Investigating the role of the centromeric histone variant CENP-A in cancer

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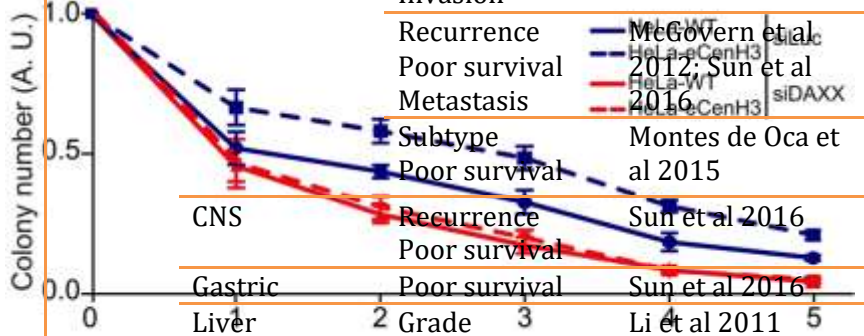
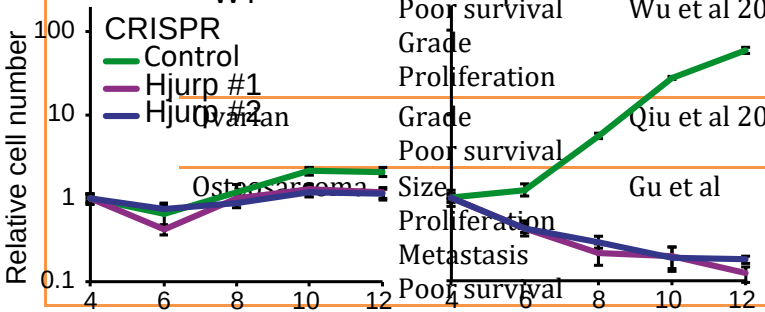
Overexpression of CENP-A and HJURP is observed in a range of aggressive cancers

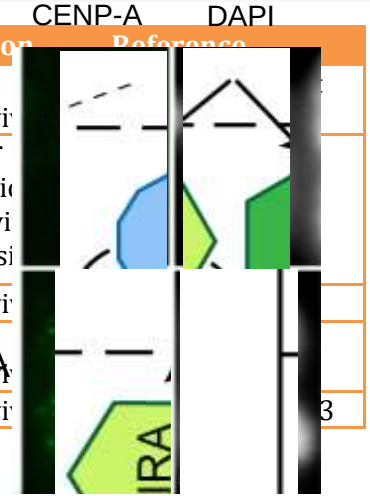
Is this just a correlation or does CENP-A/HJURP excess give an advantage to cancer cells?

Factor	Cancer	Correlation	Reference
CENP-A	Breast	Grade	Ma et al 2003
		Invasion	
		Recurrence	McGovern et al 2012; Sun et al 2016
		Poor survival	
		Metastasis	
		Subtype	Montes de Oca et al 2015
		Poor survival	
	CNS	Recurrence	Sun et al 2016
		Poor survival	
	Gastric	Poor survival	Sun et al 2016
	Liver	Grade	Li et al 2011
		Proliferation	
	Lung	Recurrence	Sun et al 2016
		Poor survival	
		Poor survival	Wu et al 2012
		Grade	
		Proliferation	
	Ovarian	Grade	Qiu et al 2013
		Poor survival	
	Osteosarcoma	Size	Gu et al
		Proliferation	
		Metastasis	
		Poor survival	





Factor	Cancer	Correlation	Reference
HJURP	Breast	Subtype	
		Poor survi	
		Grade	
		Proliferati	
		Poor Survi	
		Radiosensi	
	Lung	Poor survi	
	Glioma	Grade	
		Poor survi	
		Poor survi	3



Lacoste et al. Molecular Cell, 2014

→ CENP-A/HJURP excess (and mislocalization) provides a cancer-specific advantage?

Filipescu et al, Genes Dev, 2017

Research Question

What are the mechanisms behind this apparent CENP-A/HJURP-dependent advantage?

→Compensation by alternative pathways?
→Unusual chromatin: impinging on centromere function / DNA damage response?

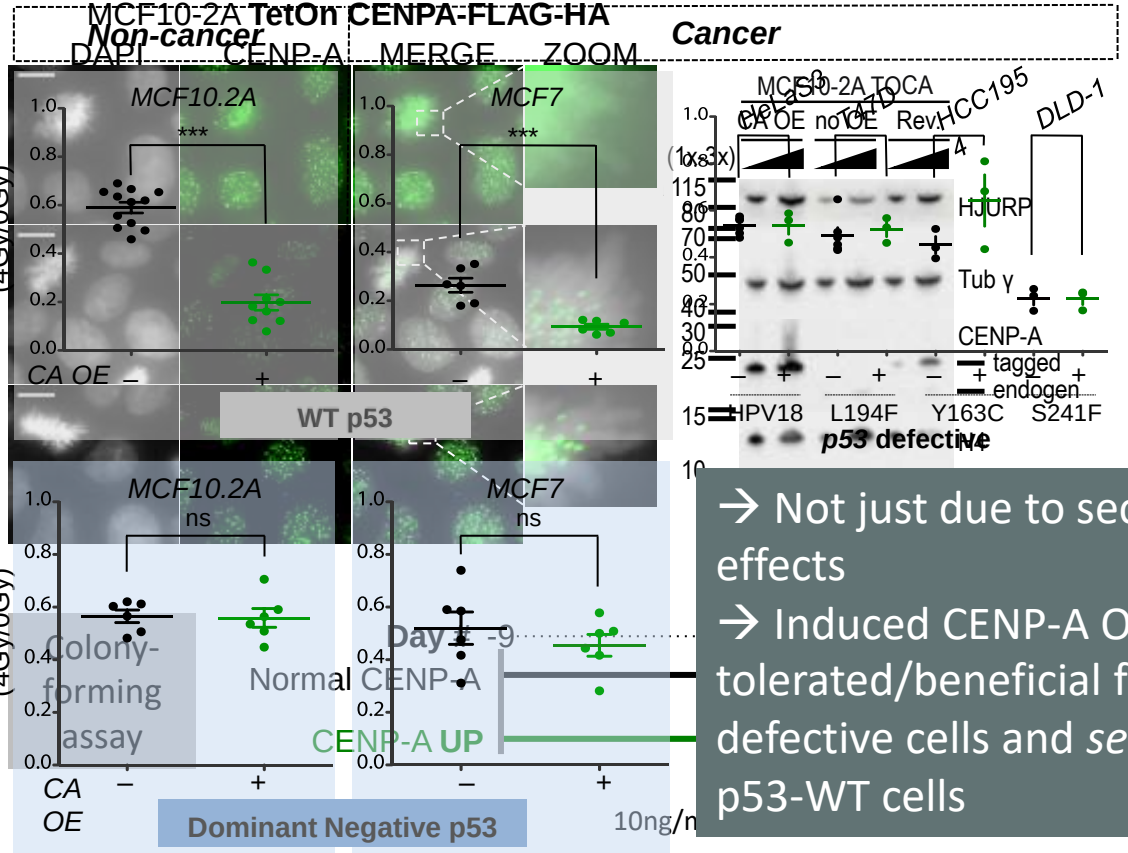
Can we exploit this for cancer treatment?

CENP-A excess: compensation by alternative pathways?

Inducible + reversible overexpression…

Human cell lines with different p53 status

Isogenic cell lines with defective p53



→ Not just due to secondary effects

→ Induced CENP-A OE is tolerated/beneficial for p53 defective cells and *sensitizes* p53-WT cells

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Thank you! And I encourage you to visit my poster for the rest of the story!