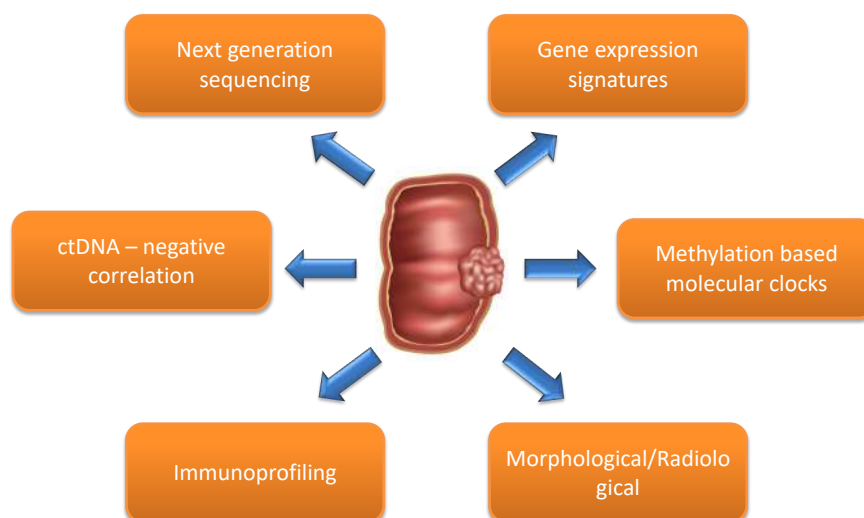
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Translational approach to ERC



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More ideas...?

