

BCB 731:

*Defense Against
the Dark Arts*



Odds & Ends

Dec 6th, 2023



Table 1:
Participant
Characteristics in
Clinical Trials

A neoantigen vaccine clinical trial

Article

Personalized RNA neoantigen vaccines stimulate T cells in pancreatic cancer

<https://doi.org/10.1038/s41586-023-06063-y>

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 Check for updates

Luis A. Rojas^{1,2,18}, Zachary Sethna^{1,2,18}, Kevin C. Soares^{2,3}, Cristina Olcese², Nan Pang², Erin Patterson², Jayon Lihm⁴, Nicholas Ceglia⁴, Pablo Guasp^{1,2}, Alexander Chu⁴, Rebecca Yu^{1,2}, Adrienne Kaya Chandra^{1,2}, Theresa Waters^{1,2}, Jennifer Ruan^{1,2}, Masataka Amisaki^{1,2}, Abderezak Zebboudj^{1,2}, Zagaa Odgerel^{1,2}, George Payne^{1,2}, Evelyn Derhovanessian⁵, Felicitas Müller⁵, Ina Rhee⁶, Mahesh Yadav⁶, Anton Dobrin^{7,8}, Michel Sadelain^{7,8}, Marta Łuksza⁹, Noah Cohen¹⁰, Laura Tang¹¹, Olca Basturk¹¹, Mithat Gönen¹², Seth Katz¹³, Richard Kinh Do¹³, Andrew S. Epstein¹⁴, Parisa Momtaz¹⁴, Wungki Park^{3,14}, Ryan Sugarman¹⁴, Anna M. Varghese¹⁴, Elizabeth Won¹⁴, Avni Desai¹⁴, Alice C. Wei^{2,3}, Michael I. D'Angelica^{2,3}, T. Peter Kingham^{2,3}, Ira Mellman⁶, Taha Merghoub¹⁵, Jedd D. Wolchok¹⁵, Ugur Sahin⁵, Özlem Türeci^{5,16}, Benjamin D. Greenbaum^{4,17}, William R. Jarnagin^{2,3}, Jeffrey Drebin^{2,3}, Eileen M. O'Reilly^{3,14} & Vinod P. Balachandran^{1,2,3}

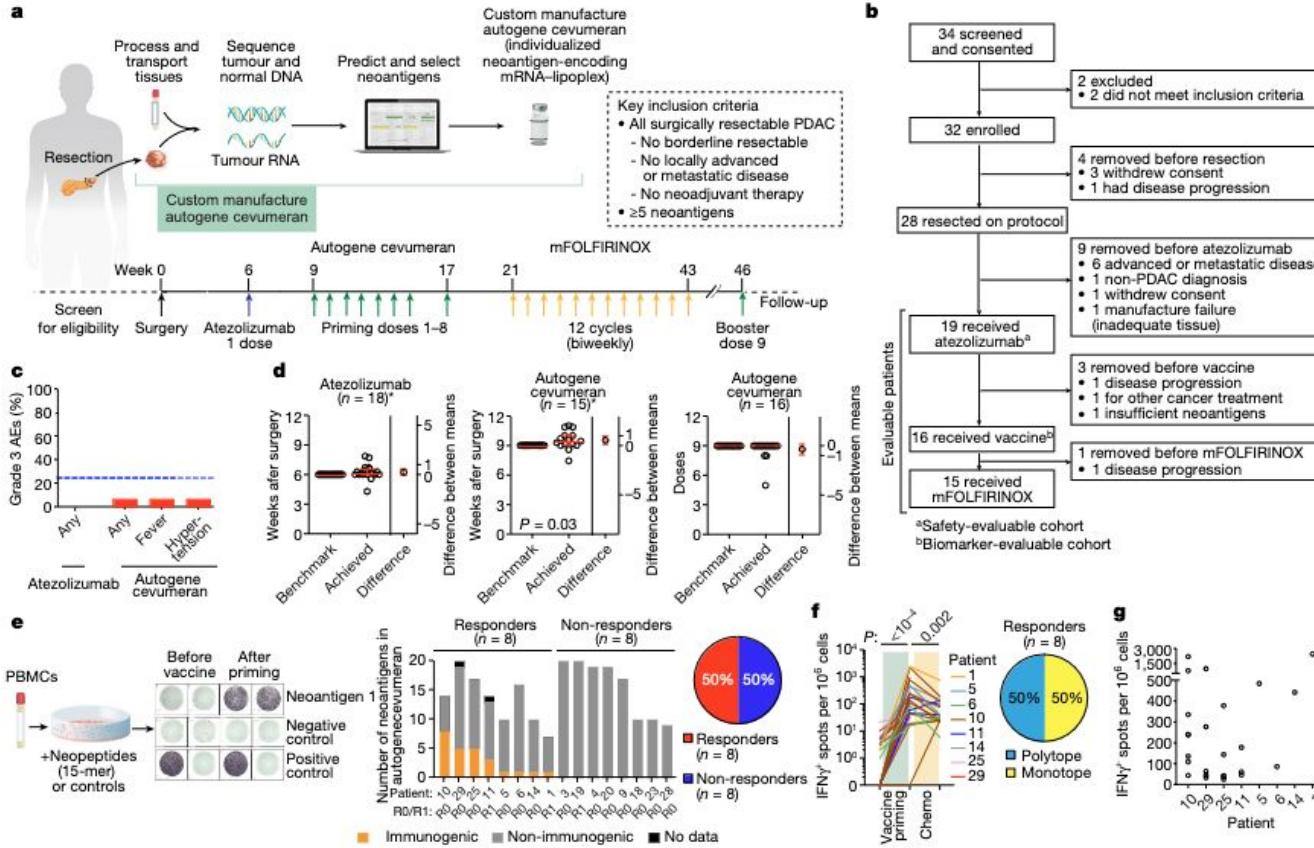
Some familiar authors

A neoantigen fitness model predicts tumour response to checkpoint blockade immunotherapy

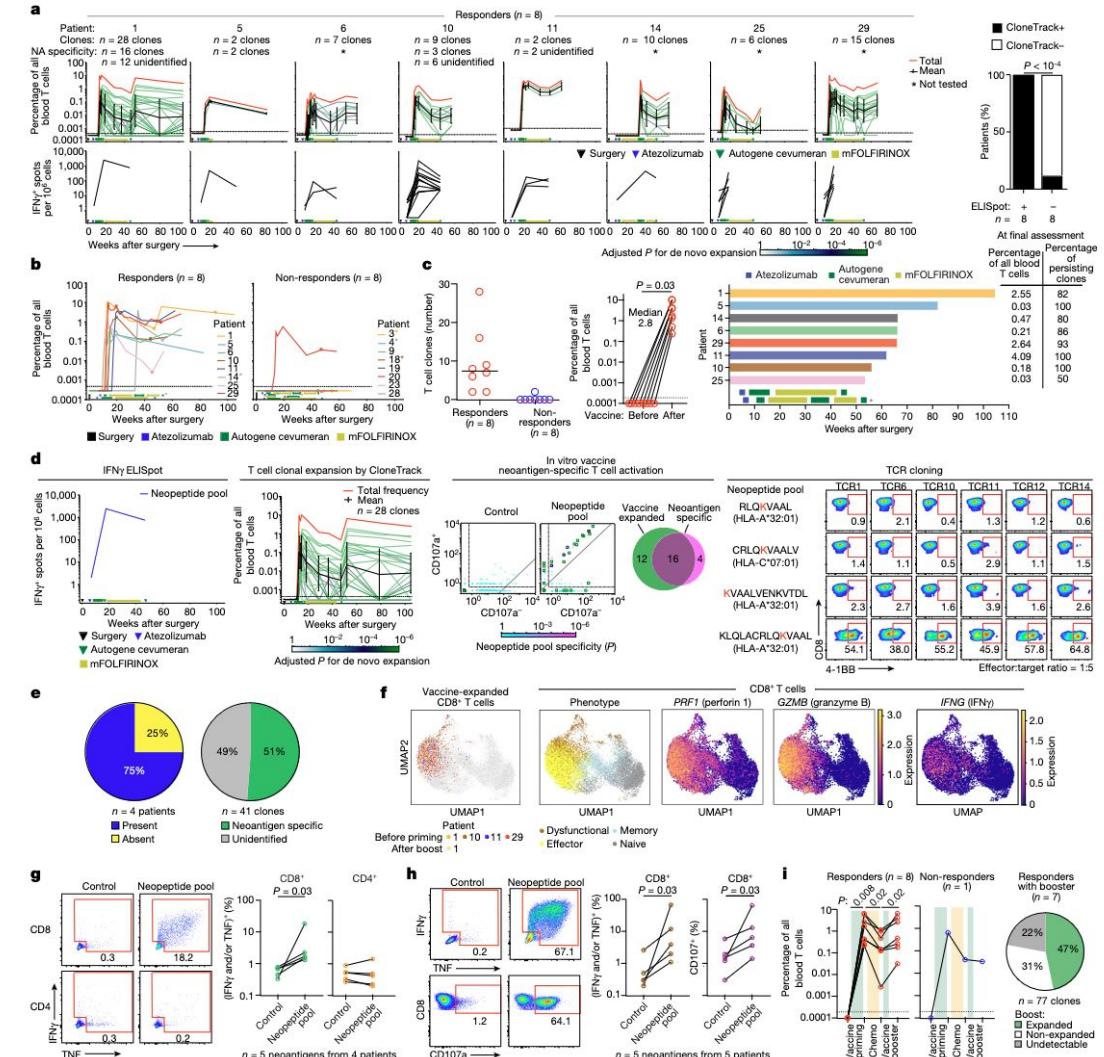
Marta Łuksza¹, Nadeem Riaz^{2,3}, Vladimir Makarov^{3,4}, Vinod P. Balachandran^{5,6,7}, Matthew D. Hellmann^{7,8,9}, Alexander Solovyov^{10,11,12,13}, Naiyer A. Rizvi¹⁴, Taha Merghoub^{7,15,16}, Arnold J. Levine¹, Timothy A. Chan^{2,3,4,7}, Jedd D. Wolchok^{7,8,15,16} & Benjamin D. Greenbaum^{10,11,12,13}

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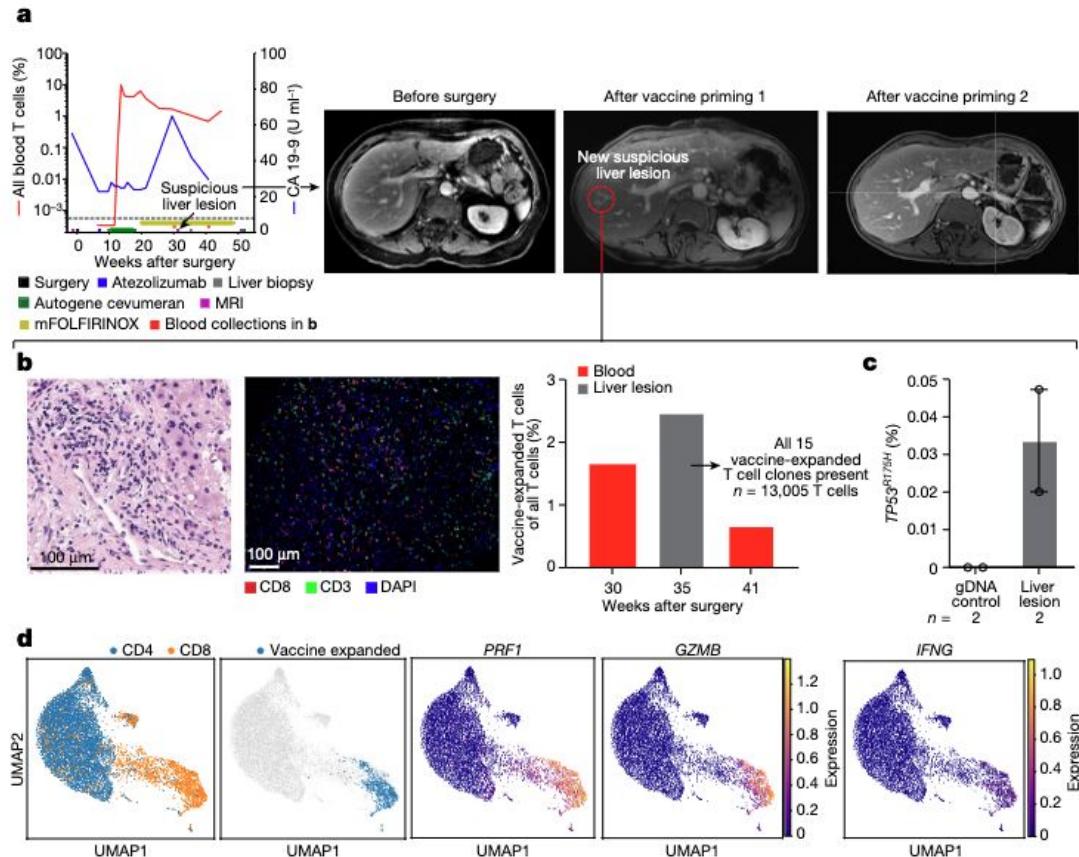
16 vaccinated PDAC patients



We're going to ignore Figure 2

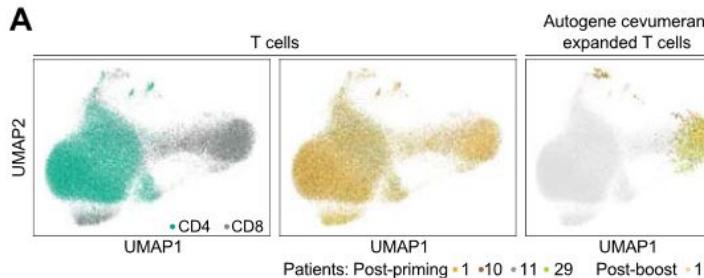


...and the
“interesting
anecdote” of
Figure 4

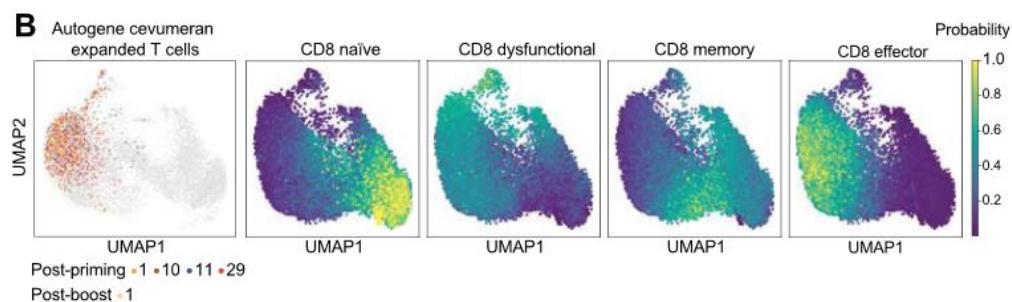


...and the obligatory scRNAseq UMAP art

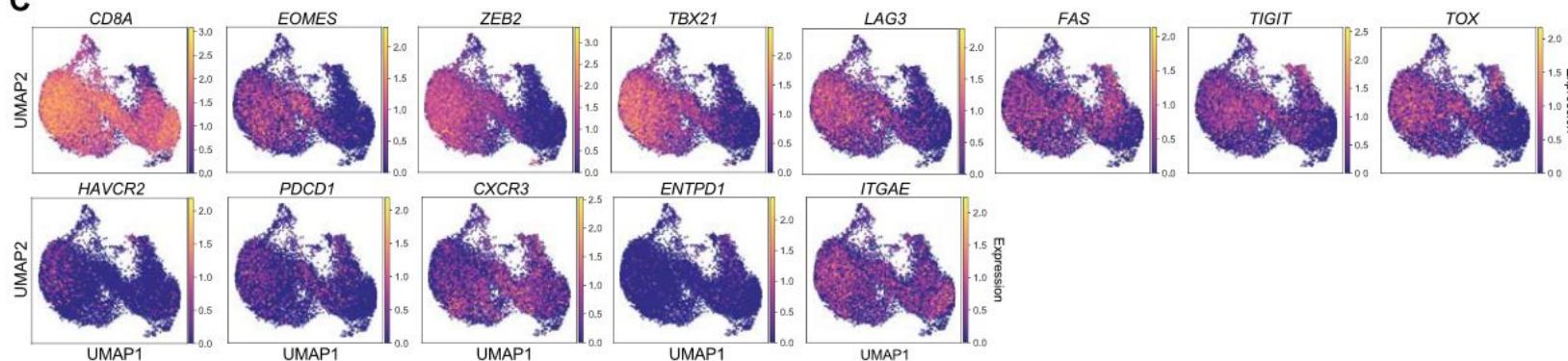
A



B

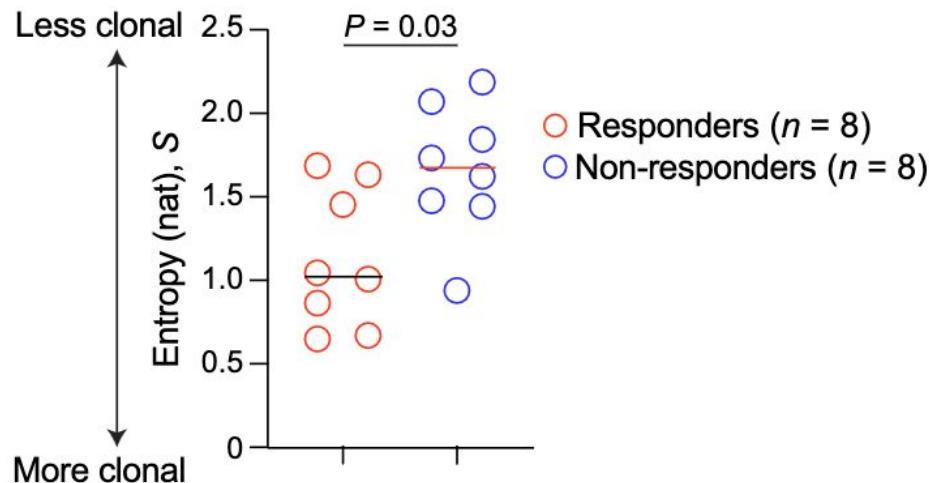


C

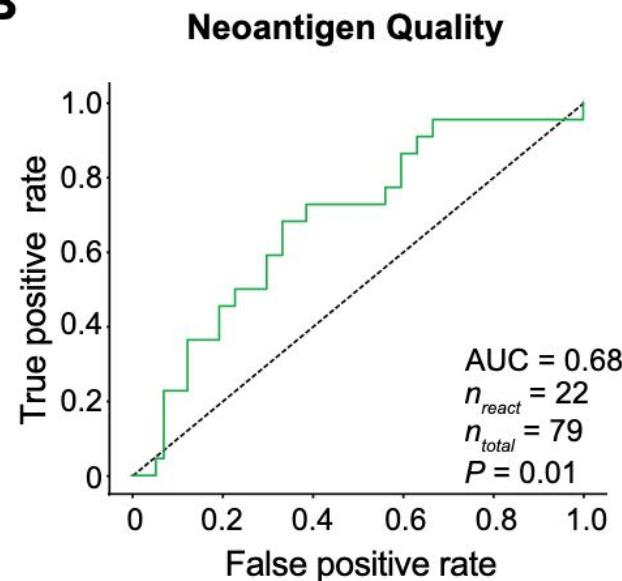


...and all the wacky post-hoc analyses like Extended Data Figure 10

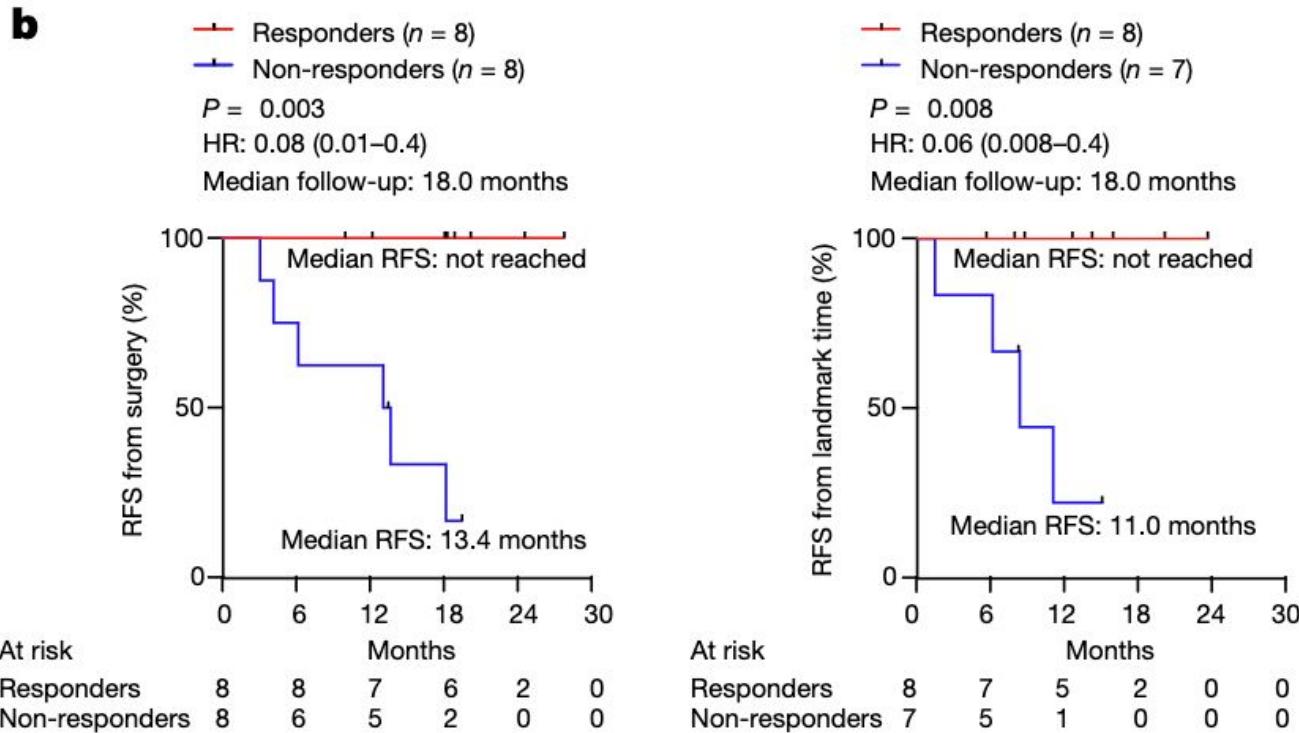
A

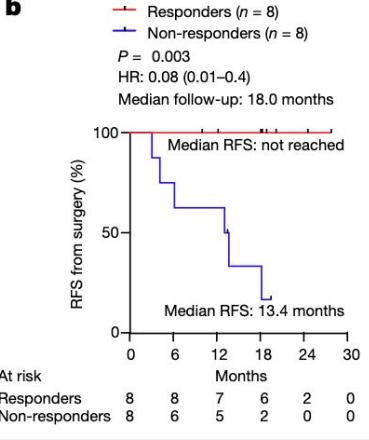


B



Published in Nature because of Figure 3



b

Pancreatic Cancer Vaccine Shows Promise in Small Trial

Using mRNA tailored to each patient's tumor, the vaccine may have staved off the return of one of the deadliest forms of cancer in half of those who received it.

On Wednesday, the scientists [reported results](#) that defied the long odds. The vaccine provoked an immune response in half of the patients treated, and those people showed no relapse of their cancer during the course of the study, a finding that outside experts described as extremely promising.

Where's “Table 1”? (actually Extended Data Figure 1B)

Biomarker evaluable patients							
Characteristic	Responders (n = 8)	Non-responders (n = 8)	P value	Surgical procedure			
Age at diagnosis (y)				Pancreatoduodenectomy	6 (75)	3 (37.5)	0.3
Median (range)	70.5 (59-80)	71.5 (55-76)		Distal pancreatectomy	2 (25)	5 (62.5)	
Mean ± SD	70.5 ± 8.3	71.5 ± 7.8					
Sex				Arterial/venous involvement			>0.99
Female	6 (75)	2 (25)	0.1	Yes	2 (25)	1 (12.5)	
Male	2 (25)	6 (75)		No	6 (75)	7 (87.5)	
Race/ethnicity				Pathology			
White	8 (100)	8 (100)	NA	Stage I	4 (50)	1 (12.5)	0.3
Black	0 (0)	0 (0)		Stage II	3 (37.5)	4 (50)	
Asian	0 (0)	0 (0)		Stage III	1 (12.5)	3 (37.5)	
Unknown	0 (0)	0 (0)		Surgical margin			
Tumor location				R0	6 (75)	7 (87.5)	>0.99
Head	6 (75)	3 (37.5)	0.3	R1	2 (25)	1 (12.5)	
Body/tail	2 (25)	5 (62.5)		Lymph node status			
Primary tumor size (cm)				N0	4 (50)	2 (25)	0.6
Median (range)	2.3 (1.0-2.9)	3 (1.9-4.2)	0.04	N1/N2	4 (50)	6 (75)	
Mean ± SD	2.2 ± 0.6	3.2 ± 0.9		Atezolizumab response			
				Yes	4 (50)	5 (62.5)	>0.99
				No	4 (50)	3 (37.5)	

What else is different about “responders”?

Biomarker evaluable patients

Characteristic	Responders (n = 8)	Non-responders (n = 8)	P value	Surgical procedure			
Age at diagnosis (y)				Pancreatoduodenectomy	6 (75)	3 (37.5)	0.3
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Mean ± SD	70.5 ± 8.3	71.5 ± 7.8					>0.99
Sex				Arterial/venous involvement			
Female	6 (75)	2 (25)	0.1	Yes	2 (25)	1 (12.5)	
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Mean ± SD	2.2 ± 0.6	3.2 ± 0.9		Atezolizumab response			
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				No	4 (50)	3 (37.5)	

Tumor location

Biomarker evaluable patients

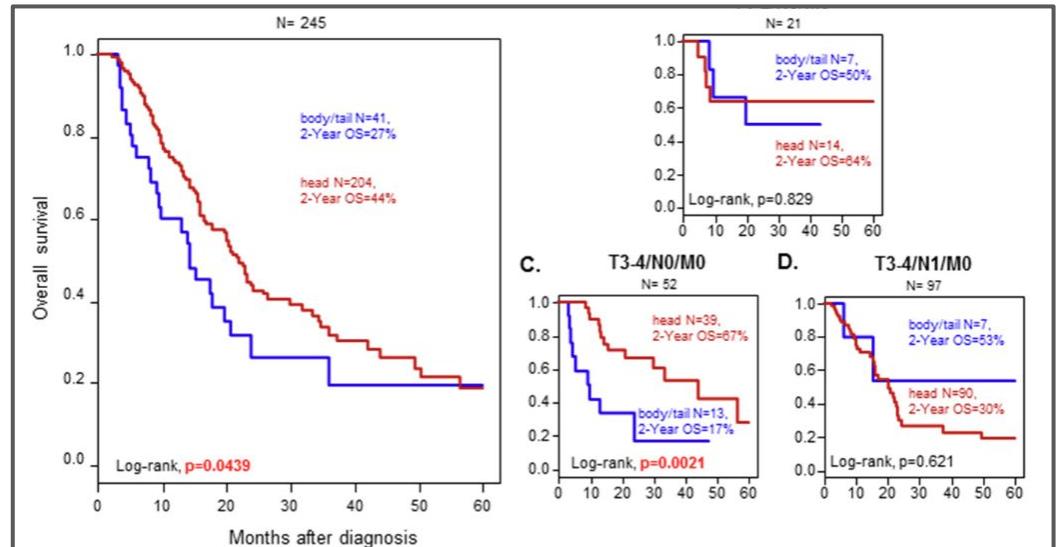
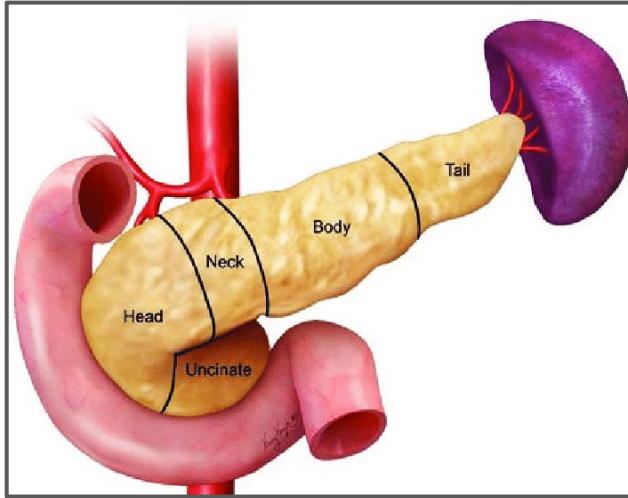
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				Yes	4 (50)	5 (62.5)	>0.99
				No	4 (50)	3 (37.5)	

Tumor location (responders: 6/8 in head)

Article

Head and Body/Tail Pancreatic Carcinomas Are Not the Same Tumors

David Jérémie Birnbaum ^{1,2,3,*}, François Bertucci ^{1,2,4}, Pascal Finetti ¹, Daniel Birnbaum ¹ and Emilie Mamessier ¹



Tumor size

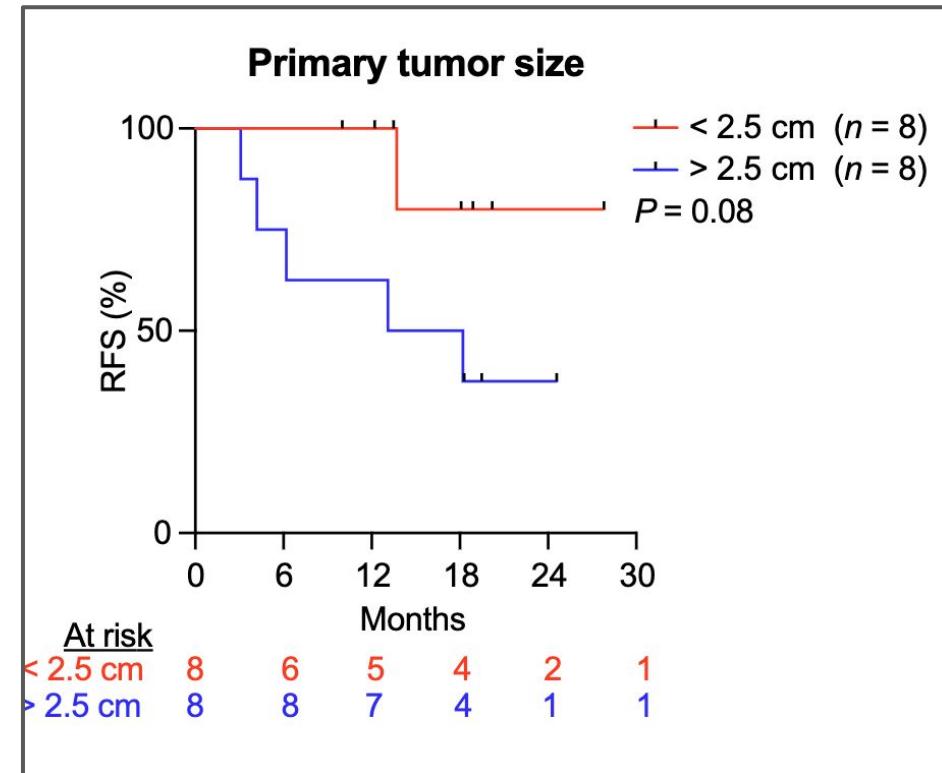
Biomarker evaluable patients

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Unknown	0 (0)	0 (0)		Surgical margin			
Tumor location				R0	6 (75)	7 (87.5)	>0.99
Head	6 (75)	3 (37.5)	0.3	R1	2 (25)	1 (12.5)	
Body/tail	2 (25)	5 (62.5)		Lymph node status			
Primary tumor size (cm)				N0	4 (50)	2 (25)	0.6
Median (range)	2.3 (1.0-2.9)	3 (1.9-4.2)	0.04	N1/N2	4 (50)	6 (75)	
Mean ± SD	2.2 ± 0.6	3.2 ± 0.9		Atezolizumab response			
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				No	4 (50)	3 (37.5)	

Tumor size

Biomarker evaluable patients

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Age at diagnosis (y)			
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Sex			
Female	6 (75)	2 (25)	0.1
Male	2 (25)	6 (75)	
Race/ethnicity			NA
White	8 (100)	8 (100)	
Black	0 (0)	0 (0)	
Asian	0 (0)	0 (0)	
Unknown	0 (0)	0 (0)	
Tumor location			
Head	6 (75)	3 (37.5)	0.3
Body/tail	2 (25)	5 (62.5)	
Primary tumor size (cm)			
Median (range)	2.3 (1.0-2.9)	3 (1.9-4.2)	0.04
Mean ± SD	2.2 ± 0.6	3.2 ± 0.9	



Lymph node invasion

Biomarker evaluable patients

Characteristic	Responders (n = 8)	Non-responders (n = 8)	P value	Surgical procedure			
Age at diagnosis (y)				Pancreatoduodenectomy	6 (75)	3 (37.5)	0.3
Median (range)	70.5 (59-80)	71.5 (55-76)		Distal pancreatectomy with splenectomy	2 (25)	5 (62.5)	
Mean ± SD	70.5 ± 8.3	71.5 ± 7.8					>0.99
Sex				Arterial/venous involvement			
Female	6 (75)	2 (25)	0.1	Yes	2 (25)	1 (12.5)	
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Head	6 (75)	3 (37.5)	0.3	R1	2 (25)	1 (12.5)	
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Lymph node invasion

Ann Surg Oncol (2020) 27:3898–3912
https://doi.org/10.1245/s10434-020-08354-4

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

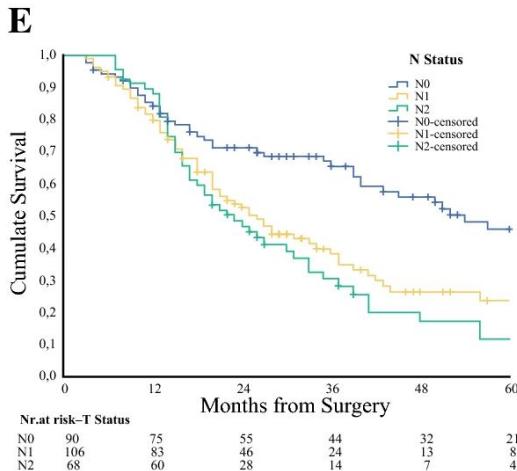
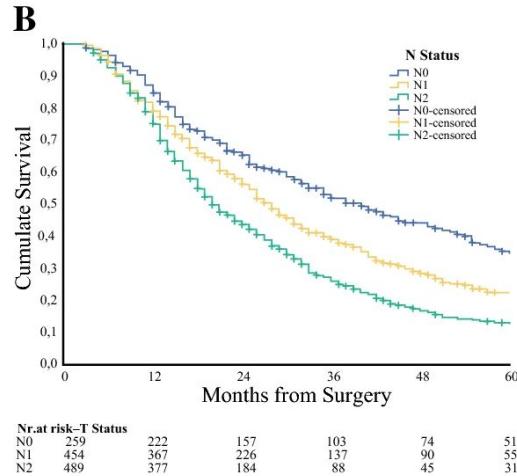


ORIGINAL ARTICLE – PANCREATIC TUMORS

Does Site Matter? Impact of Tumor Location on Pathologic Characteristics, Recurrence, and Survival of Resected Pancreatic Ductal Adenocarcinoma

Giuseppe Malleo, MD, PhD¹, Laura Maggino, MD¹, Cristina R. Ferrone, MD, FACS², Giovanni Marchegiani, MD, PhD¹, Claudio Luchini, MD³, Mari Mino-Kenudson, MD⁴, Salvatore Paiella, MD, PhD¹, Motaz Qadan, MD, PhD, FACS², Aldo Scarpa, MD³, Keith D. Lillemoe, MD, FACS², Claudio Bassi, MD, FACS¹, Carlos Fernández-del Castillo, MD, FACS², and Roberto Salvia, MD, PhD¹

¹Unit of General and Pancreatic Surgery, Department of Surgery and Oncology, G.B. Rossi Hospital, University of Verona Hospital Trust, Verona, Italy; ²Department of Surgery, Massachusetts General Hospital, Harvard Medical School, Boston, MA; ³Department of Pathology and Diagnostics, University of Verona Hospital Trust, Verona, Italy; ⁴Department of Pathology, Massachusetts General Hospital, Harvard Medical School, Boston, MA



Stage

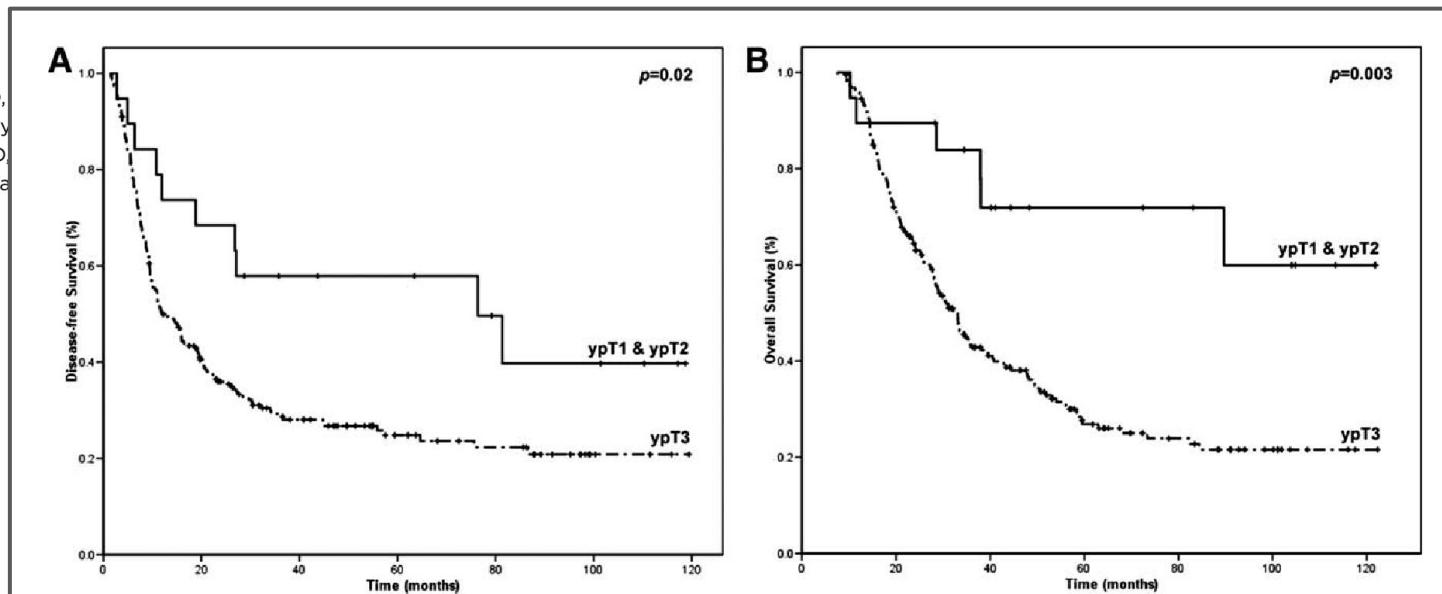
Biomarker evaluable patients

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Mean ± SD	70.5 ± 8.3	71.5 ± 7.8					>0.99
Sex				Arterial/venous involvement			
Female	6 (75)	2 (25)	0.1	Yes	2 (25)	1 (12.5)	
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White	8 (100)	8 (100)	NA	Stage I	4 (50)	1 (12.5)	0.3
Black	0 (0)	0 (0)		Stage II	3 (37.5)	4 (50)	
Asian	0 (0)	0 (0)		Stage III	1 (12.5)	3 (37.5)	
Unknown	0 (0)	0 (0)					
Tumor location				Surgical margin			
Head	6 (75)	3 (37.5)	0.3	R0	6 (75)	7 (87.5)	>0.99
Body/tail	2 (25)	5 (62.5)		R1	2 (25)	1 (12.5)	
Primary tumor size (cm)				Lymph node status			
Median (range)	2.3 (1.0-2.9)	3 (1.9-4.2)	0.04	N0	4 (50)	2 (25)	0.6
Mean ± SD	2.2 ± 0.6	3.2 ± 0.9		N1/N2	4 (50)	6 (75)	
				Atezolizumab response			
				Yes	4 (50)	5 (62.5)	>0.99
				No	4 (50)	3 (37.5)	

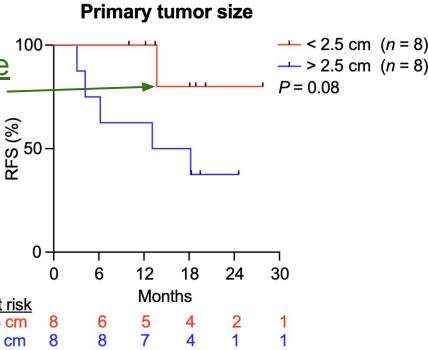
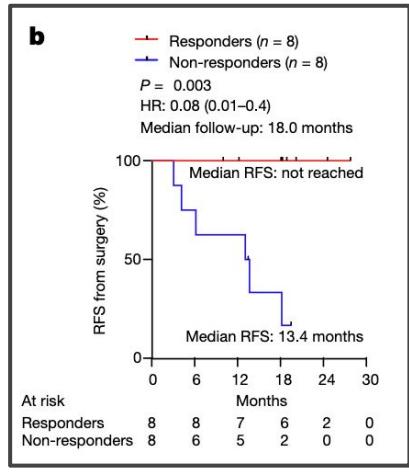
Stage

Post-Therapy Pathologic Stage and Survival in Patients With Pancreatic Ductal Adenocarcinoma Treated With Neoadjuvant Chemoradiation

Jeannelyn S. Estrella, MD¹; Asif Rashid, MD,
Robert A. Wolf, MD³; Gauri R. Varadhachary
Jean-Nicolas Vauthey, MD²; Hua Wang, MD
James L. Abbruzzese, MD³ and Huamin Wa



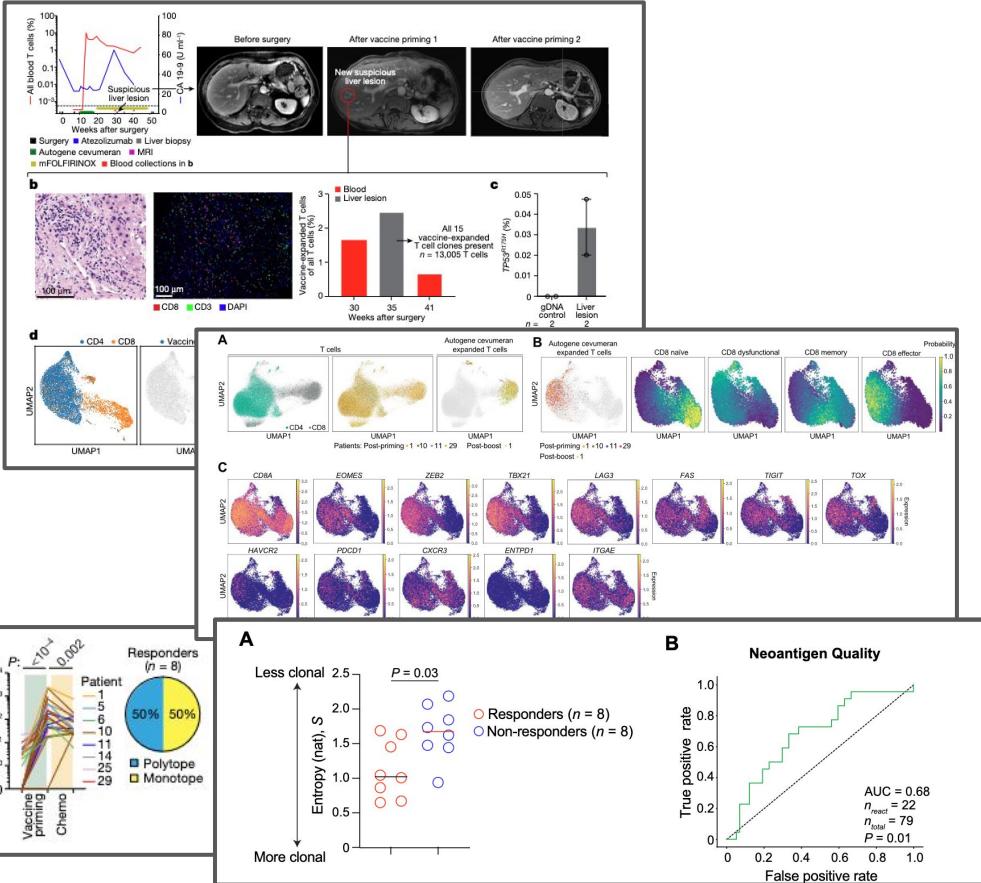
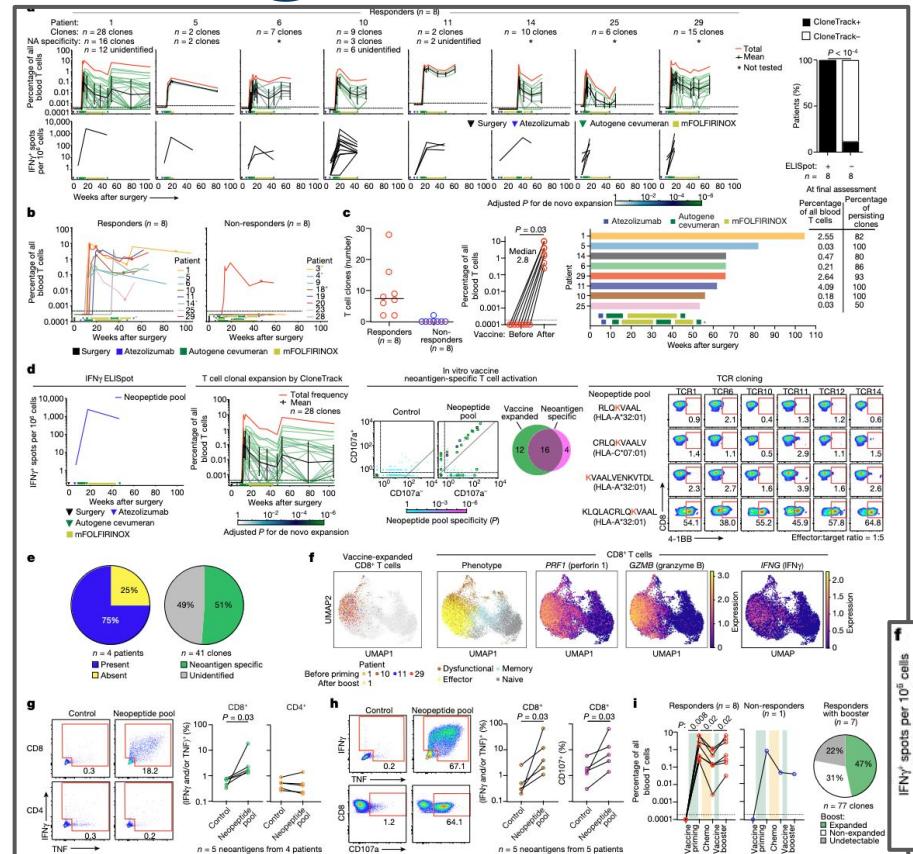
Neoantigen vaccine response drives RFS?



Tumor location	Head 6 (75)	Body/tail 2 (25)	3 (37.5) 5 (62.5)	0.3
Primary tumor size (cm)	Median (range) 2.3 (1.0-2.9)	Mean \pm SD 2.2 \pm 0.6	3 (1.9-4.2) 3.2 \pm 0.9	0.04
Pathology	Stage I 4 (50)	Stage II 3 (37.5)	Stage III 1 (12.5)	0.3
Surgical margin	R0 6 (75)	R1 2 (25)	7 (87.5) 1 (12.5)	>0.99
Lymph node status	N0 4 (50)	N1/N2 4 (50)	2 (25) 6 (75)	0.6
Atezolizumab response	Yes 4 (50)	No 4 (50)	5 (62.5) 3 (37.5)	>0.99



Ignore this stuff, look at “Table 1”



...and, lastly, fraud

“Vertical irregularities”

Cell, Vol. 97, 927–941, June 25, 1999, Copyright ©1999 by Cell Press

A Ligand-Gated Association between Cytoplasmic Domains of UNC5 and DCC Family Receptors Converts Netrin-Induced Growth Cone Attraction to Repulsion

Kyonsoo Hong,^{*§} Lindsay Hinck,^{†\$||}
Makoto Nishiyama,^{*} Mu-ming Poo,^{*}
Marc Tessier-Lavigne,^{†‡} and Elke Stein^{†§}

elongation and branching of embryonic sensory axons
(reviewed in Van Vactor and Flanagan, 1999).
Several types of mechanisms could in principle under-

“Vertical irregularities”

Cell, Vol. 97, 927–941, June 25, 1999, Copyright ©1999 by Cell Press

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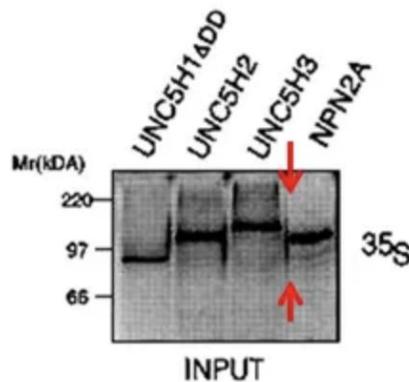
Kyonsoo Hong,^{*§} Lindsay Hinck,^{†\$||}
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Marc Tessier-Lavigne,^{†‡} and Elke Stein^{†§}

elongation and branching of embryonic sensory axons
(reviewed in Van Vactor and Flanagan, 1999).
Several types of mechanisms could in principle under-

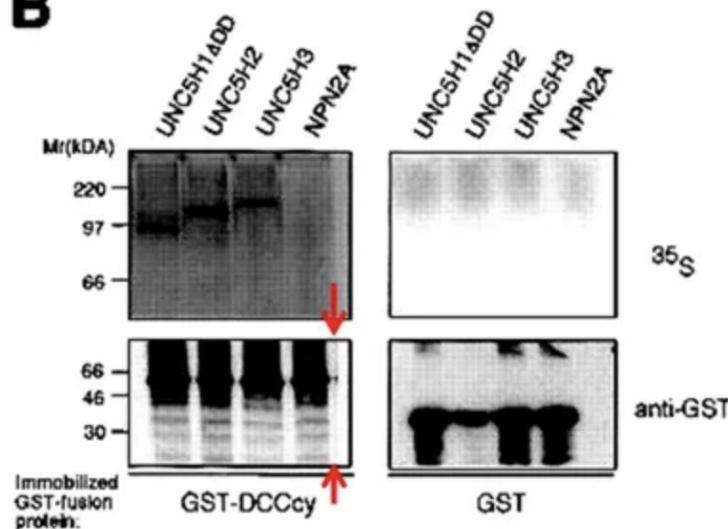
“Vertical irregularities”

Fig 5

A



B



“Vertical irregularities”

A

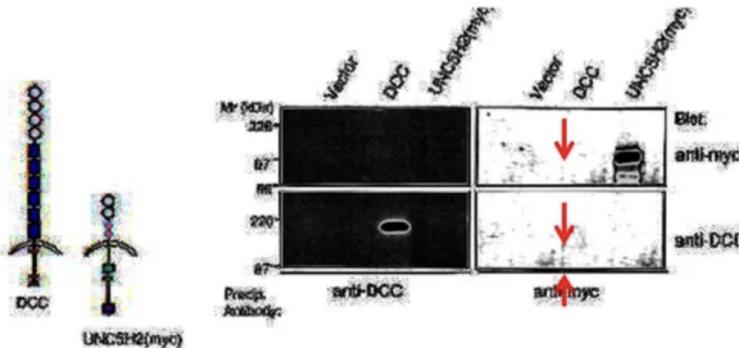


Fig 3

DOI: [http://dx.doi.org/10.1016/S0092-8674\(00\)80804-1](http://dx.doi.org/10.1016/S0092-8674(00)80804-1)

C

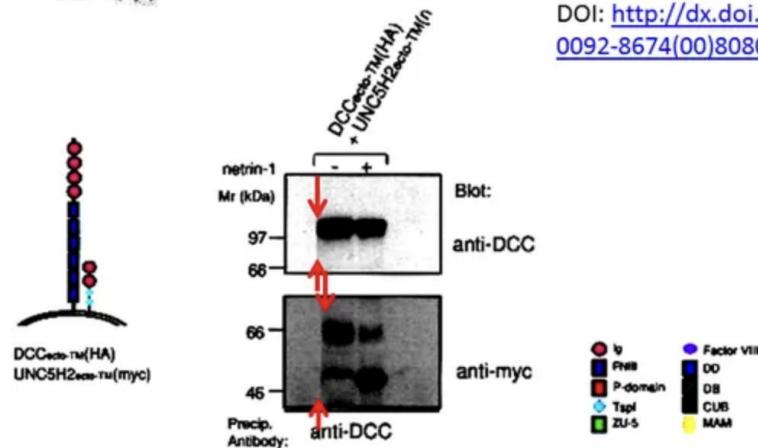
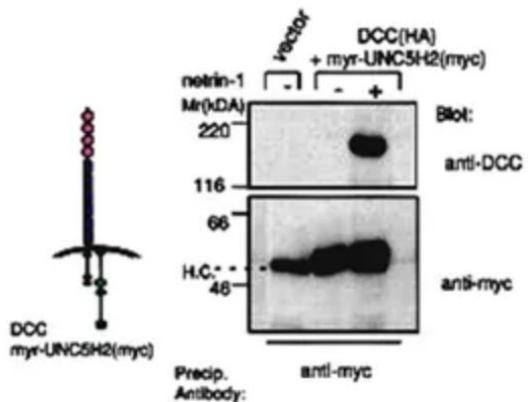
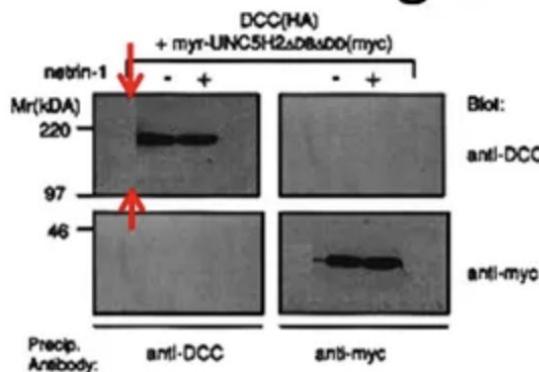


Fig 7

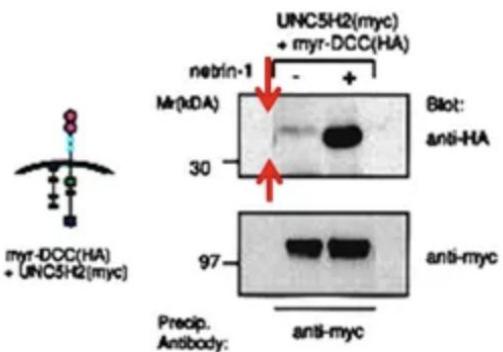
A



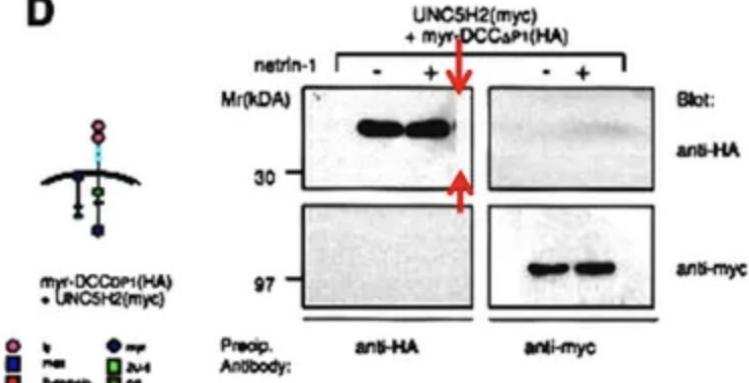
C



B



D



Outcome

HOME > NEWS > SCIENCEINSIDER > STANFORD PRESIDENT TO STEP DOWN DESPITE PROBE EXONERATING HIM OF RESEARCH MISCONDUCT

SCIENCEINSIDER | PEOPLE & EVENTS

Stanford president to step down despite probe exonerating him of research misconduct

University investigation finds data manipulation by others in Marc Tessier-Lavigne's lab and says he should have corrected work more "decisively"

Tessier-Lavigne, 63, is best known for his work in the 1990s discovering netrins, proteins that guide the growth of nerve cell projections known as axons in the developing spinal cord. His resignation brings an end to an extraordinary 8 months that began in late November 2022, when Stanford's student paper, *The Stanford Daily*, reported that *The EMBO Journal* was investigating alleged image manipulation in a 2008 paper and that [Bik](#) had confirmed similar possible problems in other articles on which he was a co-author. The image issues had come to the newspaper's attention via a discussion of them on [PubPeer](#), a forum where scientists, often anonymously, discuss irregularities in papers. Stanford's Board of Trustees announced it was forming a special committee to investigate.

The Other Kind of Cloning

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RESEARCH ARTICLE | RADIATION TOXICITY



Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice

VINCENT FAVAUDON, LAURA CAPLIER, VIRGINIE MONCEAU, FRÉDÉRIC POUZOULET, [...], AND MARIE-CATHERINE VOZENIN

+8 authors

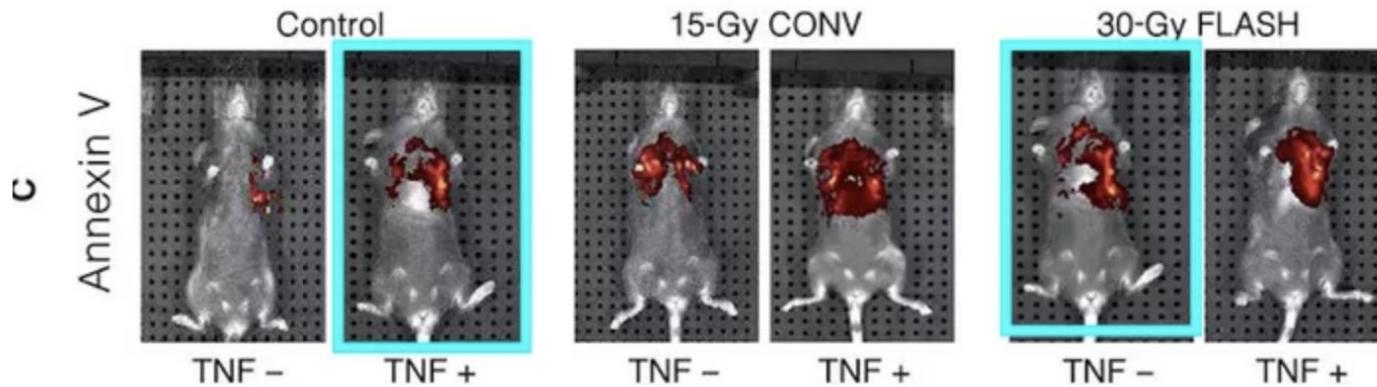
[Authors Info & Affiliations](#)

The Other Kind of Cloning

#1 Elisabeth M Bik commented September 2019

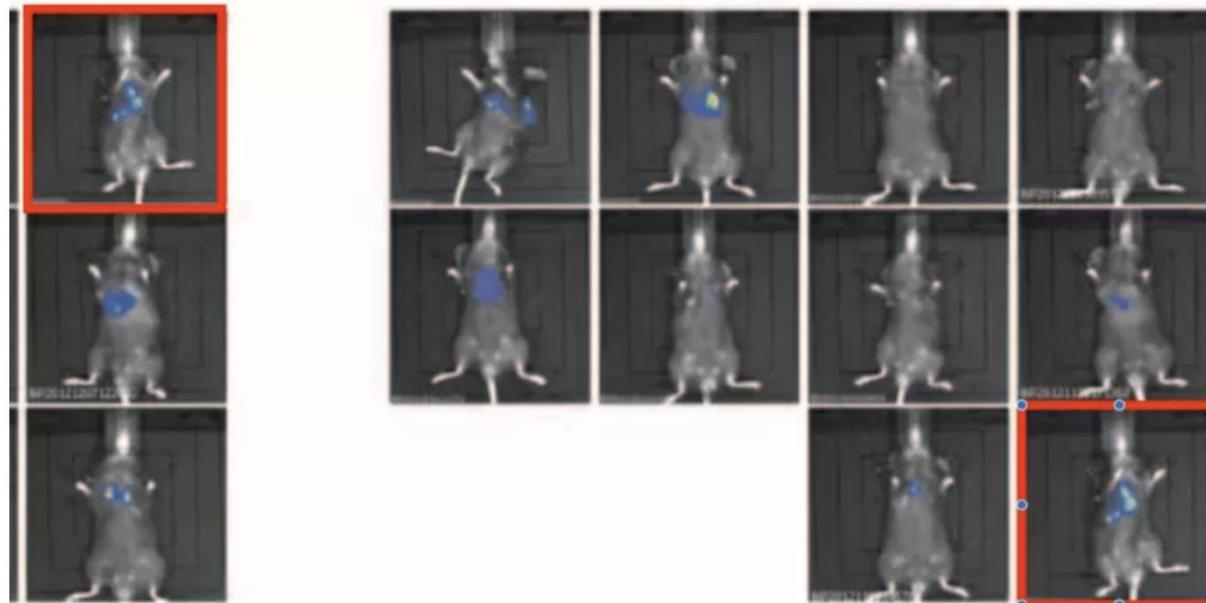
Figure 2C. The same mouse appears to be visible twice. The measured signal is slightly different between the 2 panels, but similarly shaped. Could the authors please check?

Shown in aqua boxes.

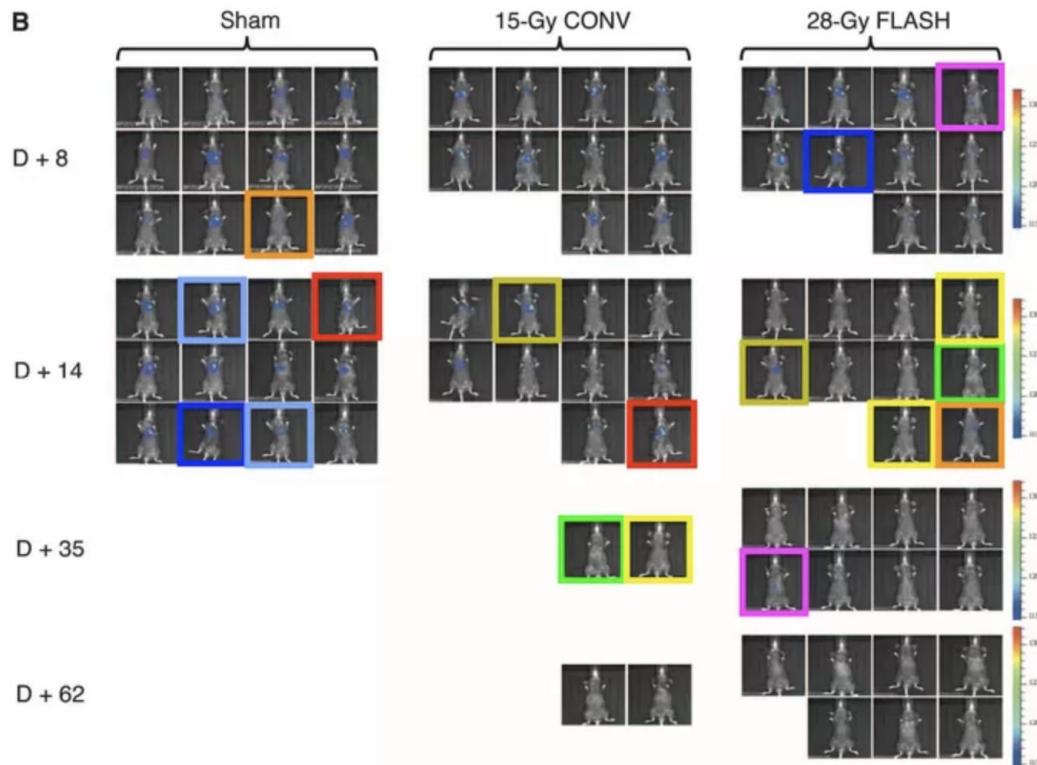


The Other Kind of Cloning

Same question for Figure 4



A lot of cloning!



Not just mice

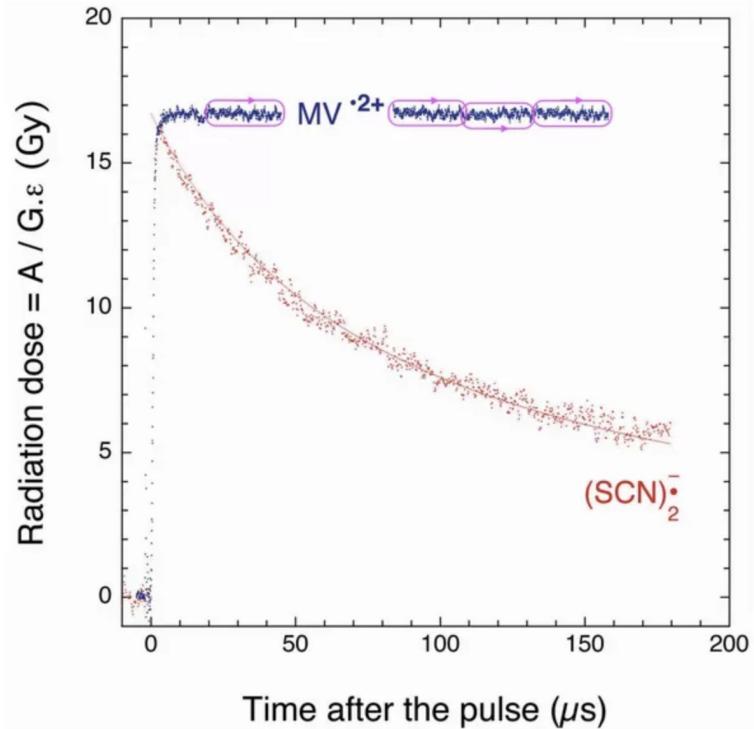


Fig. S4. Time course of the evolution of the methyl viologen MV²⁺

Response

#10 Marie-Catherine Vozenin commented August 2022

Author Response

Dear Dr Bik, Regarding the FigureS4, the chemical reaction is induced by an irradiation that lasts 2.2 micros and reaches saturation within this timeframe. The reaction is stable over seconds, therefore measuring over 20 or 50 micros does not change the signal. In 2019, we were not aware of the pubpeer website and were alerted by a colleague that mistakes were found. We checked the figures and indeed, we have found duplications in the IVIS images presented Figure 2C and Figure 4B and wrote an erratum. In 2022, Vincent Favaudon and my emails have now been added and we had a message from the website which gave us the opportunity to answer. Regarding the first comments you posted in 2019, images showed results on 1 sequence and 1 mouse whereas quantification was performed on the entire cohort of mice on the entire sequence of images. The quantification files enabled us to track the mislabeled images. The main conclusion is that FLASH spared normal tissue but that CONV and FLASH are inducing the same anti-tumor effect. This conclusion was not based on images but on IVIS quantification but supported by an array of experiments included in this paper. As explained in my previous message, the mistakes on images were random and unintentional. The fact that the main conclusions of this paper have now been reproduced by many groups over the world showed the validity of the work and support the fact that no mystification was intended. We realize that such mistakes were unfortunate despite multiple readings by the authors and co-authors, events that transpired almost 10 years ago. For this specific article, a large number of images were produced by many different devices and authors were working at several different Institutions, which likely contributed to certain minor errors in image duplication that had no impact whatsoever on the overall rigorous quantification of data. Since that time, we have established a QA check before any submission and a data management plan to keep track of all raw data/image files. If you have some more suggestions/software that might help us facilitate data management across multiple platforms we would welcome your advice. I also have a question, why your doubt about FigS4 was not posted in 2019? In the end, we stand by our conclusions that were published in this paper, and do not feel these conclusions were misrepresented in any way.

 *Fin*