Presenting your Data in Talks and Manuscripts

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SITC Cancer Immunotherapy Winter School

Houston Texas

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THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Disclosure information
SITC Cancer Immunotherapy Winter School

Presenting your Data in Talks and Manuscripts

Jennifer A. Wargo MD MMSc

- I have the following financial relationships to disclose:

- Speaker's bureau: Imedex, Dava, Omniprex, Illumina, BMS
- Advisory board member: Roche - Genentech, GSK, Novartis, Astra-Zeneca
- Clinical trial support: Roche - Genentech, GSK, BMS, Novartis

- *I am co –Inventor on patent submitted by The University of Texas MD Anderson Cancer Center to the US Patent and Trademark Office based on this work (Patent # PCT/US1/53717)*

I have given a lot of talks and submitted a lot of manuscripts –
but I am always learning better ways to do these from friends worldwide


Together we are making a difference in the lives of patients with cancer…
Scientific presentations and manuscripts help to spread the word about important advances

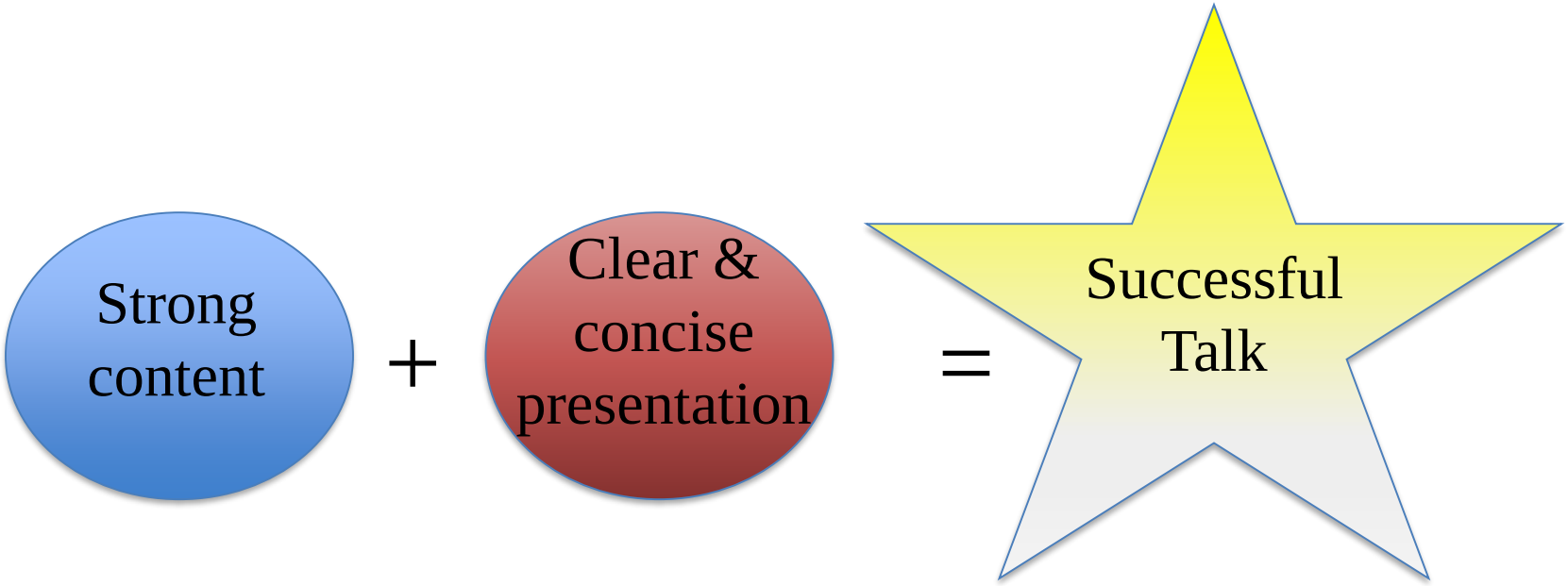
Presenting your Data in Talks and Manuscripts

I. Crafting an thoughtful and memorable scientific talk

II. Preparing and submitting an impactful scientific manuscript

III. Key points and take home messages

I. Crafting a thoughtful and memorable talk



“Proper planning and preparation prevents poor performance”

Stephen Keague – The little red handbook of public speaking and presenting

- A key first step is to know who will be viewing your presentation
    - What is the size / range of expertise of those viewing?
- What other topics are being covered in the conference / session?
- What would the session chairs / conference organizers like you to present?

As you are crafting your talk, keep the following in mind:

1) *Keep the title short if possible and introduce yourself at the beginning of the talk (convey your enthusiasm / expertise)*
2) *Provide an outline– letting the audience know what to expect – with transition slides in between*
3) *Set the stage for your talk, with a provocative concept / lead-in with a case example*

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Raising the tail in cancer immunotherapy: the tissue is the issue - but the scoop is in the poop

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American Association for Cancer Research

Rational Combination Therapies in Immune-oncology

Chicago, Illinois USA

April 17, 2018

Microbiota, Immune-tonus, and cancer: *Biology*

I. Impact of tumor microbiome on responses to cancer therapy

II. Impact of gut microbiome on responses to cancer therapy

III. Other provocative factors that should be considered

PRESENTED BY: JENNIFER A. WARGO MD MMSC

“During the first few minutes of your presentation, your job is to assure the audience members that you are not going to waste their time and attention”

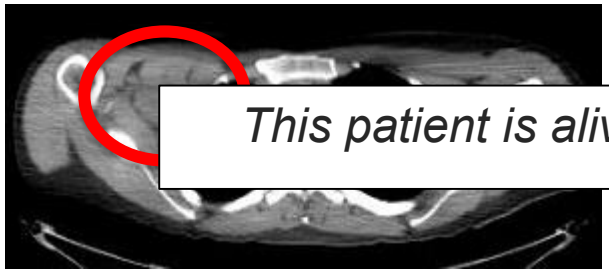
Dale Ludwig and Greg Owenboger

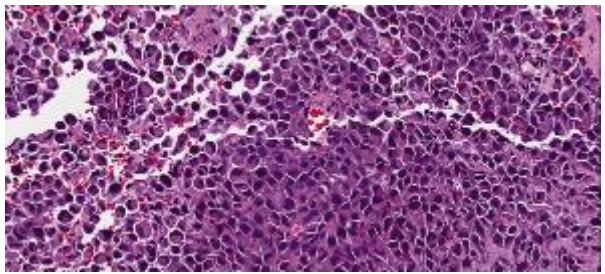
Why should we study the microbiome?

There are more genes in the human microbiome than there are stars in the galaxy

Case example

- 45 yo female with prior hx of R arm melanoma presented in October 2013 with bulky adenopathy in R axilla (unresectable). She was offered palliative radiation and was told to “get her affairs in order.”
  - She presented to MDACC where a biopsy showed a $BRAF^{V600E}$ mutation



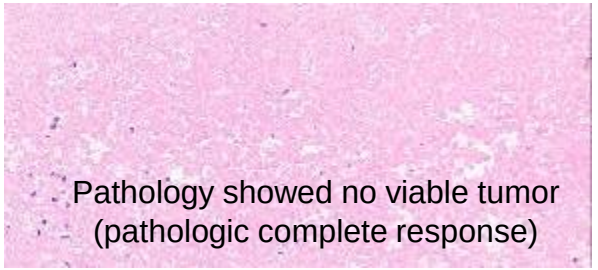


October 2013

neoadjuvant BRAF/MEK inhibitors and restaging showed a complete response

She was taken to surgery for an axillary lymph node dissection

This patient is alive, well, and free of disease 6 years later…



December 2013

As you present data in your slides,

Remember that it is best if you try to tell a story,

And best to use figures rather than extensive text

(with smooth transitions and text on slides highlighting conclusions)

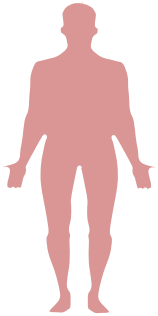
An example of one of my slides from a decade ago

Melanoma vaccination strategies

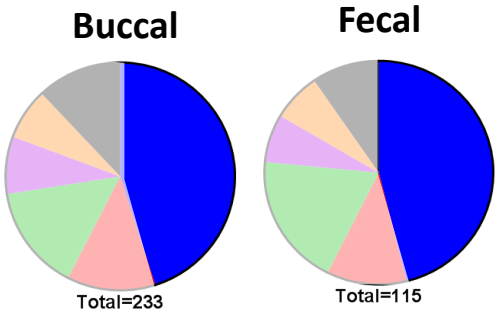
- Whole cell vaccines (autologous and allogeneic)
- Peptide vaccines (+ adjuvants, helper peptides, GM-CSF)
- Viral vectors (antigen peptides + co-stimulatory molecules)
- Dendritic cells based vaccines
- DNA vaccines (most of the work done in animal model human validation is scarce – few trials with mostly negative results so far)
- Ganglioside vaccines (glycolipids present on cell surface, minimally expressed in normal cells but highly expressed on melanoma cells – generate only humoral response)

Wargo slide from 2010 – while Instructor at Harvard / MGH

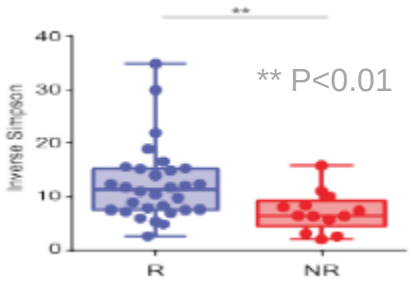
We studied oral and gut (fecal) microbiome in a large cohort of patients with metastatic melanoma going onto systemic therapy

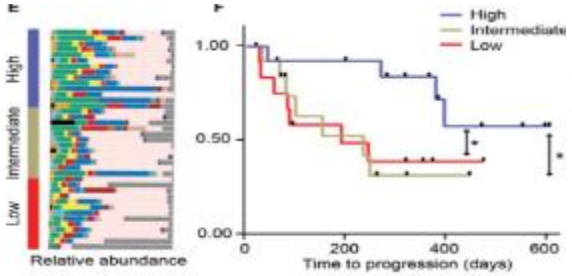


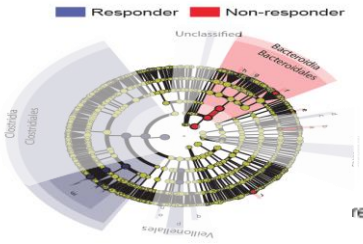
n = 233 patients

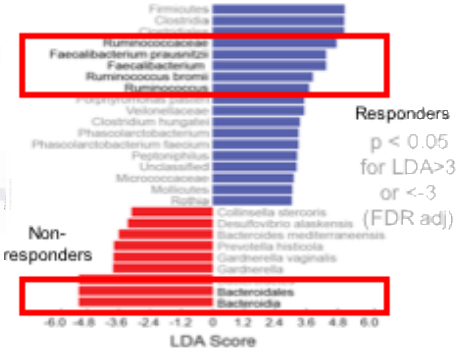


Microbiome sequencing & immune profiling was performed









Responders to anti-PD-1 had a higher diversity of gut bacteria associated with prolonged PFS (along with additional compositional differences)

Deepak Gopalakrishnan PhD

Gopalakrishnan et al, Science 2018

Christine Spencer PhD

As a general rule:

1) *Allocate about a minute per slide for the presentation (depending on complexity)*
2) *Walk the audience through the data on each slide, remember the diversity of your audience*
3) *Present unpublished data (refreshing for the audience and provides an opportunity for feedback and collaboration)*

The lasting health toll of chemical warfare *p. 20*

Hidden impacts of air pollution *p. 39*

Flying through Saturn's ionosphere *p. 66*

Science

$15
5 JANUARY 2018
sciencemag.org

AAAS

GUT MICROBES AND CANCER

The microbiome influences patient response to immunotherapy

pp. 32, 91, 97, & 104

Gut microbiome modulates response to anti–PD-1 immunotherapy in melanoma patients

V. Gopalakrishnan,[1,2*] C. N. Spencer,[2,3*] L. Nezi,[2*] A. Reuben,[1] M. C. Andrews,[1] T. V. Karpinets,[3] P. A. Prieto,[1†] D. Vicente,[1] K. Hoffman,[3] S. C. Wei,[3] A. P. Cogdill,[1,3] L. Zhao,[3] C. W. Hudgens,[3] D. S. Hutchinson,[3] T. Manzo,[3] M. Petaccia de Macedo,[4‡] T. Cotechini,[4] T. Kumar,[4] W. S. Chen,[5] S. M. Reddy,[10] R. Szczepaniak Sloane,[1] J. Galloway-Pena,[11] H. Jiang,[1] P. L. Chen,[2§] E. J. Shpall,[12] K. Rezvani,[12] A. M. Alousi,[12] R. F. Chemaly,[11] S. Shelburne,[3,11] L. M. Vence,[2] P. C. Okhuysen,[11] V. B. Jensen,[13] A. G. Swennes,[7] F. McAllister,[14] E. Marcelo Riquelme Sanchez,[14] Y. Zhang,[14] E. Le Chatelier,[15] L. Zitvogel,[16] N. Pons,[15] J. L. Austin-Breneman,[1‖] L. E. Haydu,[1] E. M. Burton,[1] J. M. Gardner,[1] E. Sirmans,[17] J. Hu,[13] A. J. Lazar,[5,9] T. Tsujikawa,[5] A. Diab,[17] H. Tawbi,[17] I. C. Glitza,[17] W. J. Hwu,[17] S. P. Patel,[17] S. E. Woodman,[17] R. N. Amaria,[17] M. A. Davies,[17] J. E. Gershenwald,[1] P. Hwu,[17] J. E. Lee,[1] J. Zhang,[2] L. M. Coussens,[6] Z. A. Cooper,[1,2¶] P. A. Futreal,[2] C. R. Daniel,[1,2] N. J. Ajami,[3] J. F. Petrosino,[3] M. T. Tetzlaff,[4,6] P. Sharma,[2,18] J. P. Allison,[2] R. R. Jenq,[2#] J. A. Wargo,[1,2#**]

Gut microbiome influences efficacy of PD-1–based immunotherapy against epithelial tumors

Bertrand Routy,[1,2,3] Emmanuelle Le Chatelier,[4] Lisa Derosa,[1,2,3] Connie P. M. Duong,[1,2,3] Maryam Tidjani Alou,[1,2,3] Romain Daillère,[1,2,3] Aurélie Fluckiger,[1,2,3] Meriem Messaoudene,[1,2] Conrad Rauber,[1,2,3] Maria P. Roberti,[1,5,6] Marine Fidelle,[1,5,6] Caroline Flament,[1,5,6] Vichnou Poirier-Colame,[1,5,6] Paule Opolon,[6] Christophe Klein,[7] Kristina Iribarren,[8,9,10,11,12] Laura Mondragón,[8,9,10,11,12] Nicolas Jacquelot,[1,2,3] Bo Qu,[1,2,3] Gladys Ferrere,[1,2,3] Céline Clémenson,[1,12] Laura Mezquita,[1,14] Jordi Remon Masip,[1,14] Charles Naltet,[12] Solenn Brosseau,[13] Courtecbe Kaderbhai,[10] Corentin Richard,[10] Hira Rizvi,[17] Florence Levenez,[4] Nathalie Galleron,[4] Benoît Quinquis,[4] Nicolas Pons,[4] Bernhard Ryffel,[18] Véronique Minard-Colin,[1,19] Patrick Gonin,[1,20] Jean-Charles Soria,[1,14] Eric Deutsch,[1,2,12] Yohann Loriot,[1,2,12] François Ghiringhelli,[16] Gérard Zalcman,[13] François Goldwasser,[8,21,22] Bernard Escudier,[1,14,22] Matthew D. Hellmann,[23,24] Alexander Eggermont,[1,2,14] Didier Raoult,[25] Laurence Albiges,[1,2,14] Guido Kroemer,[8,9,10,11,12,27,28*]

The commensal microbiome is associated with anti–PD-1 efficacy in metastatic melanoma patients

Vyara Matson,[1*] Jessica Fessler,[1*] Riyue Bao,[2,3*] Tara Chongsuwat,[4] Yuanyuan Zha,[4] Maria-Luisa Alegre,[4] Jason J. Luke,[4] Thomas F. Gajewski[1,4†]

When preparing for your talk,

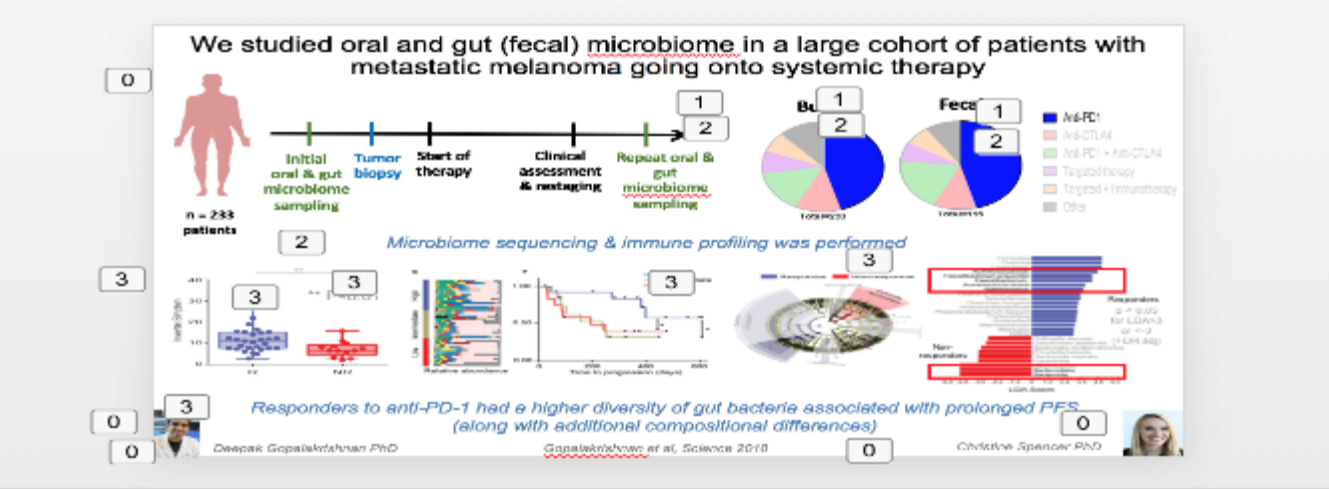
Practice, practice, practice!

** It is useful to craft a “script” that can be embedded in the slide deck*

*and printed out in notes pages,**

and practice / refine your slides and script with mentors and peers

Preparation of a “script” allows you to print out notes to practice talk, and even use them during talk with “presenter view” or printed / on a tablet (if needed)



To test this hypothesis, we collected samples from over 200 patients with metastatic melanoma going onto systemic therapy.
Oral and gut microbiome samples were collected at the start of systemic therapy
and tumor biopsies were also performed when feasible.
Repeat oral and gut microbiome samples were collected again in a subset of patients
(click)
You can see here that the majority of patients were treated with immune checkpoint blockade
Oral microbiome samples were obtained via cheek swab in clinic and there was 100% compliance with this
For fecal samples, patients were given a kit in clinic and were asked to mail this back after the sample was obtained, and over half of patients returned the kit
(click)
The largest proportion of patients were treated on anti-PD-1, thus we studied this subset first
(click)
Microbiome samples were then profiled using 16s sequencing on all samples and whole genome shotgun sequencing on a subset,
And also deeply profiled the available tumor biopsies via molecular and immune profiling

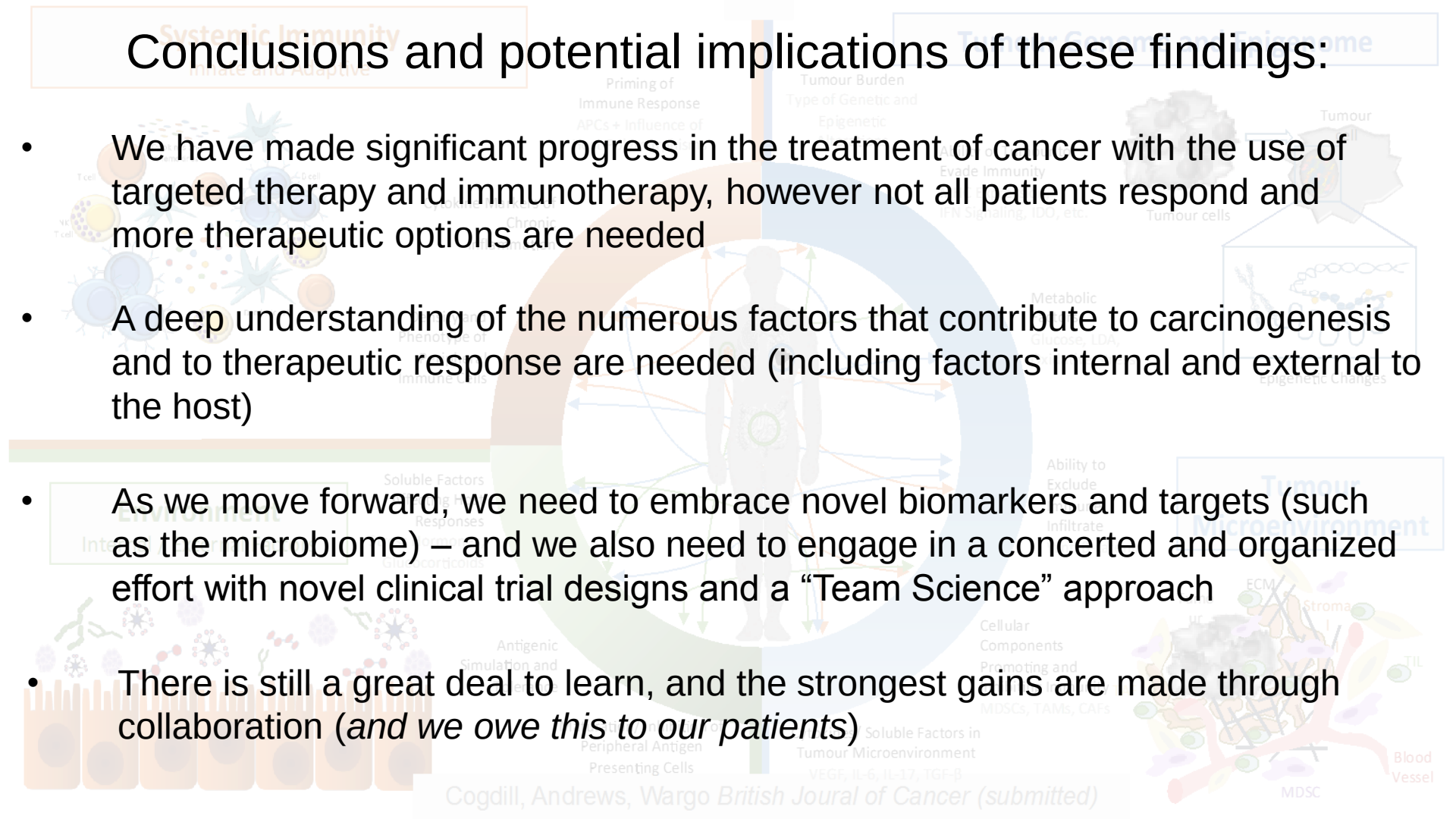
At the end of your talk,

Summarize conclusions and next steps (3-4 bullet points)

And share acknowledgements

Conclusions and potential implications of these findings:

- We have made significant progress in the treatment of cancer with the use of targeted therapy and immunotherapy, however not all patients respond and more therapeutic options are needed
- A deep understanding of the numerous factors that contribute to carcinogenesis and to therapeutic response are needed (including factors internal and external to the host)
- As we move forward, we need to embrace novel biomarkers and targets (such as the microbiome) – and we also need to engage in a concerted and organized effort with novel clinical trial designs and a “Team Science” approach
- There is still a great deal to learn, and the strongest gains are made through collaboration (*and we owe this to our patients*)



Acknowledgements

Patients and their families

Conference organizers, faculty / staff, attendees

Laboratory Investigation (Wargo lab members)

- **Christine Spencer PhD**
- **Vancheswaran Gopalakrishnan PhD**
- **Beth Helmink MD PhD**
- **Wadud Khan PhD**
- **Luigi Nezi PhD**
- **Zachary A. Cooper PhD (alumni)**
- **Alexandria P. Cogdill MS (PhD candidate)**
- **Robert Szczepaniak-Sloane BS (PhD candidate)**
- **Rohit Thakur PhD**
- Wei-Shen Chen, MD PhD
- Sangeetha Reddy MD PhD
- Liz Burton MBA

Other key collaborators

- **Laurence Zitvogel MD PhD, Giorgio Trinchieri PhD**
- **Ravid Straussman MD PhD**

MDACC Collaborators

- **Jim Allison PhD, Pam Sharma MD PhD**
- **Michael Davies MD PhD, Jeff Gershenwald MD**
- **Hussein Tawbi MD PhD, Bella Glitza MD**
- **Patrick Hwu MD, other Melanoma Med Onc Facutly / Staff**
- Jeff Lee MD, Merrick Ross MD, other Surg Onc Faculty / Staff
- Michael Tetzlaff MD PhD, Alex Lazar MD
- Robert Jenq MD PhD, other MDACC faculty / staff

Prior mentors

- **Toni Ribas MD PhD, Steve Rosenberg MD PhD**
- **Lisa Butterfield PhD, Keith Flaherty MD, Arlene Sharpe MD PhD**

Baylor CMMR

- **Joe Petrosino PhD, Nadim Ajami PhD, Diane Hutchinson PhD**

Philanthropic/Grant Support

- **MRA, BSF, AACR-SU2C, PICI, Sabin Family Foundation**
- **Melanoma Moon Shot Program**

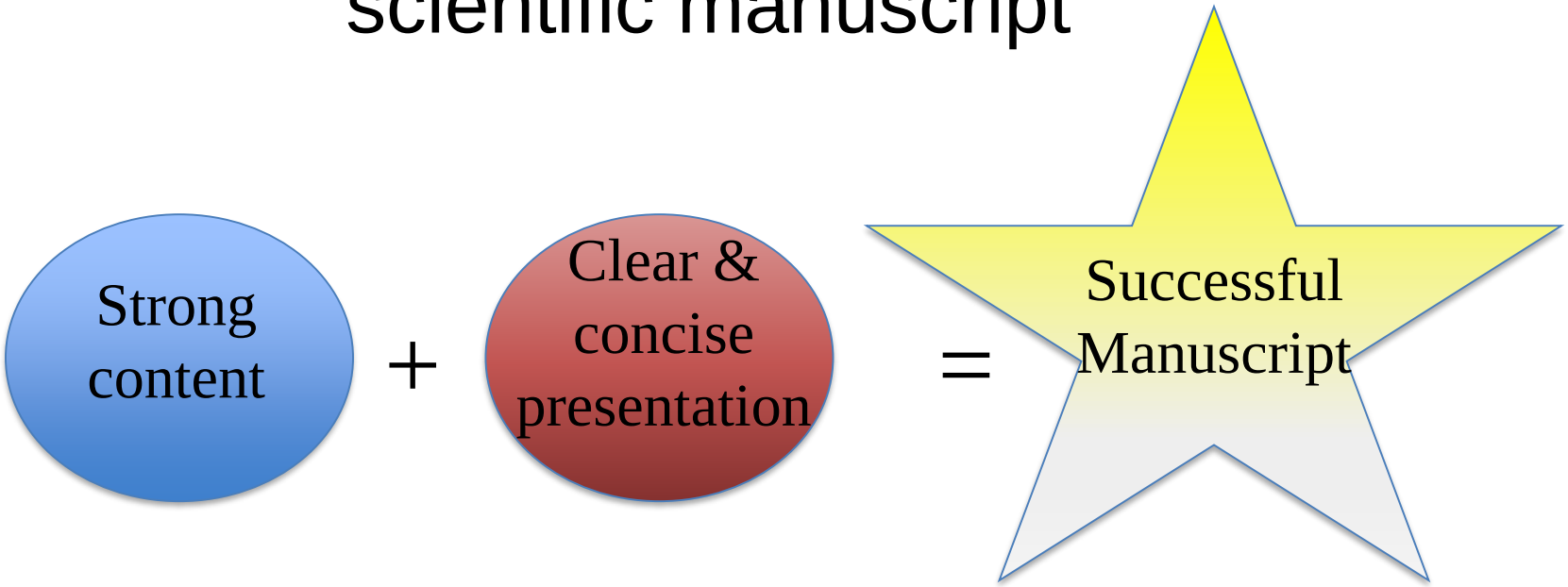
Industry Sponsors/Collaborators

Parker Institute for Cancer Immunotherapy

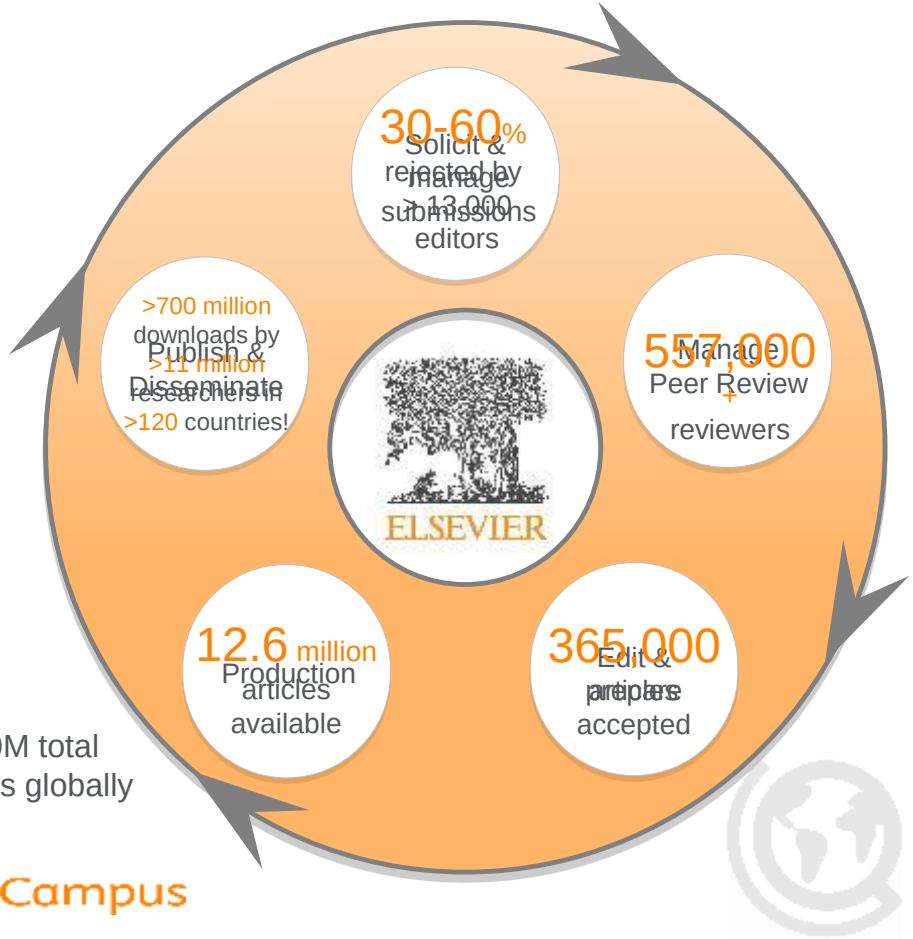
Questions at the end of a talk are a good sign!

- Write questions down if needed and repeat the question for the audience
- Try to answer thoroughly and succinctly, based on your own data and from others in the field
- After the talk, solicit feedback and incorporate changes as needed *(and celebrate your accomplishment)*

II. Preparing and submitting an impactful scientific manuscript



The academic publishing cycle & key figures (at Elsevier)



>40M total articles globally

1.4 M accepted articles globally each year

Elsevier Publishing Campus

Key ingredients for a successful scientific manuscript

- Novel / exciting research findings or methods
- Presented in a clear and logical manner allowing readers to grasp significance
- Work closely with co-authors, collaborators and editors to polish story

“Nailed it”

Unsuccessful scientific manuscript

- Outdated work with overstated conclusions
- Duplication of already published work or poorly presented novel data
- Lack of engagement with others in the scientific community

“Failed it”

It is never too early to start thinking about how to

communicate your scientific findings in manuscript form

(and thinking about it can help guide your experiments / analyses)

Identify a novel research question

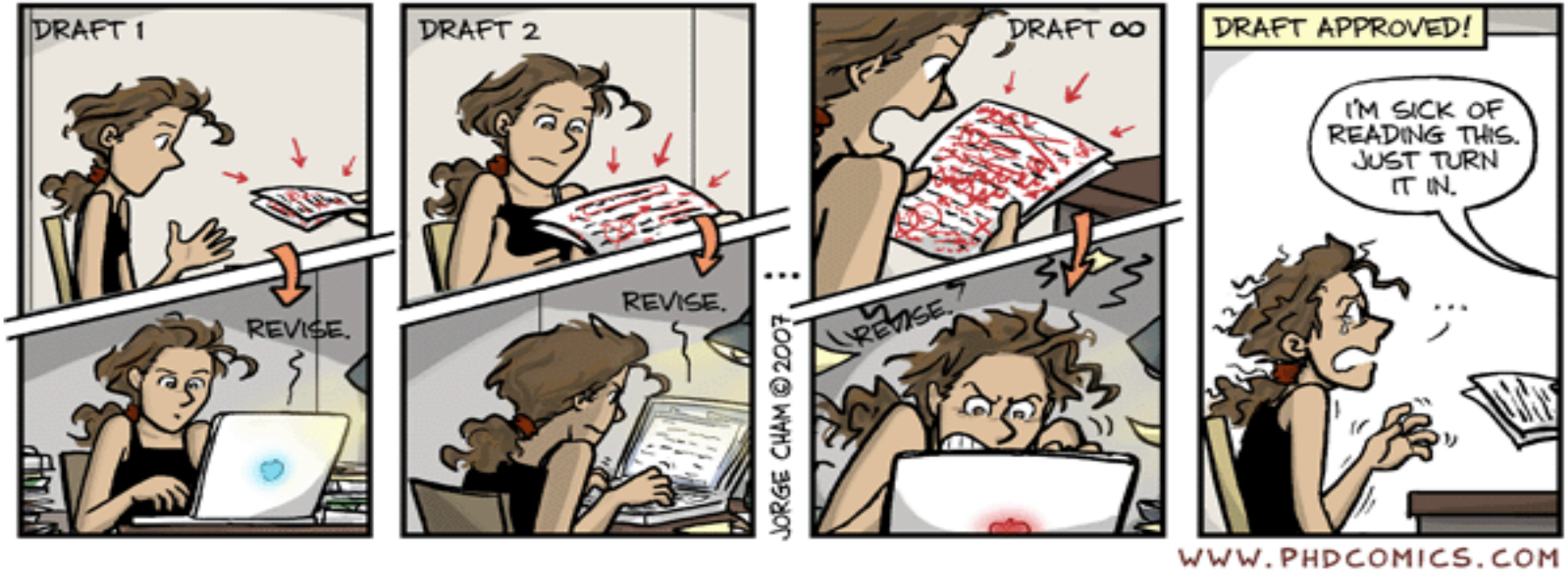


FIG 1 CLINICAL COHORTS

1) n: 13 (pCR 5&2)

2) n = 20 (pCR

3) n = 15 (pCR

RNA SEQ

↳ ALIGNING TO

FIG 2

IN VIVO DATA

- TUMOR GROWTH + SURVIVAL
- ANALYSIS OF SAMPLES

EXPANSION + CR DONORS

SCIENCE +

ADDITIONAL

FIG 1

I A. SCHEMA

B. RUN-IN

16s / WMS

C. ROC PLOT D. SCATTER PLOT

OPTIMAL DONORS

CR R NR HD

α β TYPE I (%) COMP (FUNC)

CR VS R CR VS HD

? IMMUNE PROFILING IN TUMOR (PBBF)

+ BLOOD IN

MOUSE EXP.

/SWATH1)

BRAF/MEK RX ♀ + ♂

PT SAMPLES

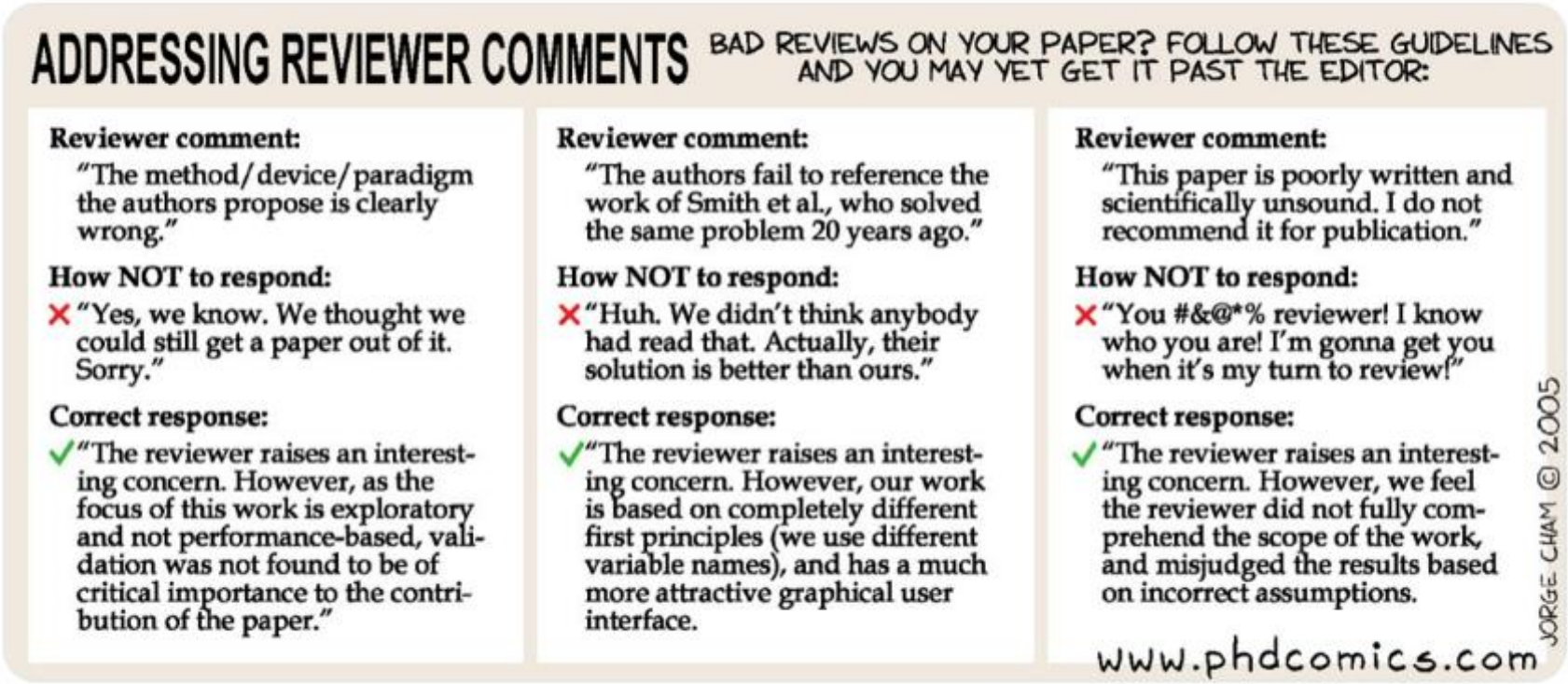
R=

SWATH1 (JEN/REGTAK31)

Tips for manuscript preparation:

1) *Remember that your reviewers (and potentially editors) are busy professionals – make their job easy!*
2) *Editors and reviewers don't know the material as well as you do – work extra hard to make findings clear and concise*
3) *Figures should be well-crafted and should be able to tell the whole story (augmented by the text)*

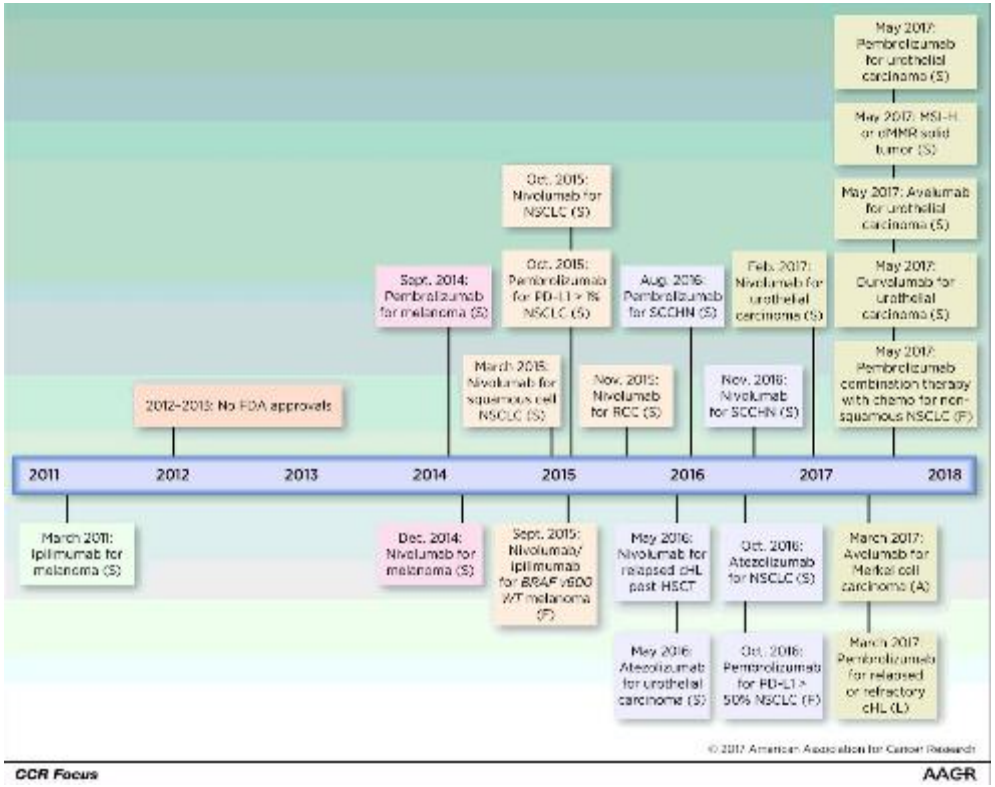
Ten simple rules for writing a response to reviewers (Noble, PLOS comp bio)

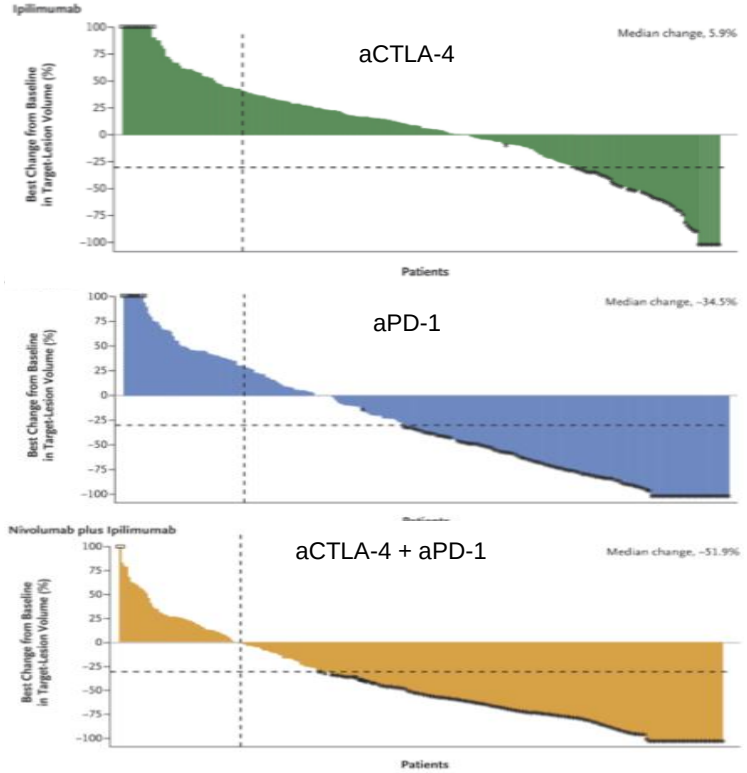


Noble, PLOS computational biology Oct 12, 2017

Example of a successful manuscript submission (with follow-up publication)

We have made tremendous advances in cancer treatment with the use of immunotherapy, however not all patients respond to therapy

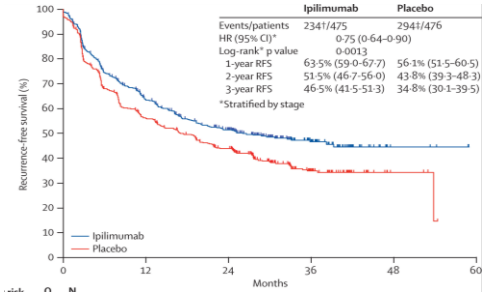




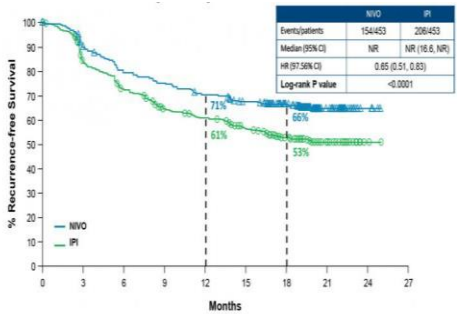
There is a critical need to better understand who will benefit from these agents, as well as proper timing, sequence, and combination regimens

Immune checkpoint blockade is being used in the adjuvant setting, and there is a strong rationale to use this in the neoadjuvant setting

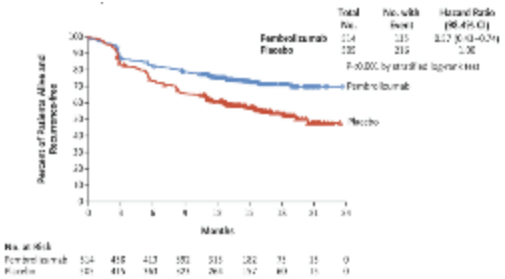
EORTC 1871

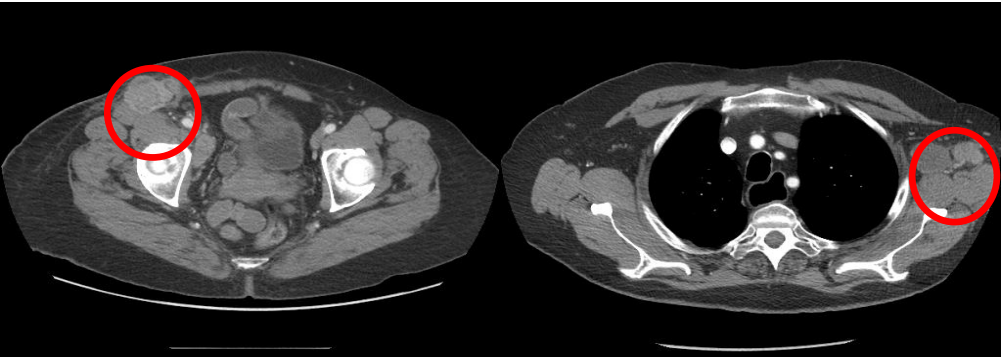


Checkmate 238

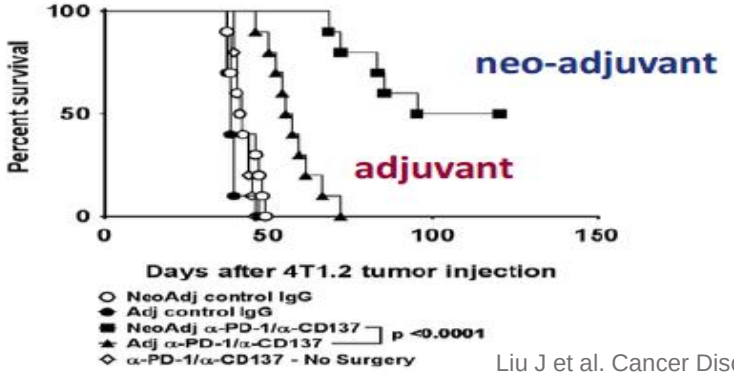


Keynote 054





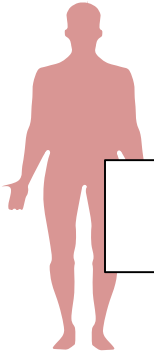
Upfront surgery is currently the standard of care for these patients, but up to 70% of patients treated in this manner will relapse and die of disease



Liu J et al. Cancer Discov 2016.

Pre-clinical models suggest improved outcomes in neoadjuvant vs. adjuvant treatment

We ran a phase II trial using neoadjuvant (+ adjuvant) checkpoint blockade in patients with high risk resectable metastatic melanoma



Patients with resectable stage IIIB/IIIC melanoma, no brain mets or prior ICB

Stratify by Stage and

Ipi 3mg/kg + Nivo 1 mg/kg q 3 wks x 3 doses (n=20)

Nivo 3mg/kg q 2 wks x 4 doses (n=20)

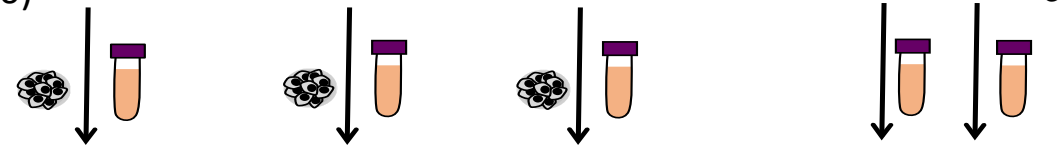
RECIST restaging and

Nivo 3 mg/kg

months

Trial was stopped early due to concerns re: progression / toxicity concerns

Primary Endpoint:
Path response
Secondary endpdoints:
-DMFS
-OS
-Toxicity
- correlatives



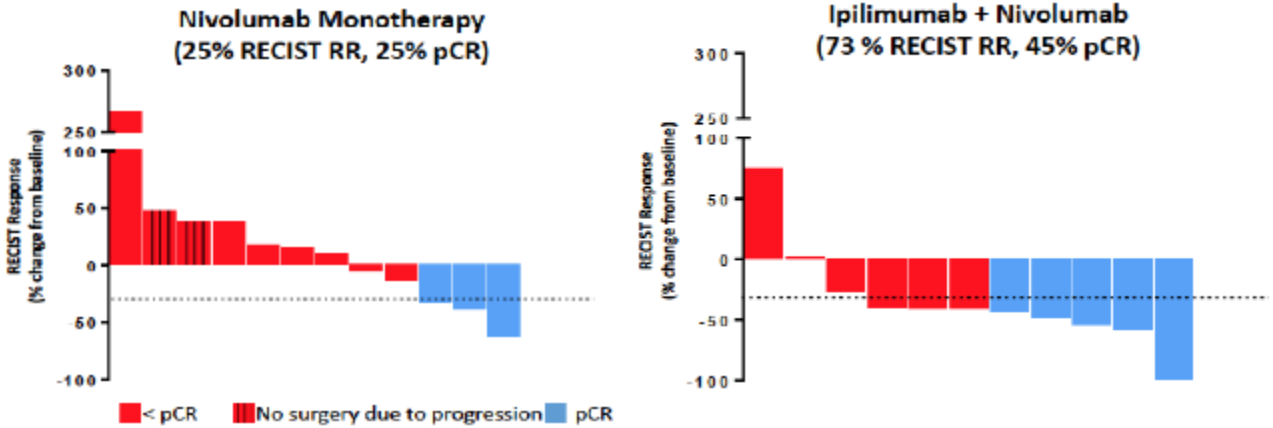
Molecular & immune profiling in longitudinal tissue and blood samples

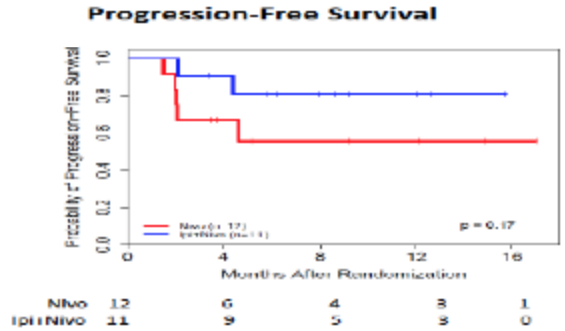
PIs: Amaria & Wargo

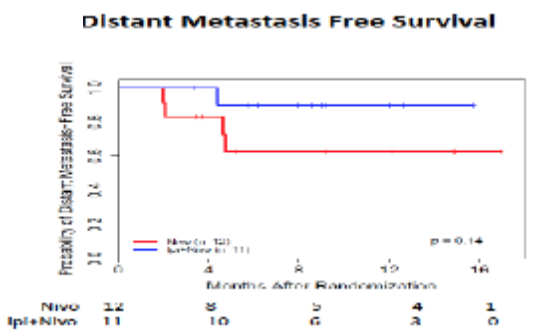
Amaria , Reddy et al, Nature Medicine 2018

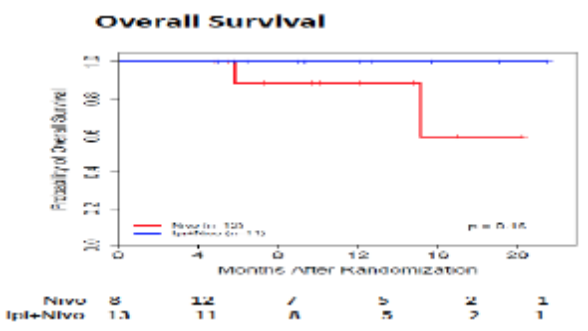
NCT02519322

Treatment with neoadjuvant Ipi Nivo was associated with a higher RECIST / pCR rate, and improved RFS over Nivo monotherapy









Roda Amaria MD

Amaria , Reddy et al, Nature Medicine 2018

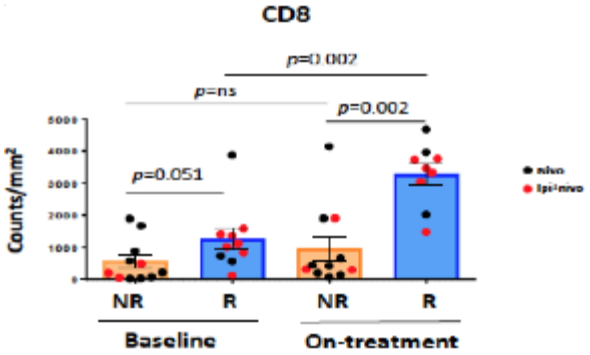
Sangeetha Reddy MD MS

However treatment with combined therapy was associated with a high rate of adverse events

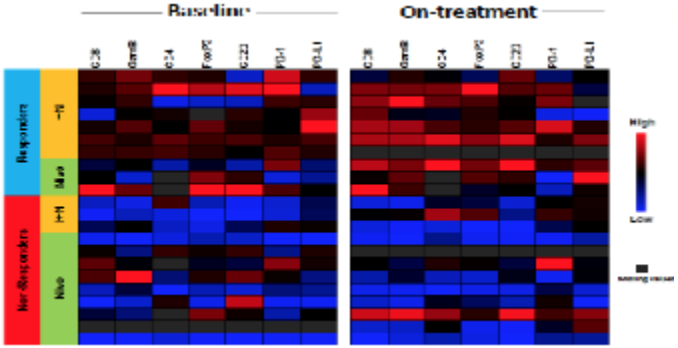
Select Treatment Related Adverse Events During Neoadjuvant Treatment				
	Nivolumab (n=12)		Ipilimumab + Nivolumab (n=11)	
	Any Grade, %	Grade 3-4, %	Any Grade, %	Grade 3-4, %
Any Treatment Related Adverse Events	**92**	**8**	**91**	**73**
Fatigue	67	0	55	0
Rash	17	0	73	0
Fevers/chills/flu like	8	0	64	0
Weight loss/anorexia	17	0	27	0
Transaminitis	17	0	55	27
Colitis/diarrhea	17	0	64	18
Hyperthyroidism	8	0	27	9
Hypothyroidism	0	0	36	0
Myositis/myalgias	8	0	18	9
Pain	25	8	27	0

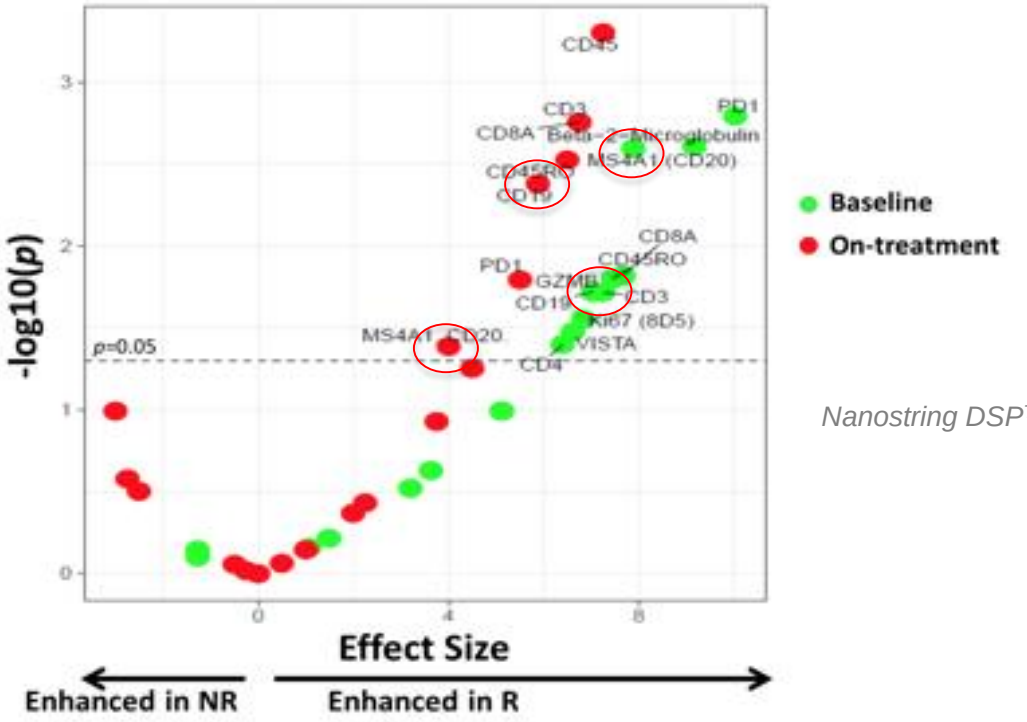
Amaria , Reddy et al, Nature Medicine 2018

Correlative analyses on samples from the neoadjuvant checkpoint blockade trial reveal known and novel biomarkers / targets for therapeutic resistance



Similar biomarkers of response (inflamed tumors)





Nanostring DSP™

Sangeetha Reddy MD MS

Amaria, Reddy et al, Nature Medicine 2018

Michael Tetzlaff MD PhD

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Slide Removed Per Presenter Request

III. Key points and take home messages

Together we are here for patients with cancer

And together we can help advance the field through research (sharing this data in presentations and manuscripts)


Effective presentation skills are key to sharing research data
“Good public speakers are made, not born”

Publishing important findings in scientific journals is critical –

And requires a team science approach from study conception to publication and beyond…

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- **Ravid Straussman MD PhD**

Patients and their families

MDACC Collaborators

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