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# High resolution molecular analysis of CD47-mediated immune escape in bladder cancer

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**Department of Pediatrics**

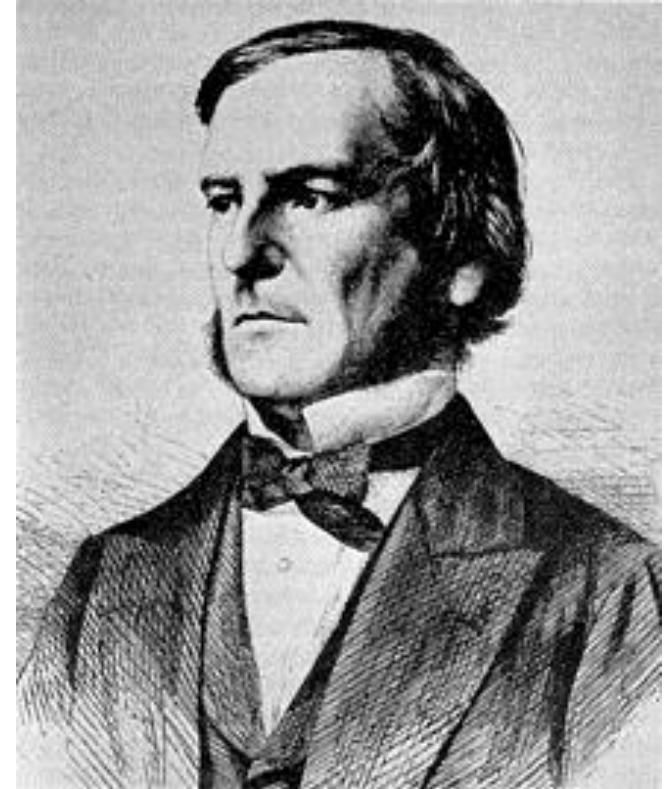
**UC San Diego**  
SCHOOL OF MEDICINE

Rady  
Children's  
Hospital  
San Diego 

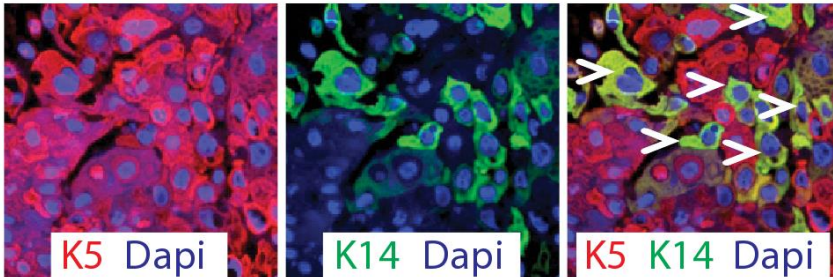
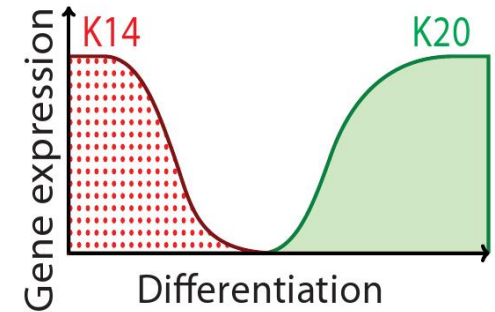
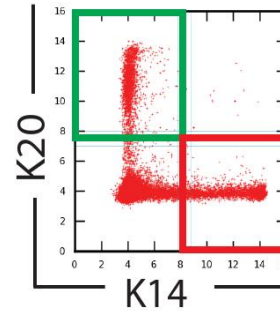
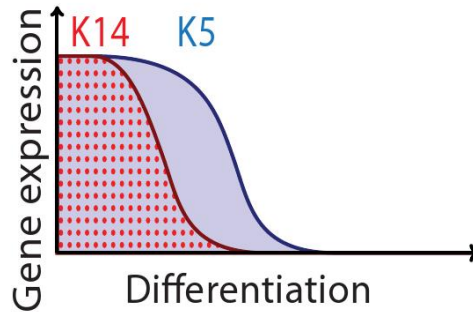
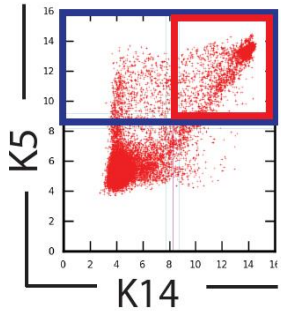
# Boolean Analysis



- George Boole (1815-1864)
- Two values
  - High, Low
  - 1, 0
- Boolean operations
  - AND, OR, NOT
  - Implication
    - $X \Rightarrow y$

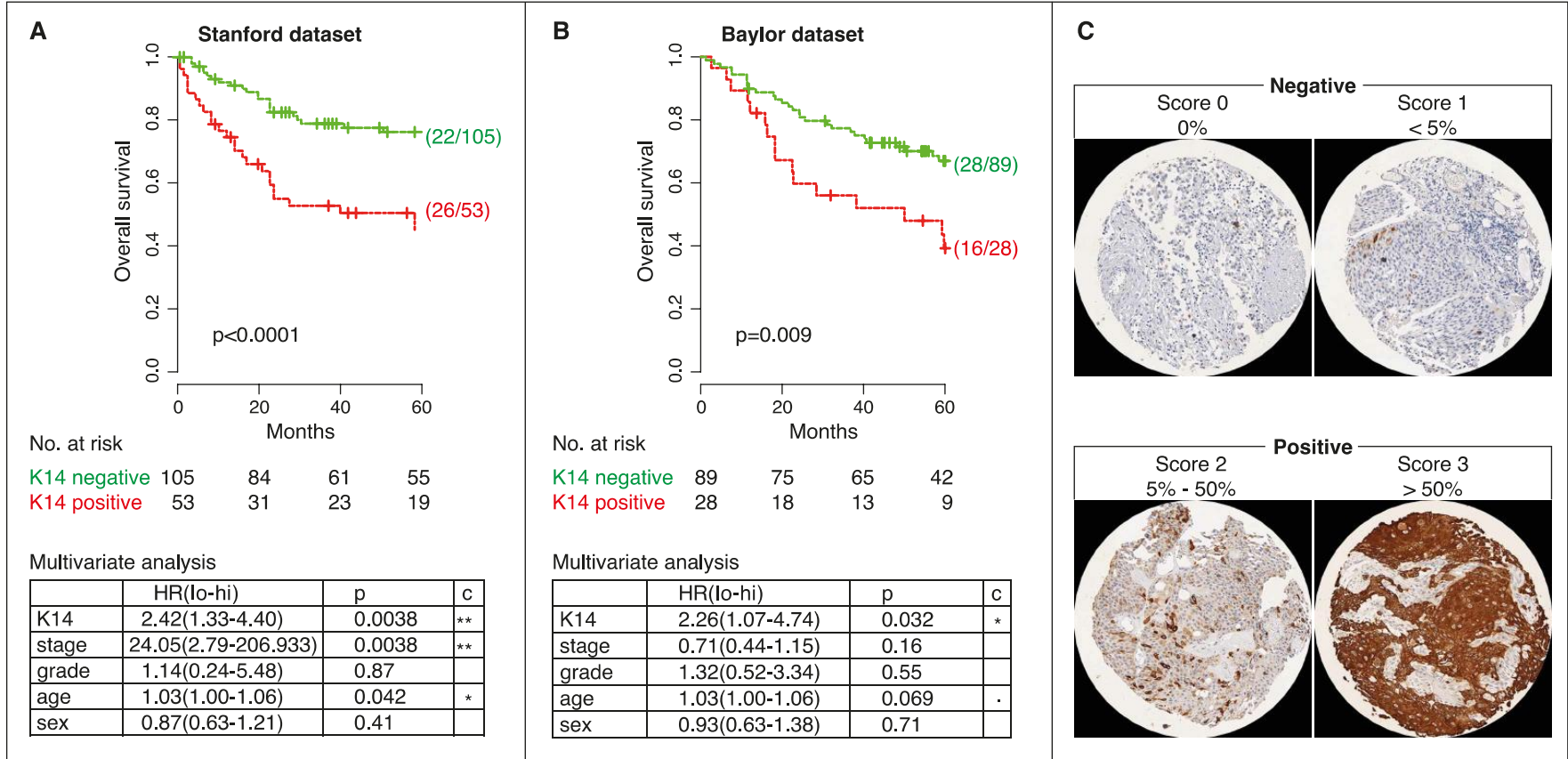


# KRT14 is an Upstream Marker



[Volkmer\*, Sahoo\*, and Chin\* et al. PNAS, 2012]

# KRT14 is Prognostic

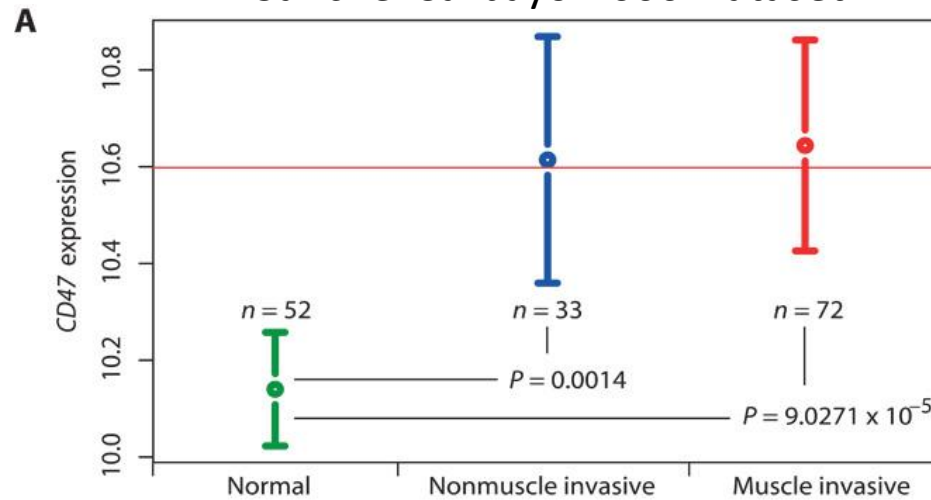


[Volkmer\*, Sahoo\*, and Chin\* et al. PNAS, 2012]

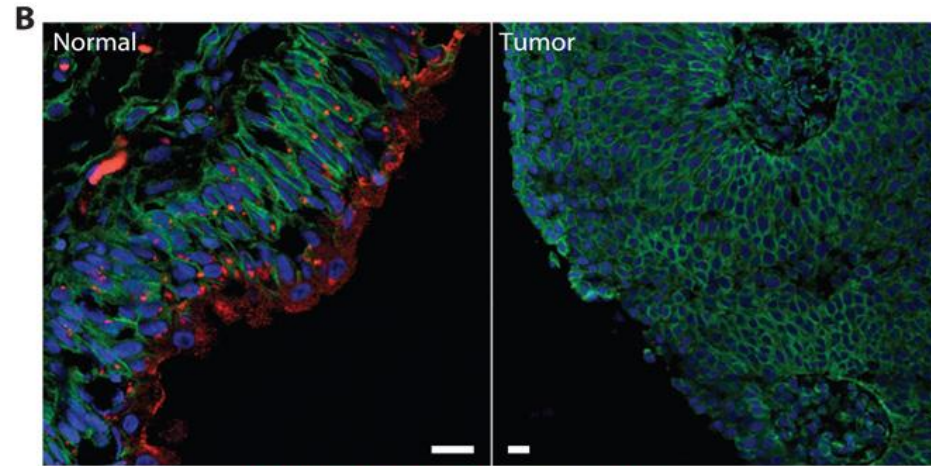
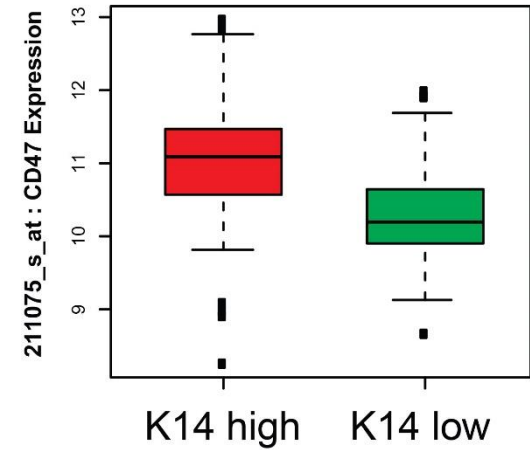
# CD47 Expression in Bladder Cancer



SanchezCarbayo-2006 Dataset

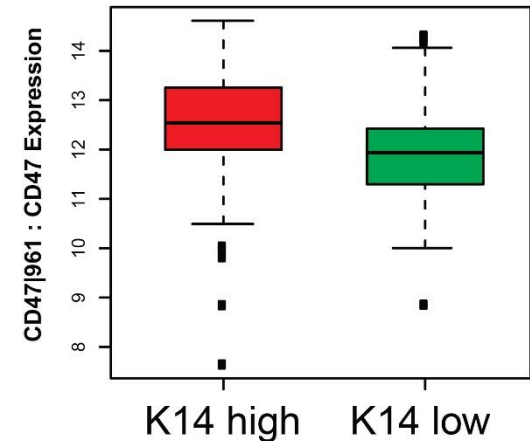


SC06 Dataset



CK18 (umbrella cells) - nuclei - CD47

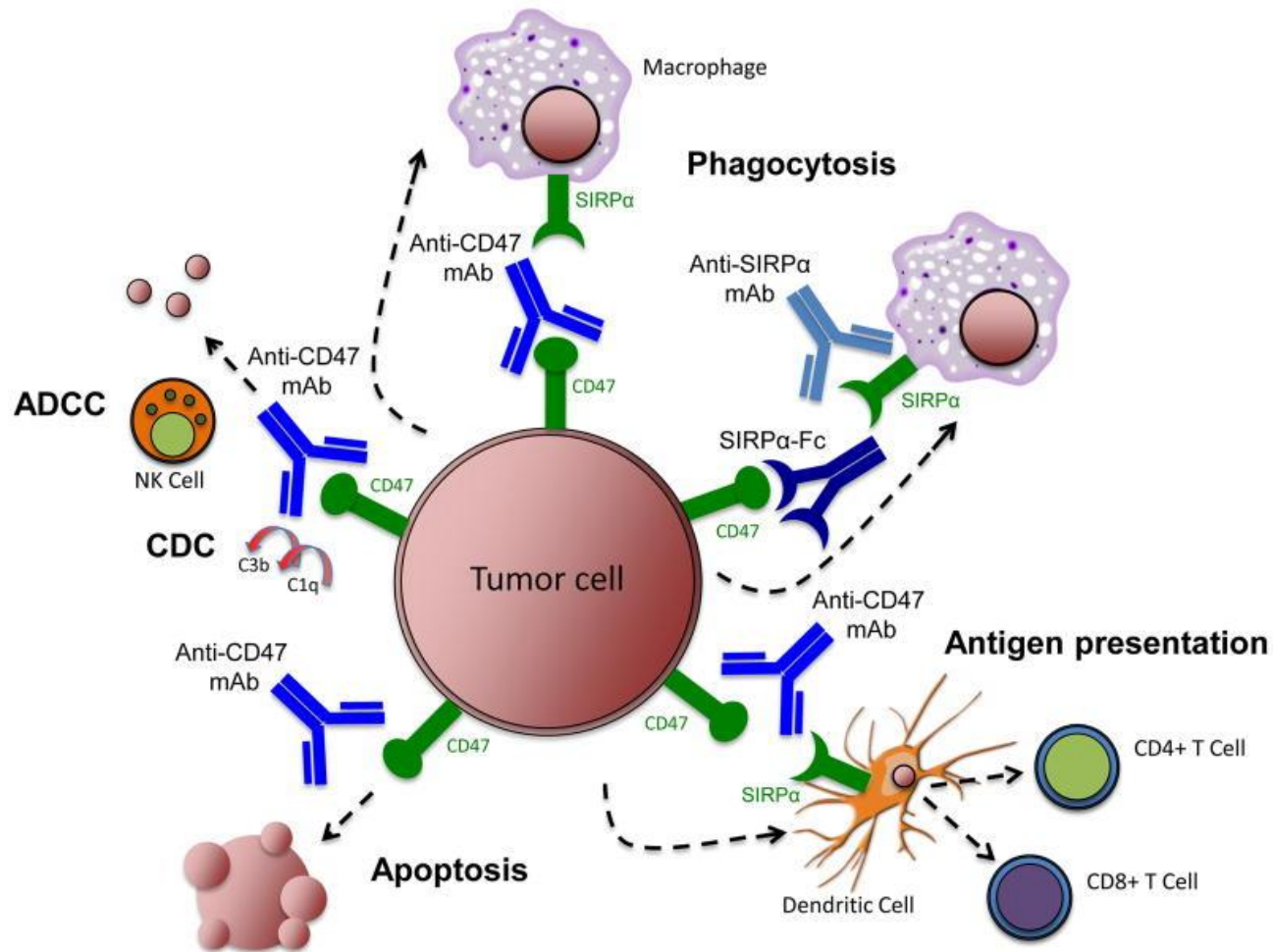
TCGA Dataset



Ying Pan et al., Sci Transl Med 2014;6:260ra148



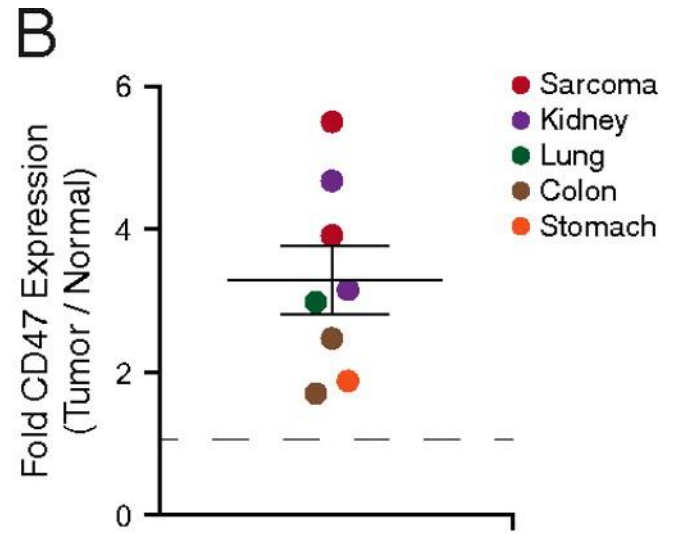
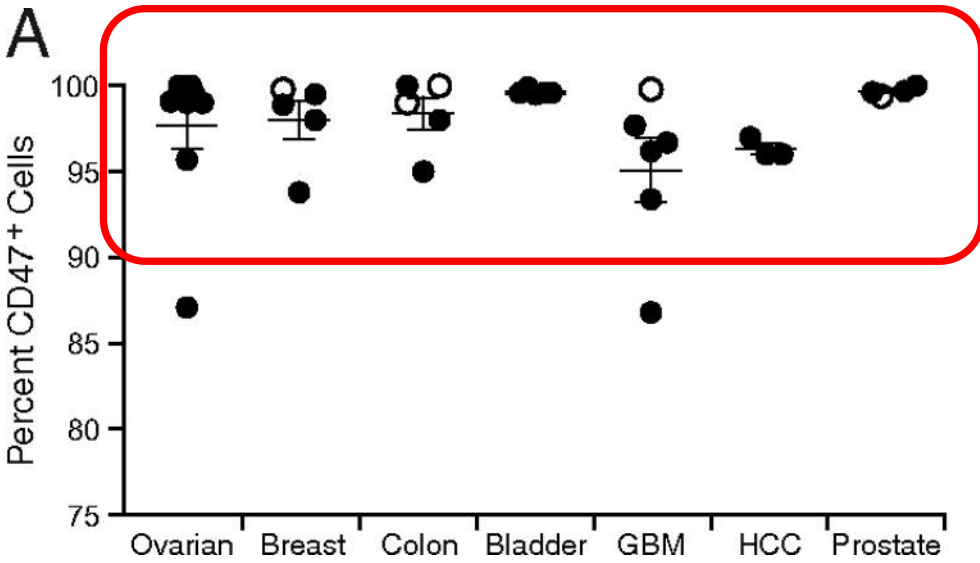
# CD47 – The Don't eat me Signal



Chao, Weissman, Majeti. *Curr Opin Immunol.* 2012 Apr; 24(2): 225–232.



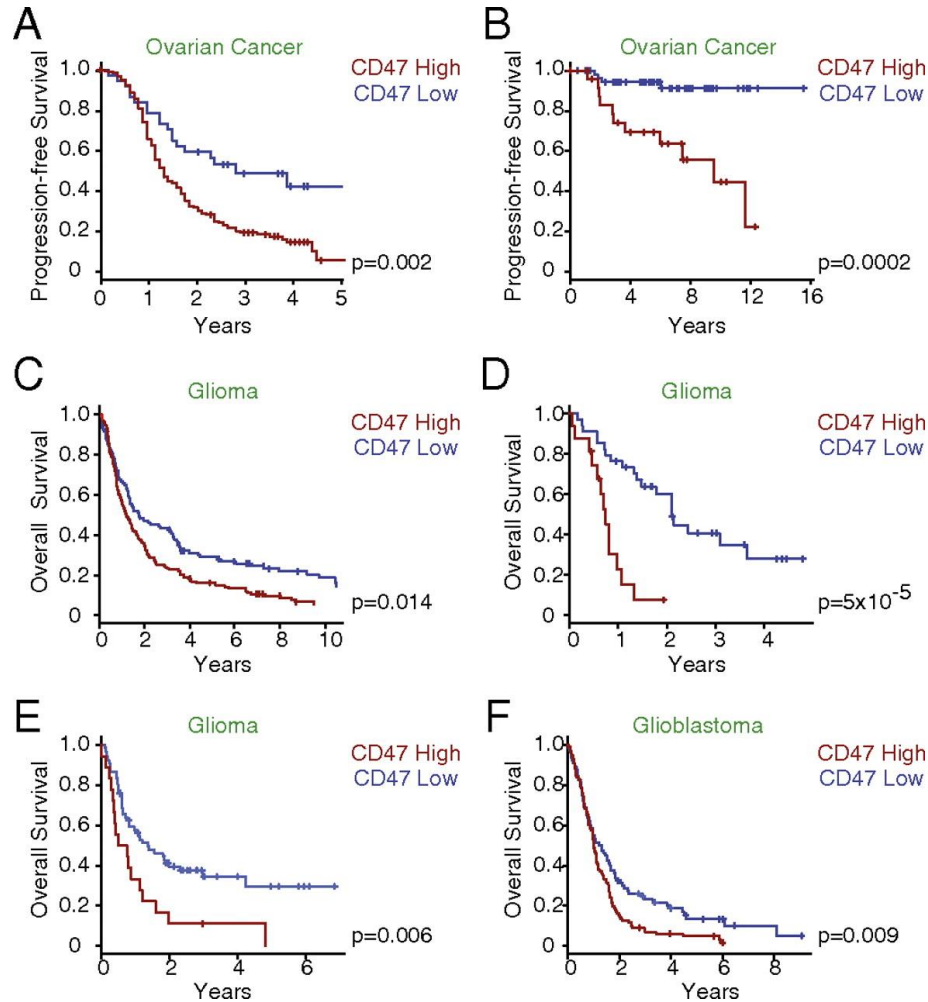
# CD47 is highly expressed on solid tumors



Stephen B. Willingham et al. PNAS 2012;109:6662-6667

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# CD47 is Prognostic

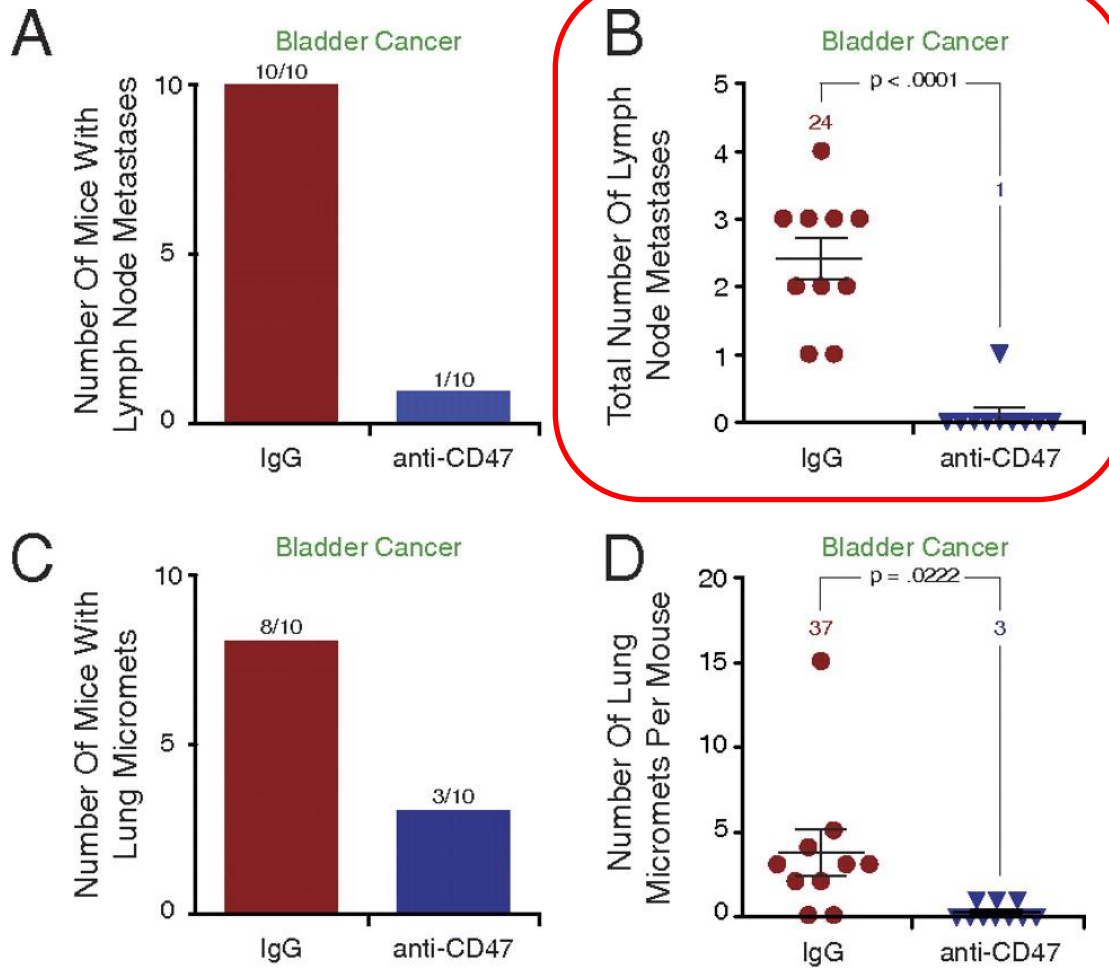


Stephen B. Willingham et al. PNAS 2012;109:6662-6667

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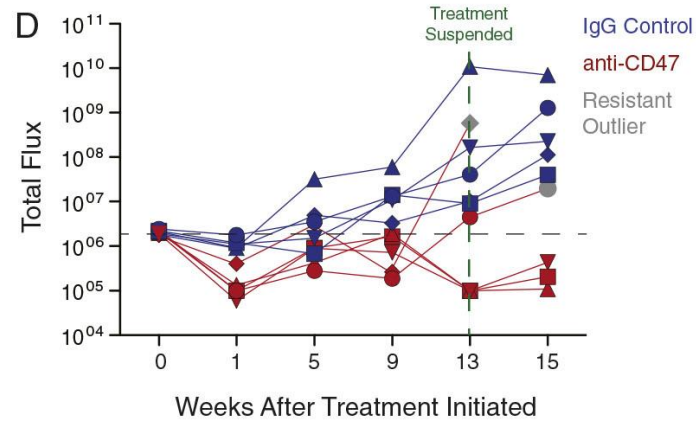
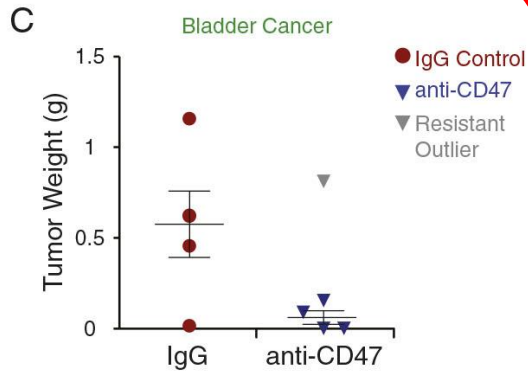
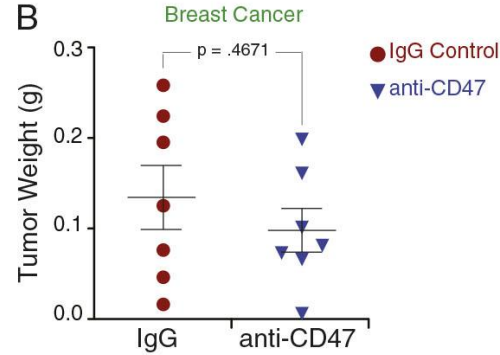
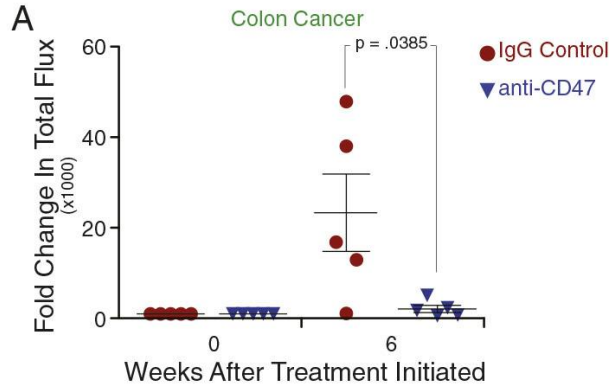
# Anti-CD47 mAbs prevent tumor metastasis



Stephen B. Willingham et al. PNAS 2012;109:6662-6667

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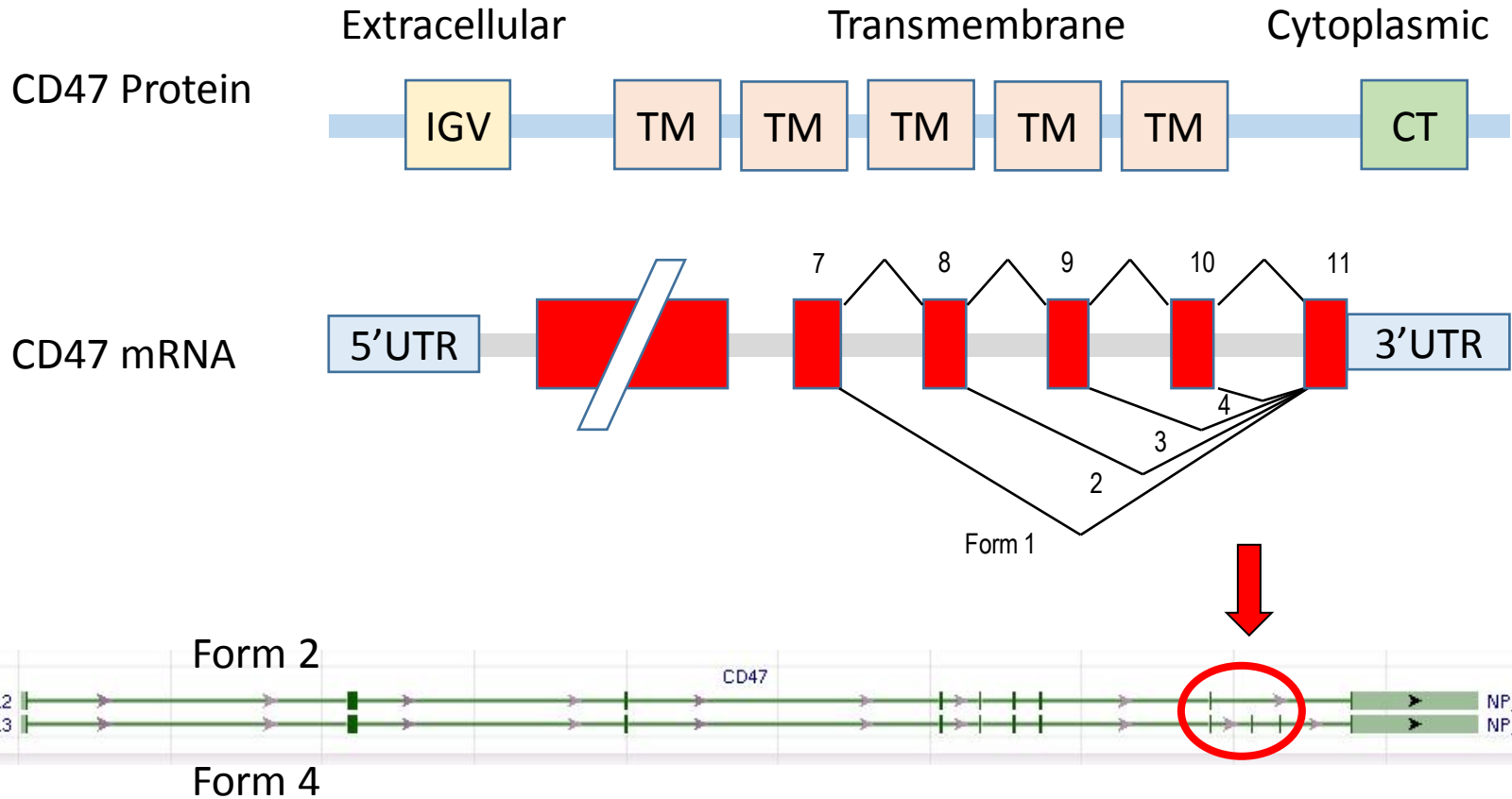
# Anti-CD47 is Therapeutic



Stephen B. Willingham et al. PNAS 2012;109:6662-6667

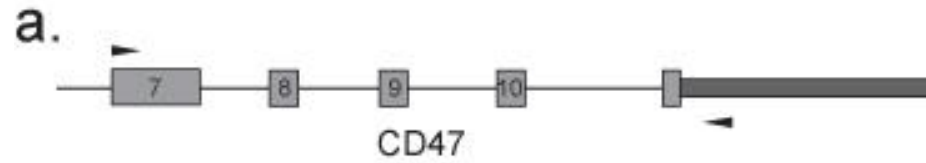
©2012 by National Academy of Sciences

# CD47 Isoforms



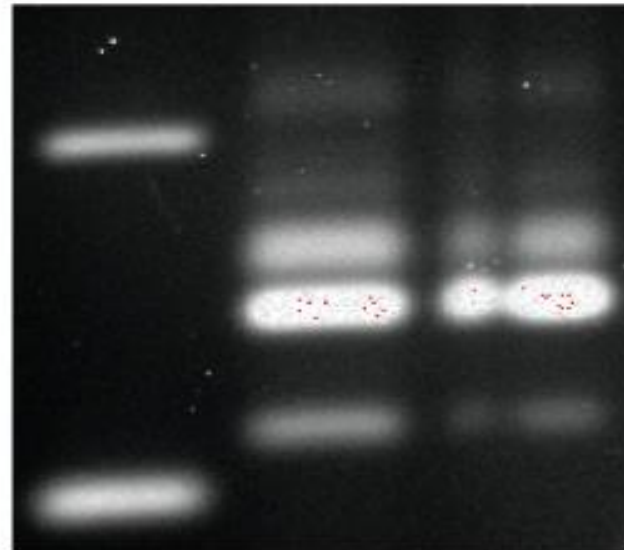
Reinhold et al., J Cell Sci. 1995 Nov;108 ( Pt 11):3419-25.

# CD47 Isoforms



b.

Marker	MOLM13	THP1
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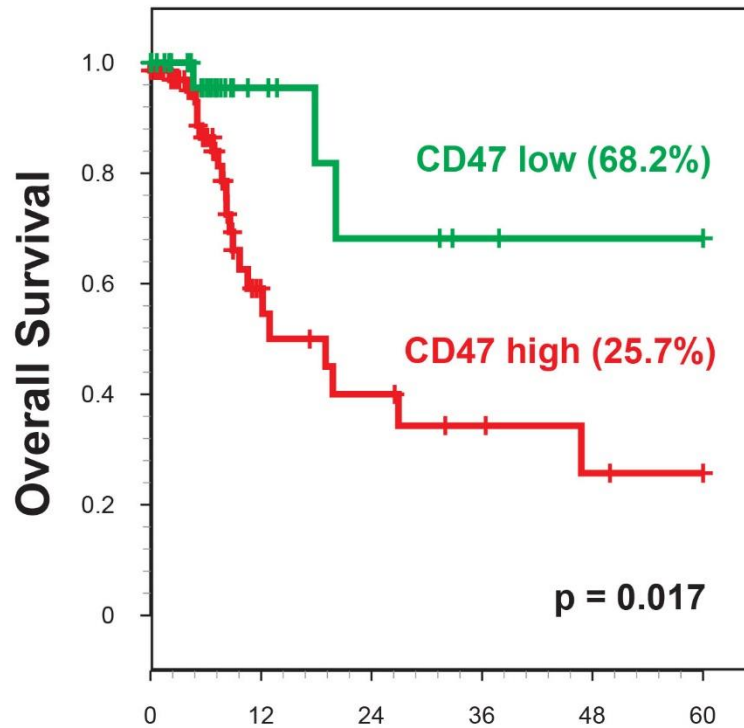


Isoform 1  
Isoform 2  
Isoform 3  
Isoform 4  
Isoform 5

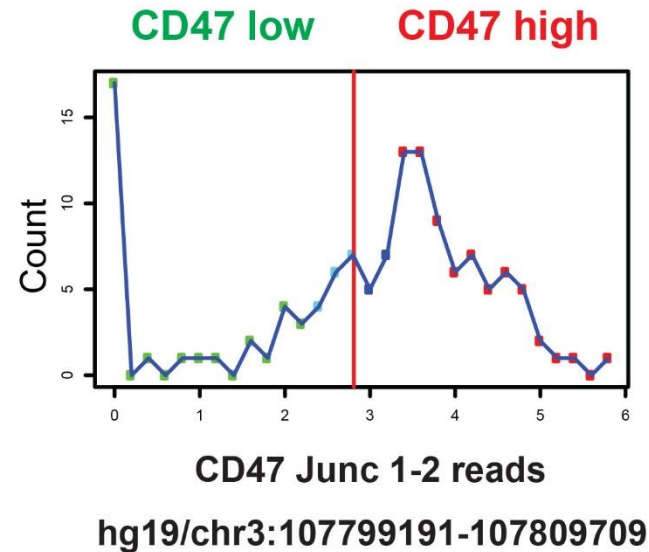
# CD47 is Associated with Survival



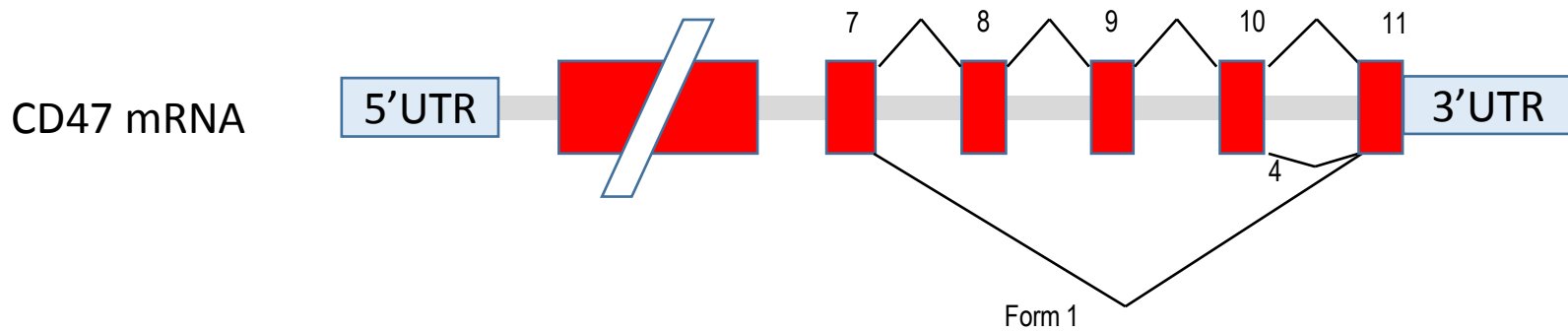
TCGA Bladder Cancer RNASeq



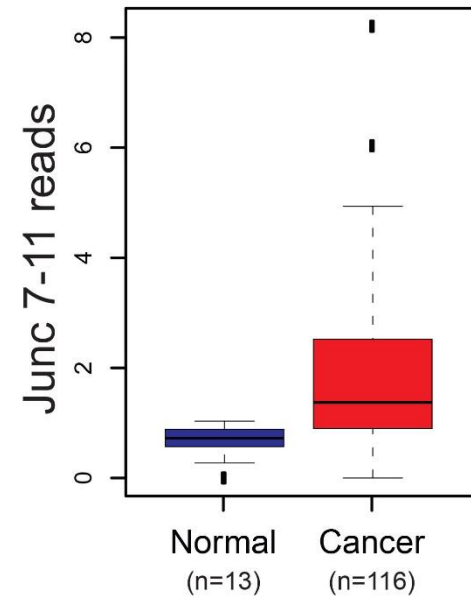
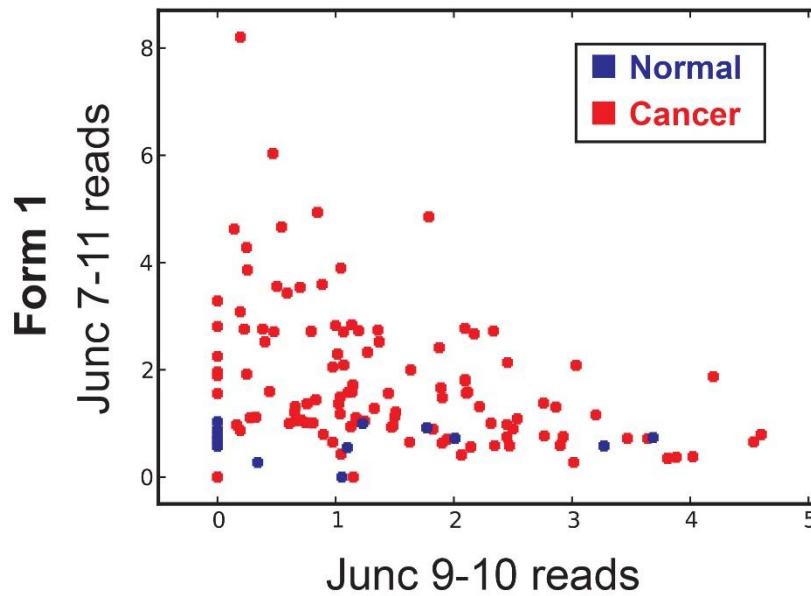
No at risk	0	12	24	36	48	60
<b>CD47 high</b>	71	13	8	5	3	2
<b>CD47 low</b>	32	9	5	3	2	2



# Cancer Specific CD47 Isoforms



TCGA Bladder Cancer RNASeq Dataset (n=129)



Form 4



# Summary



- ❖ CD47 isoforms may be important targets in the bladder cancer diagnosis and treatment
- ❖ We have identified bladder cancer specific CD47 isoforms
  
- ❖ CD47 isoform(s) may confer survival advantage to cancer cells
  - ❑ Not all cancer cells get eaten in an in-vitro phagocytosis assay
  
- ❖ CD47 isoform(s) may prime the cancer cells for efficient phagocytosis

# Acknowledgements



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