Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

What's Next for Cancer Immunotherapy?

Terence Rhodes, MD, PhD

Director of Immuno-Oncology, Intermountain Healthcare

AAEM American Academy of Emergency Medicine — Champion of the Emergency Physician

ACCC Association of Community Cancer Centers

HOPA Hematology/Oncology Pharmacy Association

sitc Society for Immunotherapy of Cancer

#LearnACI

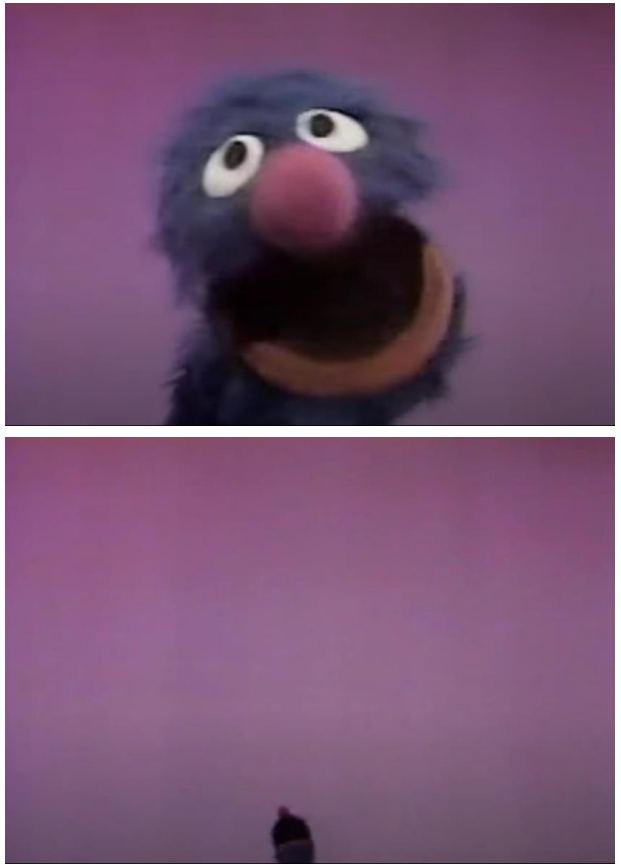
Disclosures

- Consulting Fees: AstraZeneca, BMS
- Fees for Non-CE Services Received Directly from an Ineligible Entity or their Agents : BMS

- I will be discussing non-FDA approved indications during my presentation.

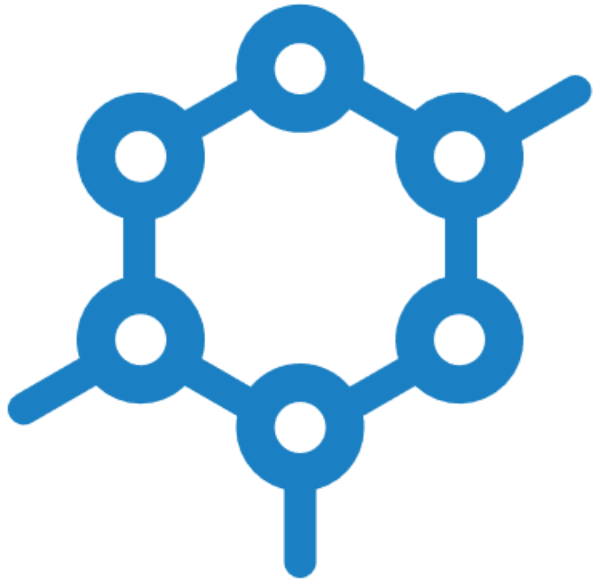
What's next for Immunotherapy?

- Near future
- Not too far
- Far



Grover teaches us the difference between near and far

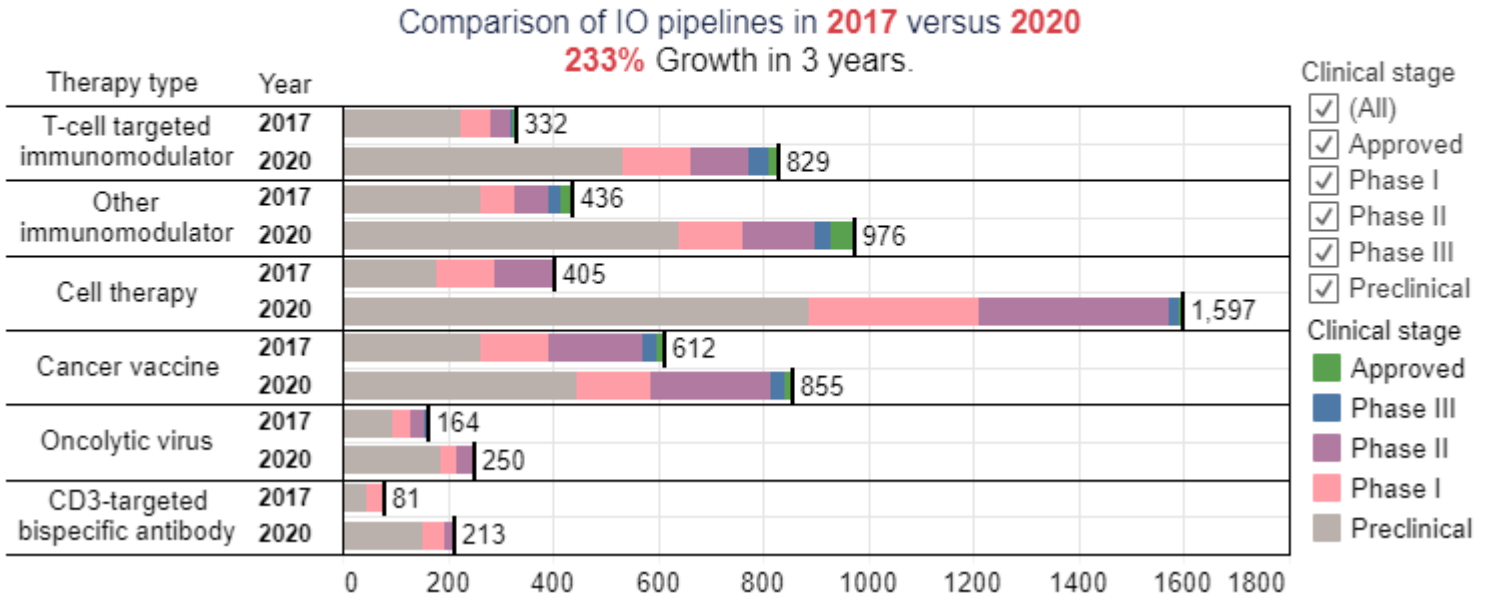
Near



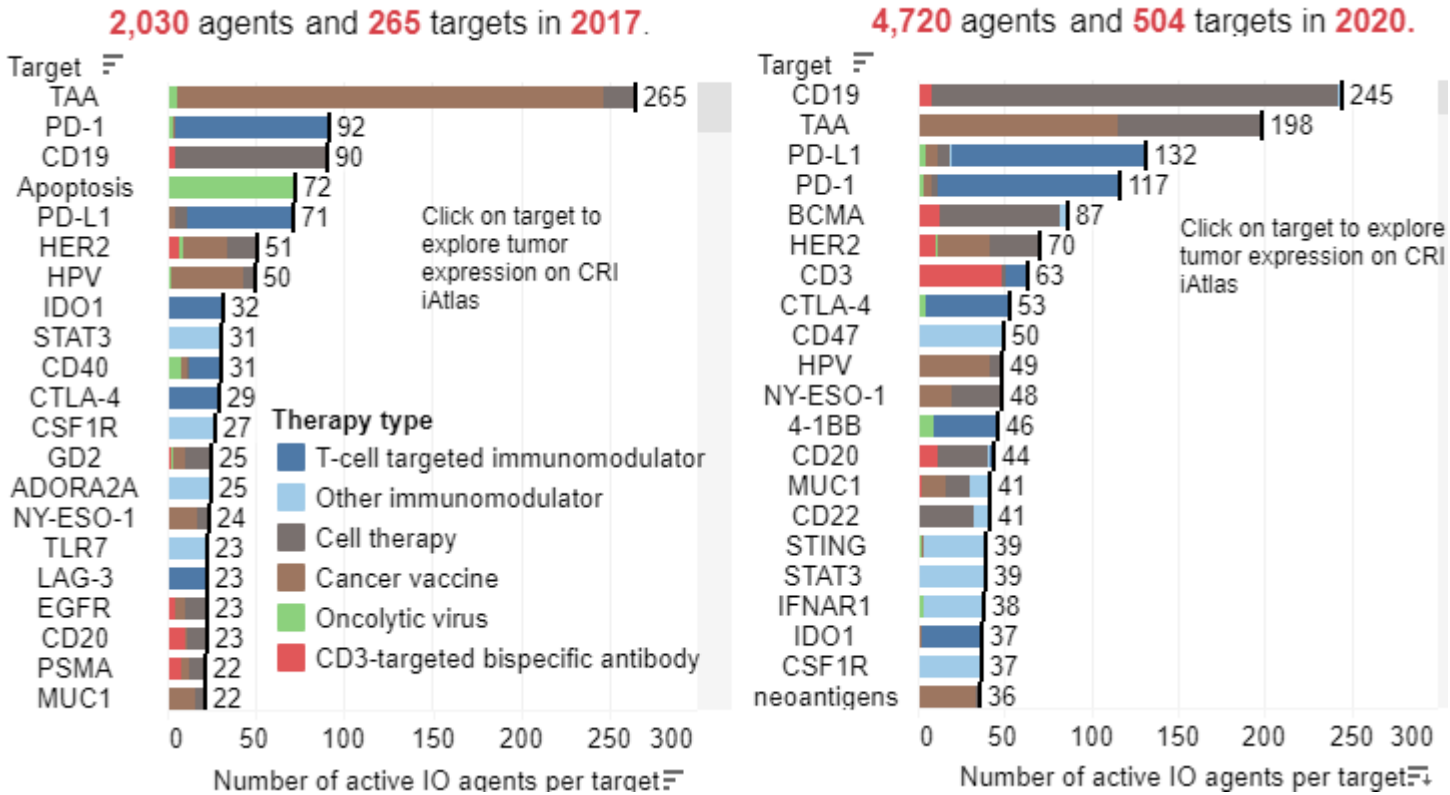
Global Immuno-Oncology Drug Development Pipeline

Published by Samik Upadhaya & Annie Yu on Sep 18, 2020
Sources: CRI, CRI Analytics, Clinicaltrials.gov, CRI-iAtlas, and GlobalData.

CANCER RESEARCH INSTITUTE® The Anna-Maria Kellen Clinical Accelerator



https://www.cancerresearch.org/scientists/immuno-oncology-landscape



https://www.cancerresearch.org/scientists/immuno-oncology-landscape

Near

- CAR-T
- TILs
- Cancer vaccines
- Oncolytic viruses
- Combination x plus immunotherapy
- Enhanced clinical response to toxicity

CAR-T in Multiple Myeloma

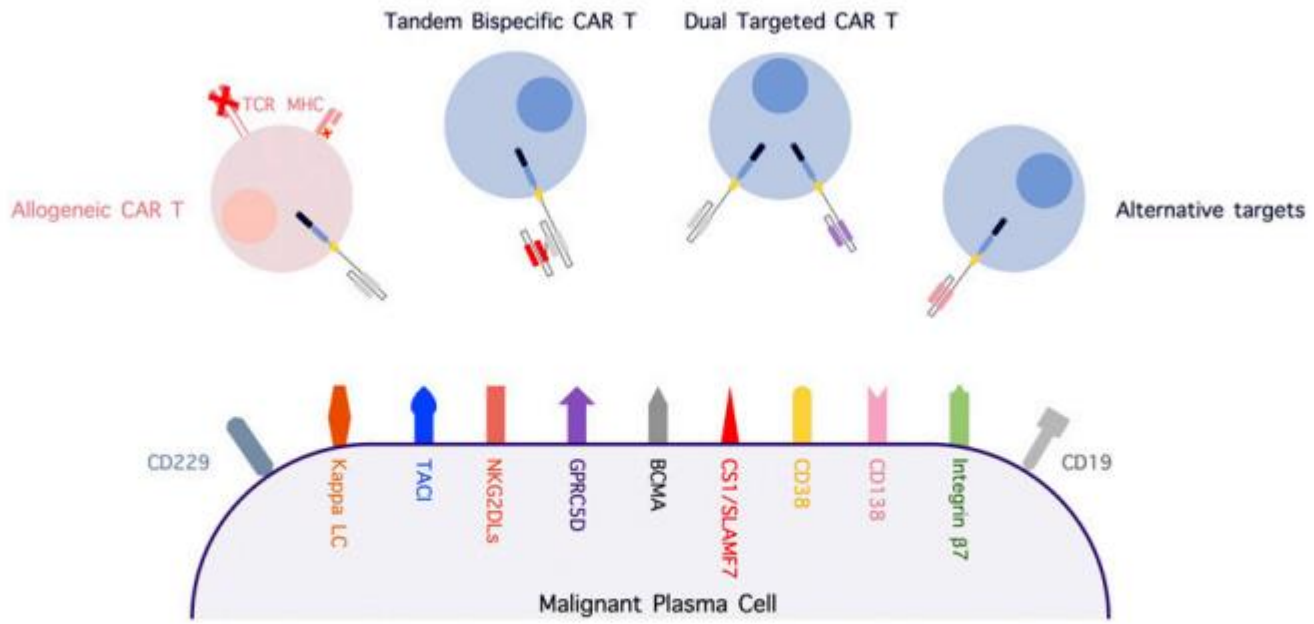
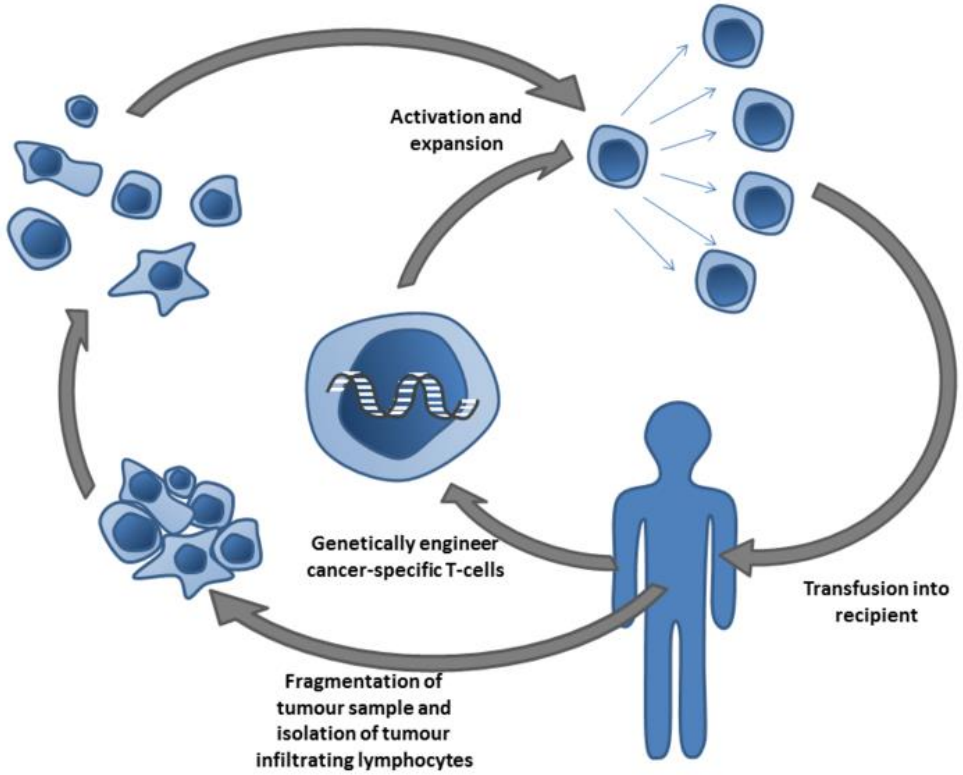


Figure 1. Alternative myeloma-associated targets for immune-based therapy and strategies involving novel CAR T-cell constructs.
CS1, CD2 subset 1; LC, light chain; MHC, major histocompatibility complex; NKG2DLs, NKG2D ligands; SLAMF7, signaling lymphocytic activation molecule family 7; TACI, transmembrane activator and CAML interactor; TCR, T-cell receptor.

Future of CAR T cells in multiple myeloma
Kitsada Wudhikarn,[1,2] Sham Mailankody,[3-5] and Eric L. Smith[6]
Hematology 2020 | ASH Education Program

Tumor Infiltrating Lymphocytes therapy

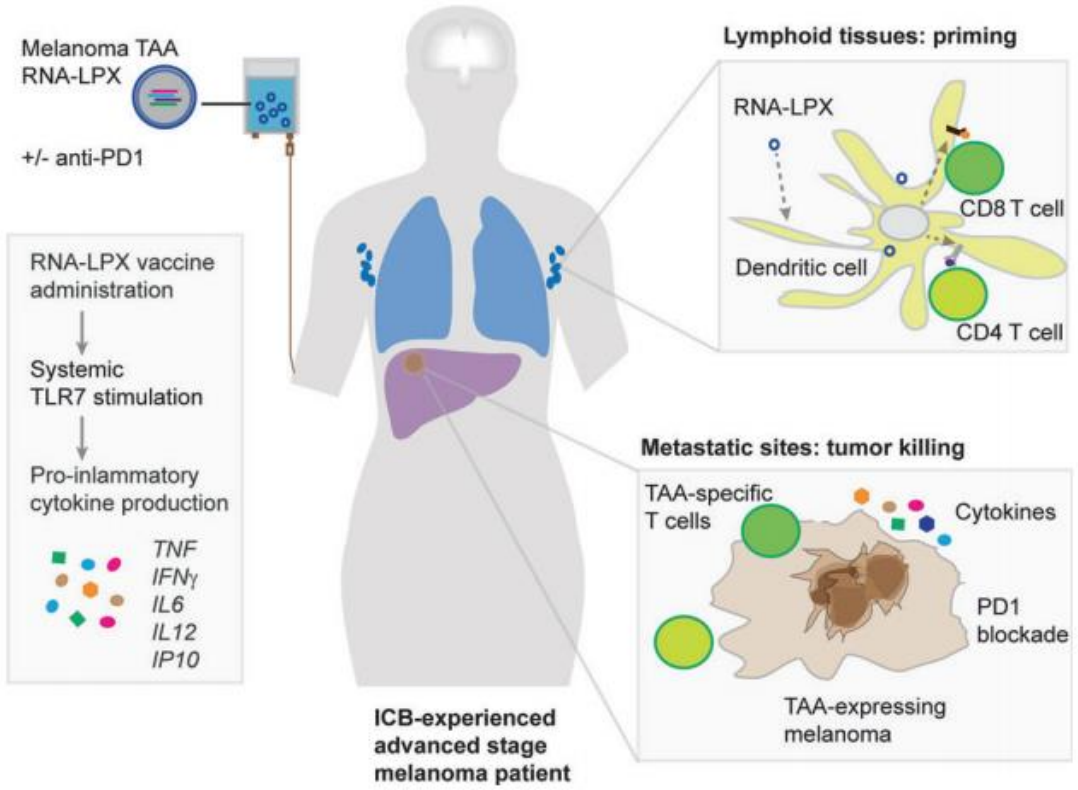


Resurgence in TIL therapy with the success of CAR-T

TIL Therapy Explained by Steven Rosenberg, MD, PhD

https://www.aacr.org/blog/2018/11/19/3944-2-til-therapy/

Cancer Vaccines



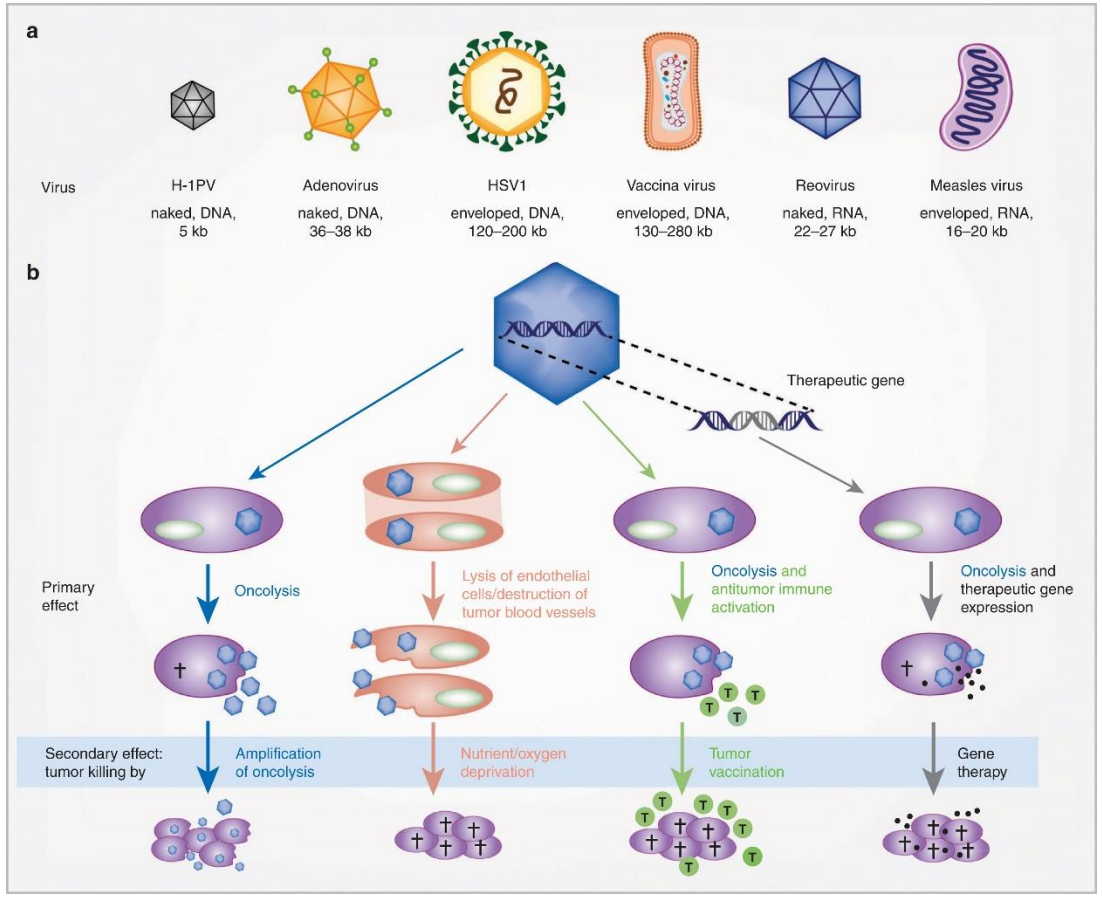
Same technology used in two COVID-19 vaccines

Cancer vaccines: shared tumor antigens return to the spotlight

Lijin Li[1], S. Peter Goedegebuure[1,2] and William Gillanders[1,2]

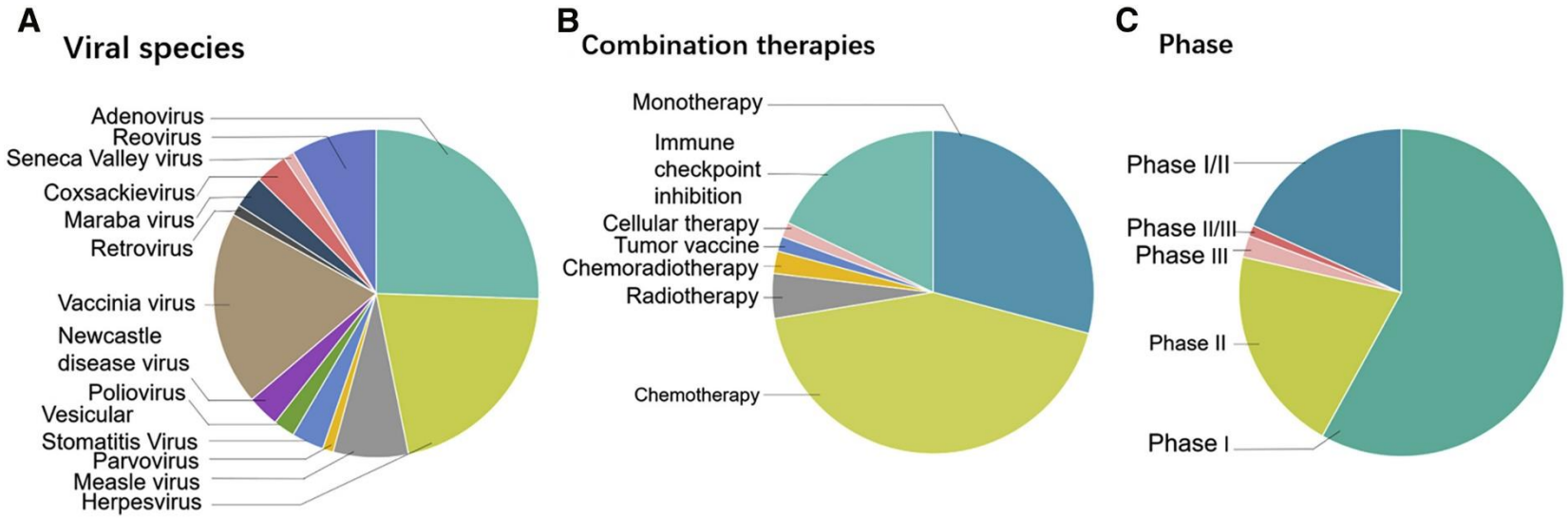
Signal Transduction and Targeted Therapy (2020)5:251 ; https://doi.org/10.1038/s41392-020-00364-8

Oncolytic viruses



Molecular Therapy - Methods & Clinical Development 2016 3DOI: (10.1038/mtm.2016.18)

Oncolytic viruses



Molecular Therapy - Oncolytics 2019 15234-247DOI: (10.1016/j.omto.2019.10.007)

Combination x plus immunotherapy

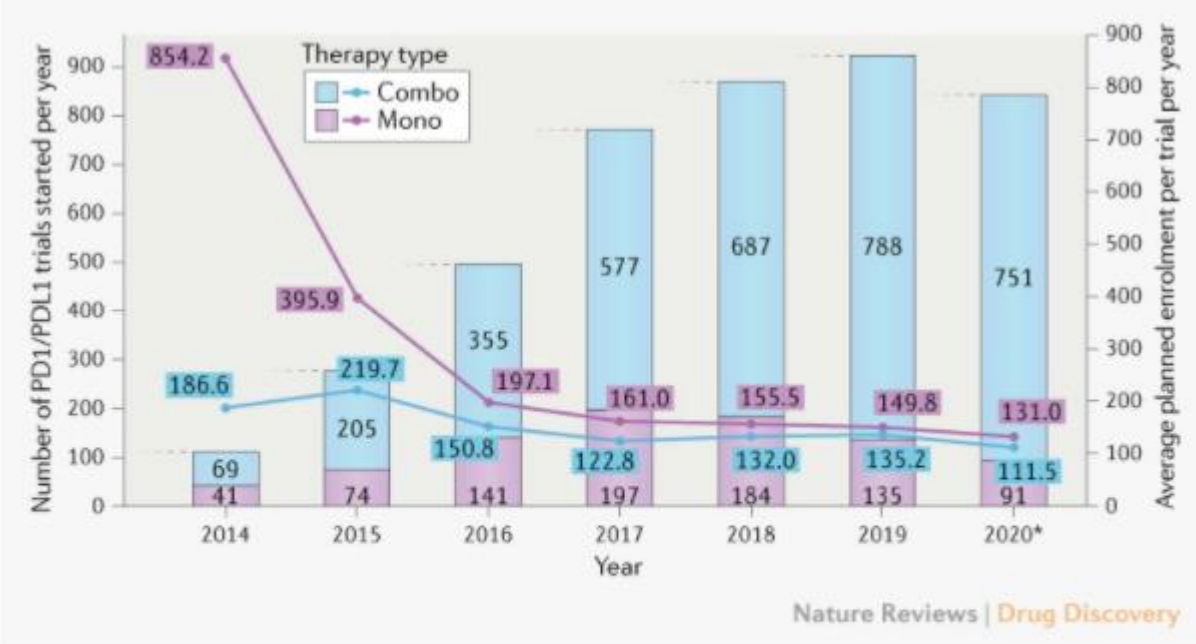


Fig. 2 | Comparison of monotherapy and combination trials. Most new trials since 2014 have been combination trials (bar graphs). The average planned patient enrolment (line graph) has decreased since 2014 for monotherapy trials more than for combination trials. *Only data from the first three quarters of 2020 were used to generate the analysis.

Upadhaya et al. Nature Reviews Drug Discovery. November 2020.

Continuous FDA approvals of combination therapies.

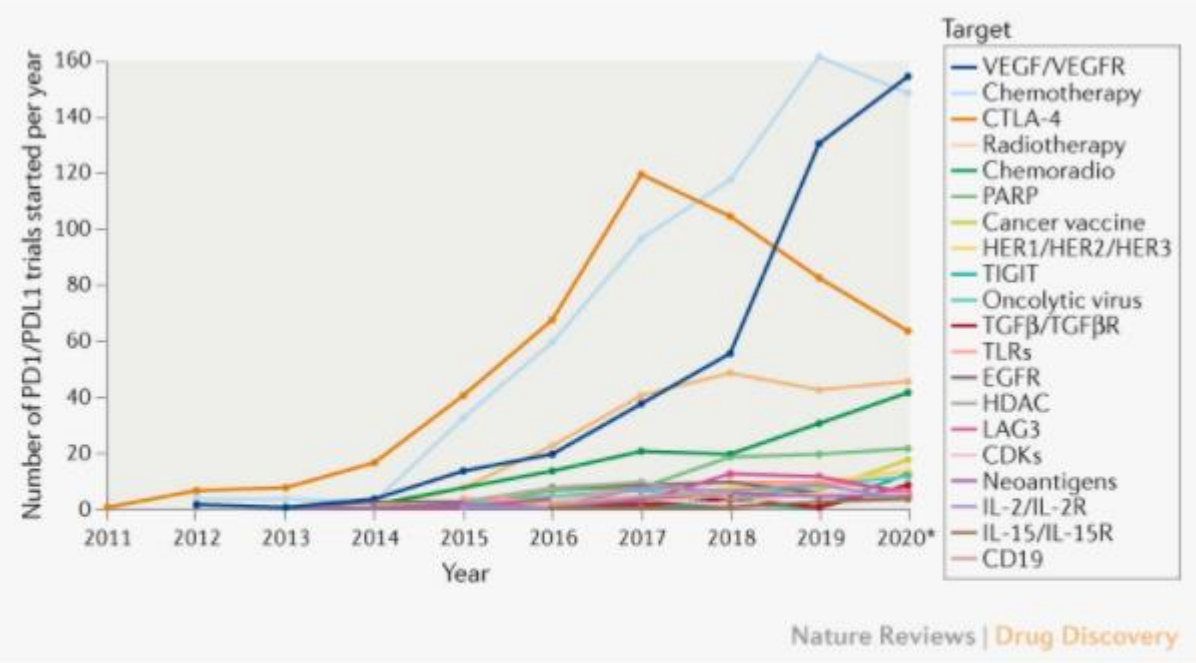


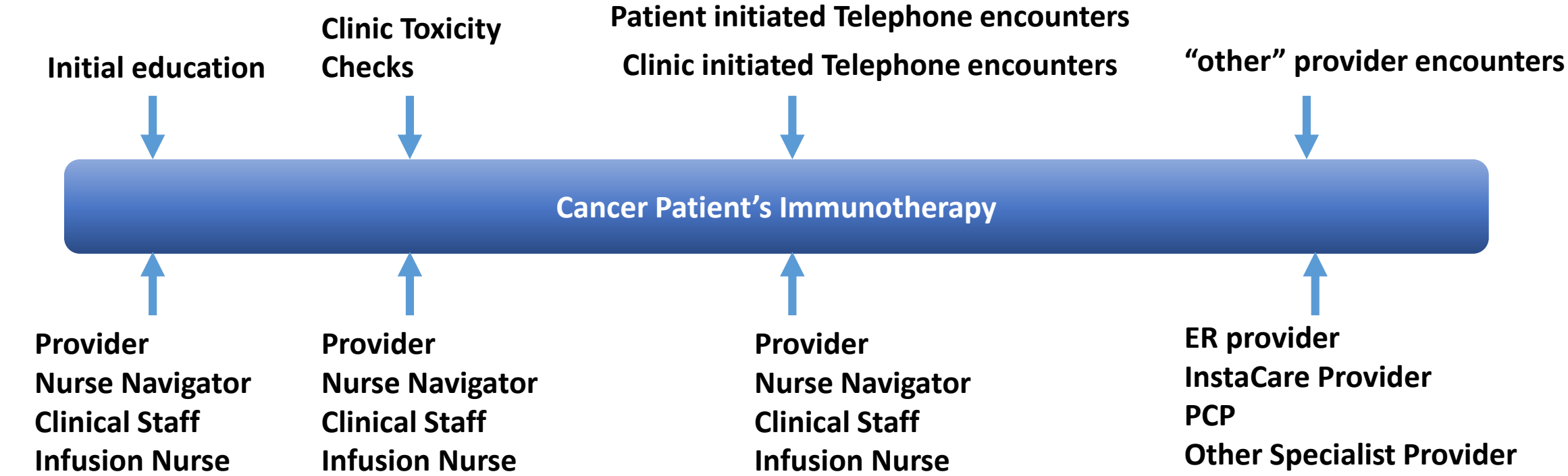
Fig. 3 | Main targets assessed in combination with anti-PD1/PDL1 mAbs. The graph shows the number of combination trials starting each year since 2011. The main 20 targets assessed in combination are shown in descending order according to the number of trials started in 2020. *Only data from the first three quarters of 2020 were used to generate the analysis.

Upadhaya et al. Nature Reviews Drug Discovery. November 2020.

Continuous FDA approvals of combination therapies.

Enhanced Clinical Response to toxicity

Multiple touch points



Immune Toxicity Registry at Intermountain

- **“Amateurs talk strategy. Professionals talk logistics.”**
  --Gen. Omar Bradley

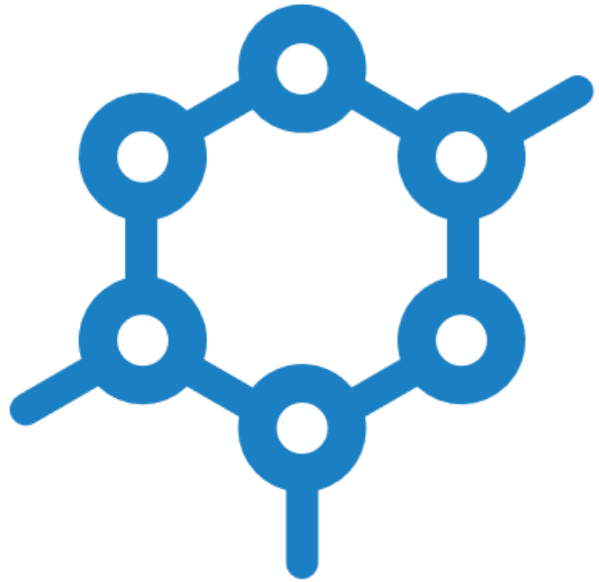
- **QC project to enhance our ability to respond and manage immune mediated toxicity**

- **Database of immune mediated toxicities**

- **Evaluation of touch points to increase our understanding of areas to improve toxicity management.**

Society for Immunotherapy of Cancer
ADVANCES IN Cancer IMMUNOTHERAPY™

Not too far

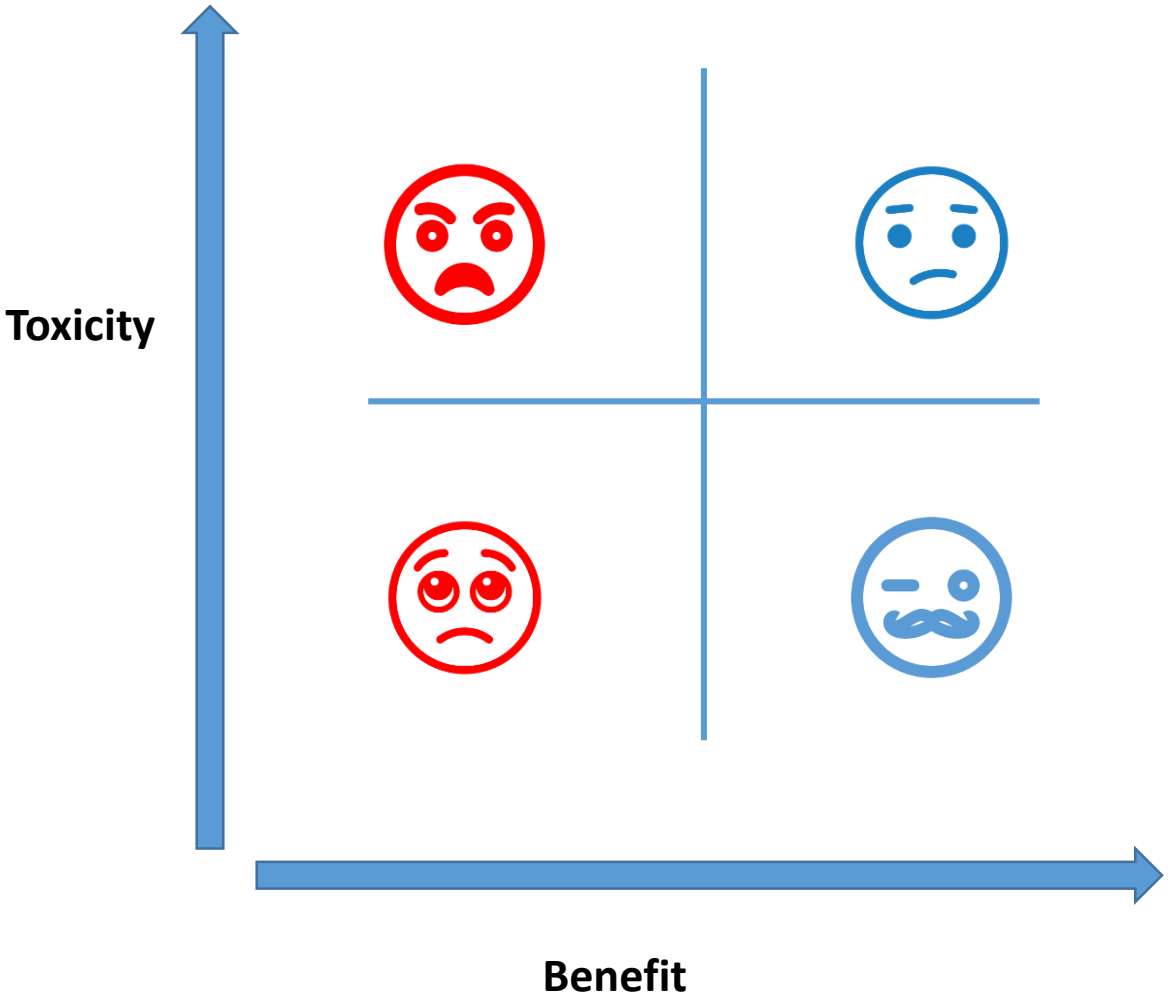


Not too far

- Enhanced Biomarkers for response

- Enhanced Biomarkers to monitor toxicity

Benefit and Toxicity of immunotherapy

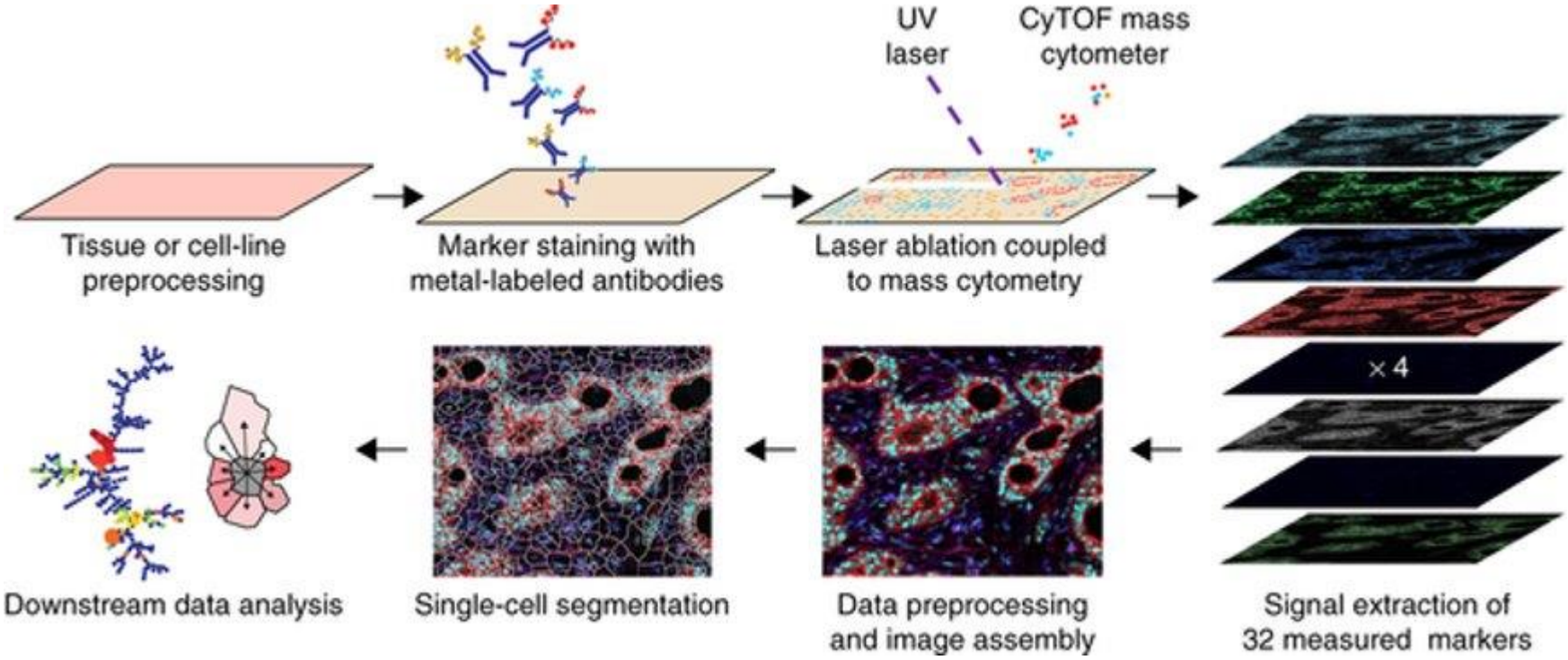


Toxicity may be monitored during therapy

Benefit may be predicted prior to therapy

Biomarkers to evaluate response

- Multiplex imaging



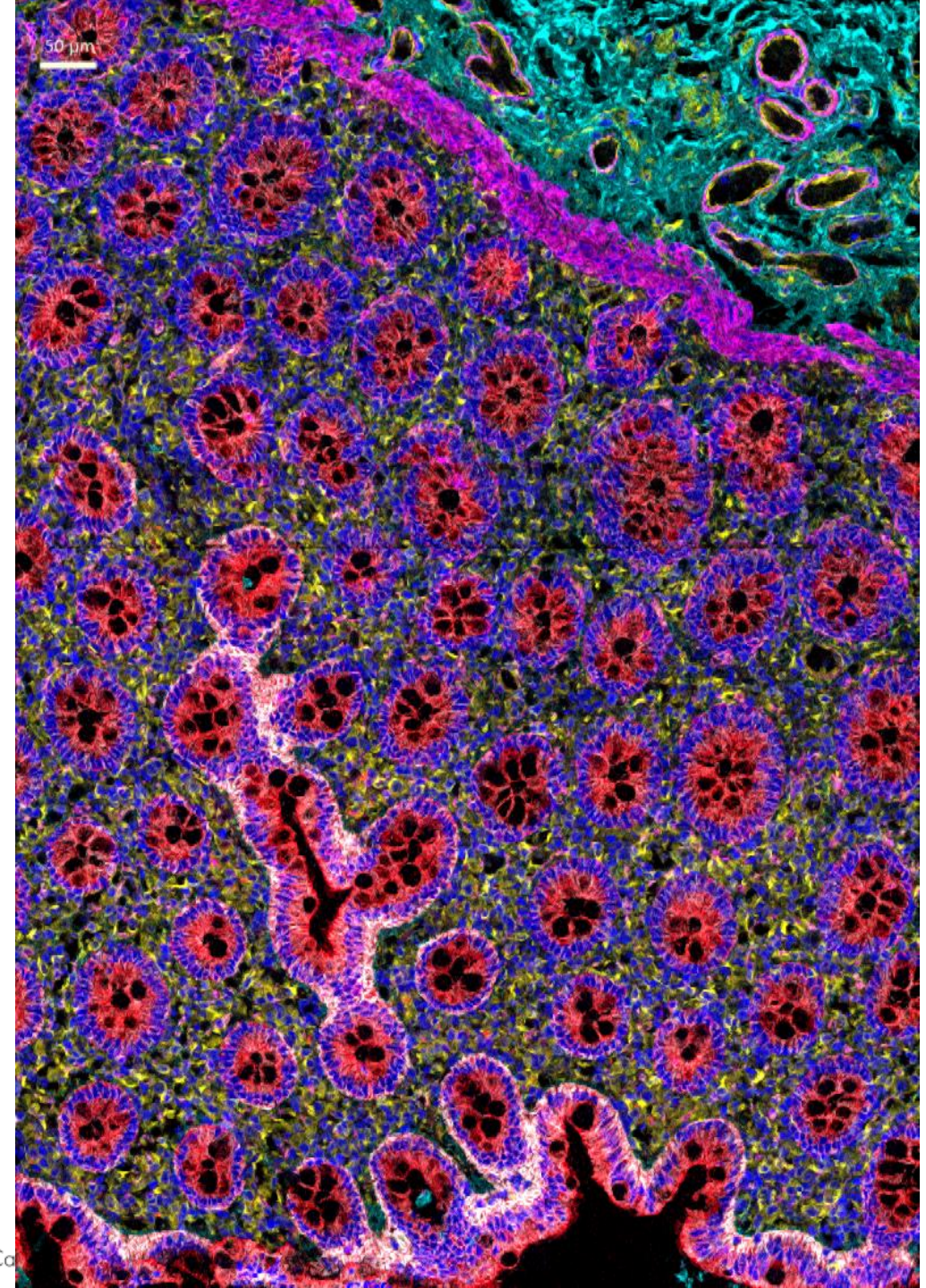
C. Giesen, et al., Nat Meth. 11:417-422

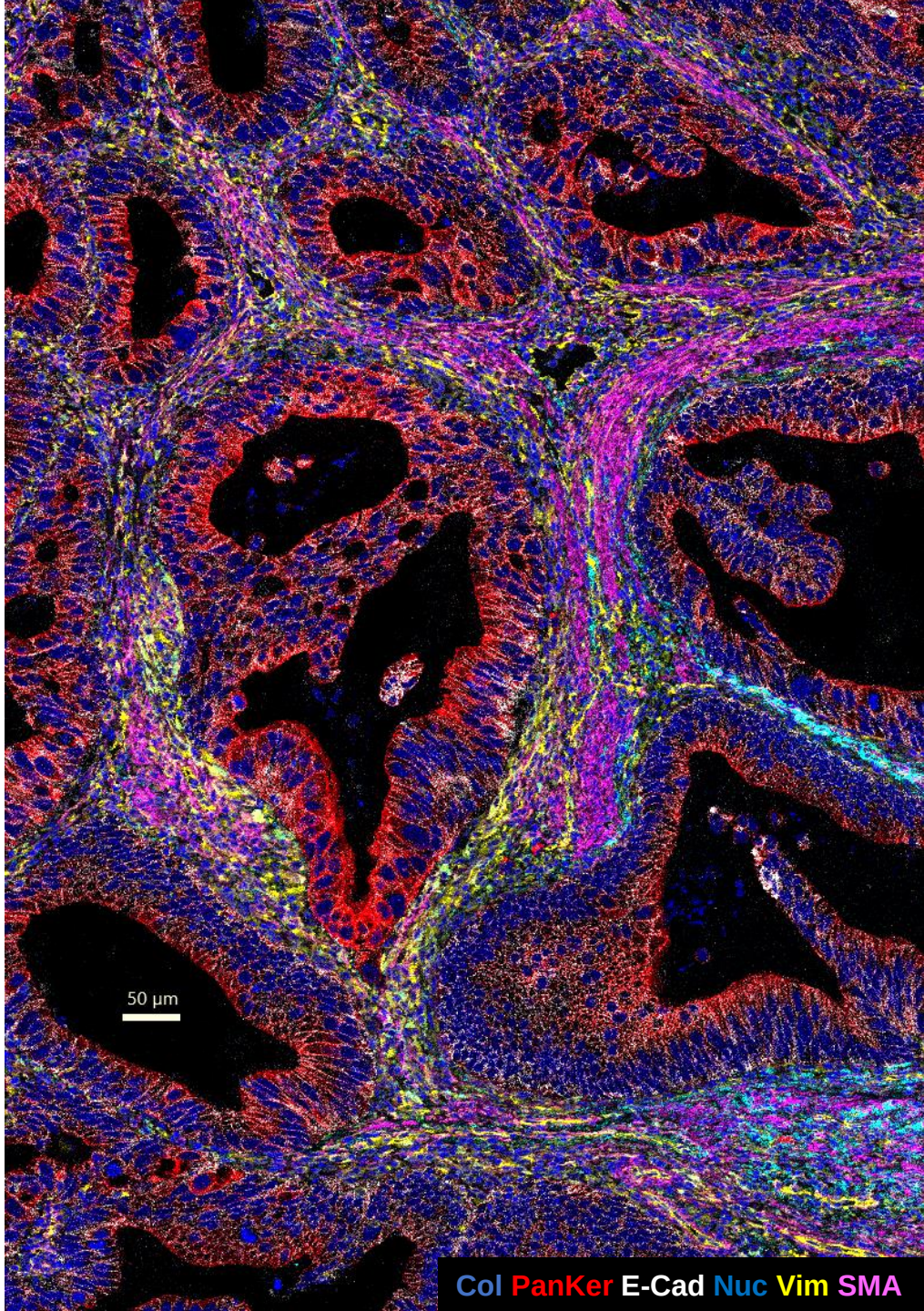
Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

COLON SLIDE

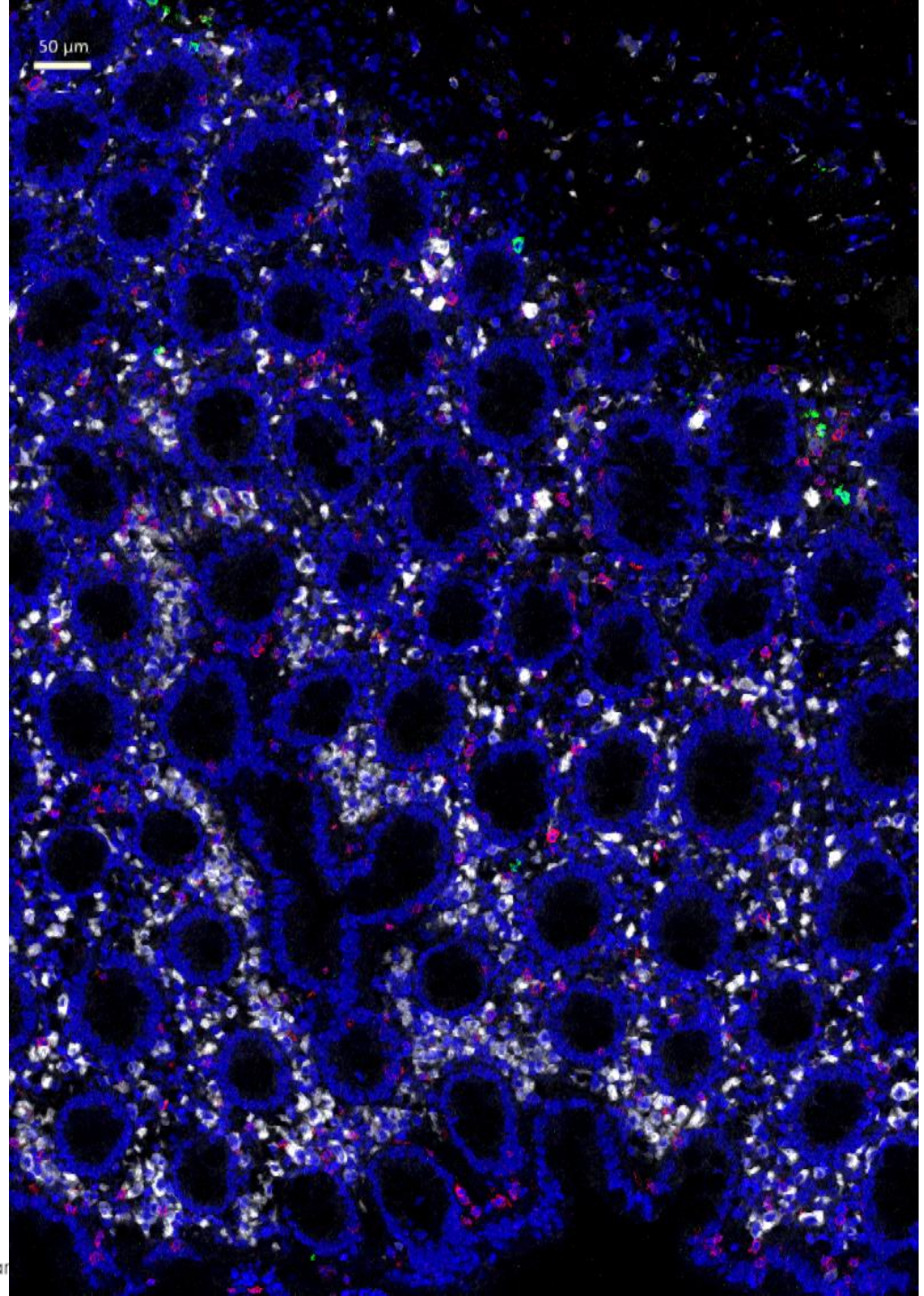
Green = B-cell
Red = T-cell
White = macrophage
Blue = nuclear marker
Yellow = Vimentin
Pink = SMA

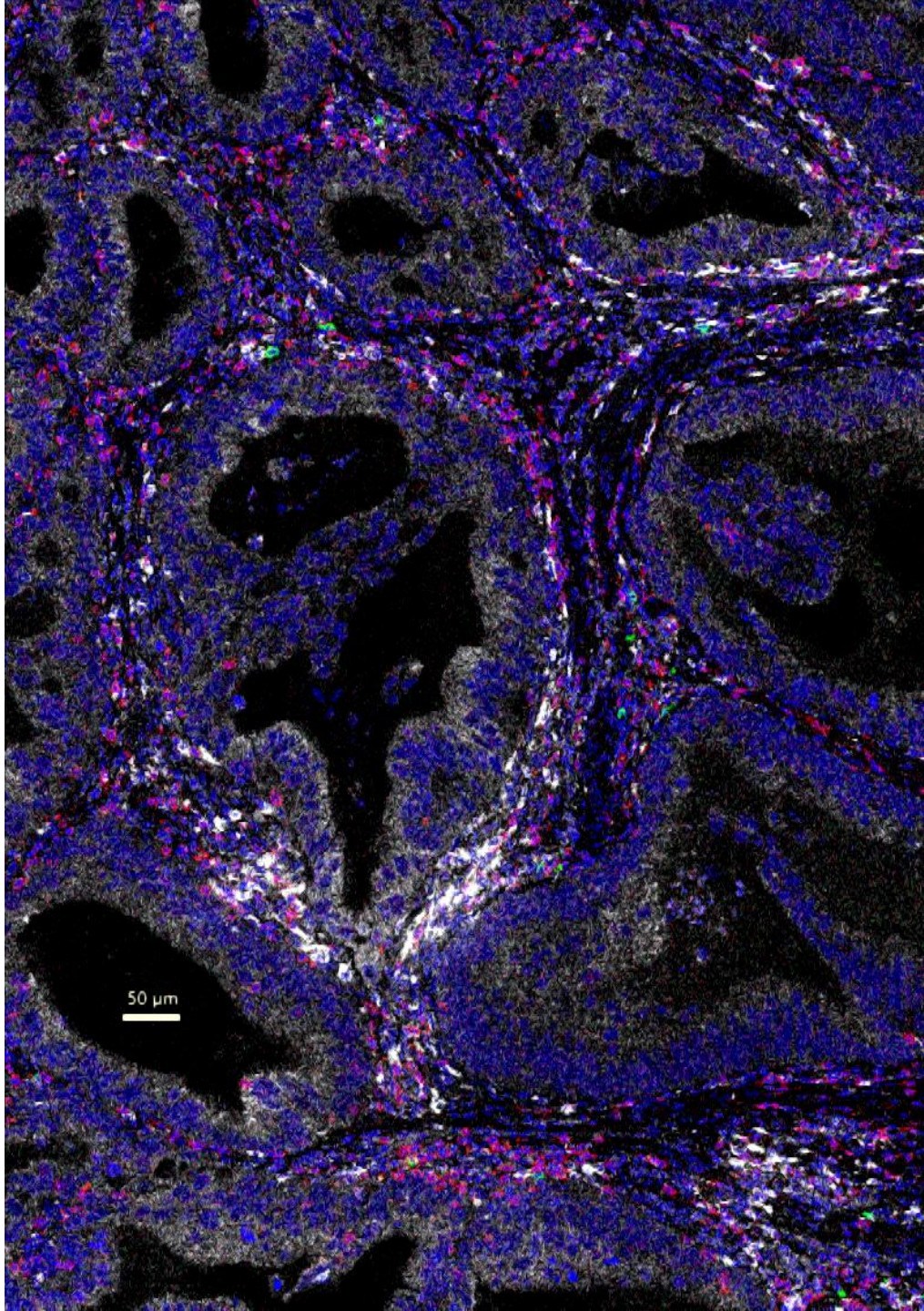




Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™





COLON SLIDE

Green = B-cell

Red = T-cell

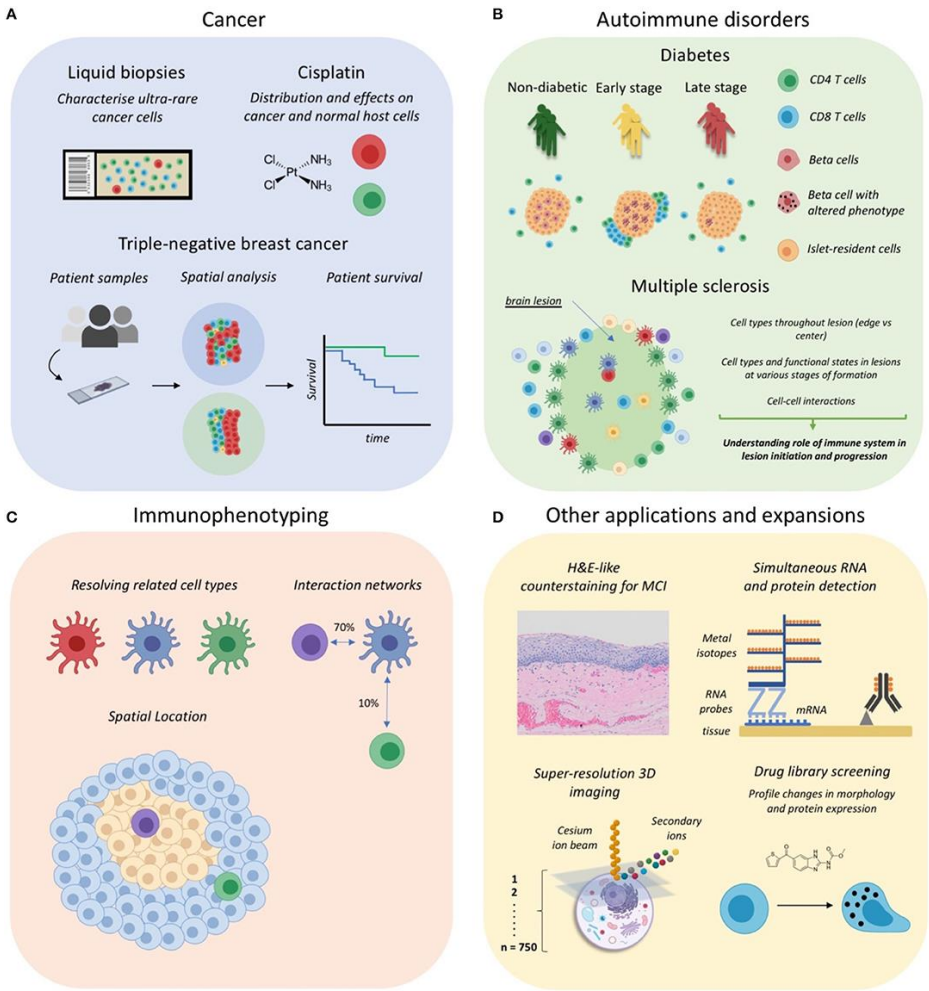
White = macrophage

Blue = nuclear marker

Society for Immunotherapy of Cancer

ADVANCES IN Cancer IMMUNOTHERAPY™

Use Cases for multiplex imaging



Front. Immunol., 14 November 2019 | https://doi.org/10.3389/fimmu.2019.02657

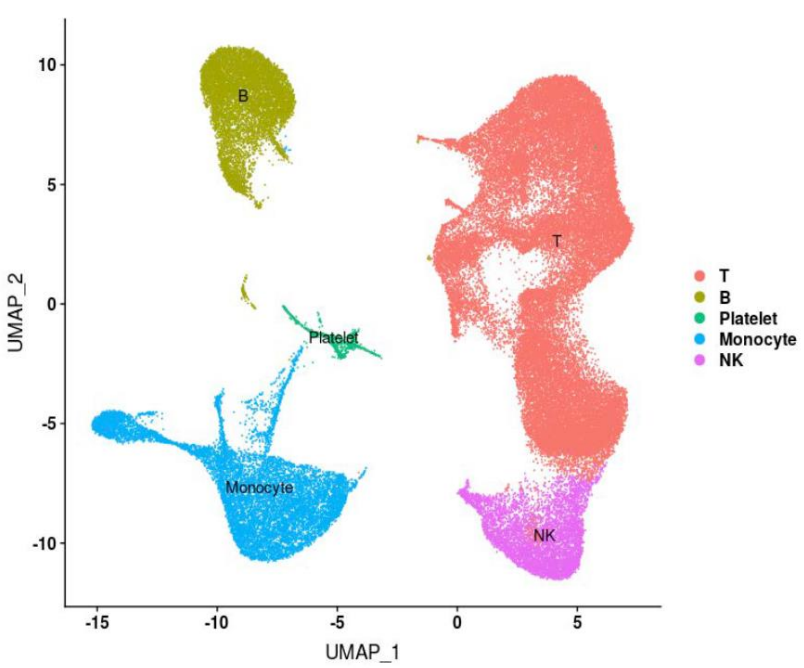
Mass Cytometry Imaging for the Study of Human Diseases—Applications and Data Analysis Strategies

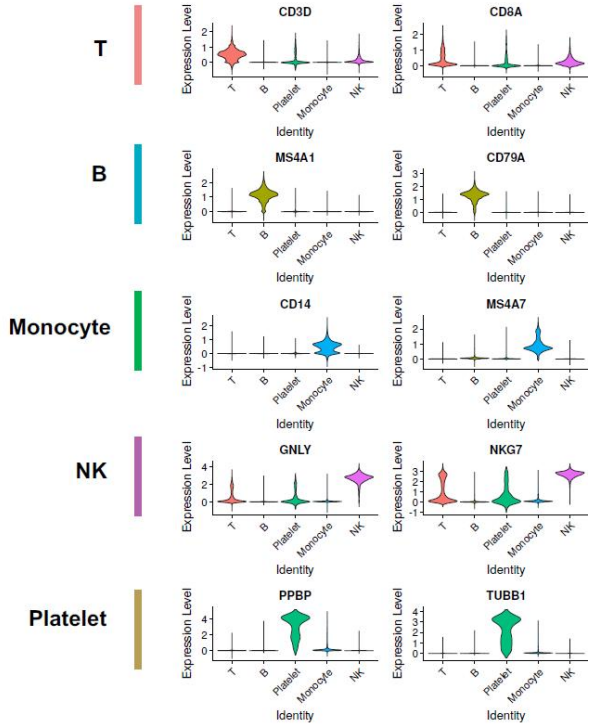
Heeva Baharlou, Nicolas P. Canete, Anthony L. Cunningham, Andrew N. Harman and Ellis Patrick

Enhanced Biomarkers to monitor toxicity

- Immune mediated toxicities lead to morbidity and mortality
- Early intervention is needed
- Biomarkers could improve time to immune mediated toxicity treatment
- Serial blood samples for biomarker discovery

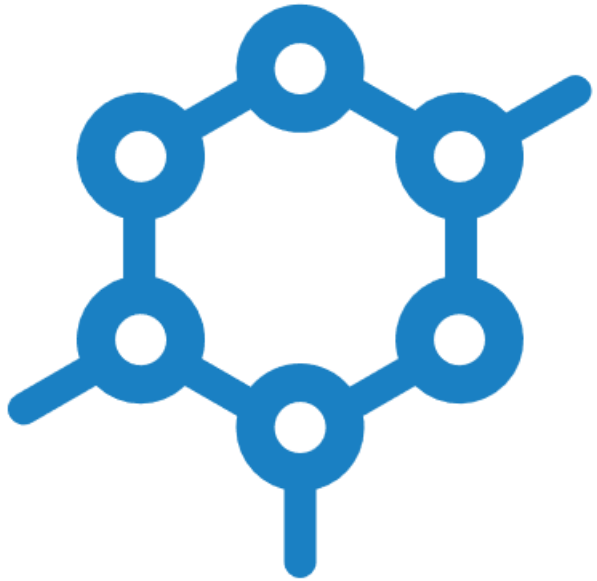
Single cell RNAseq





Single cell RNAseq of blood samples of patients who suffered immune mediated toxicities

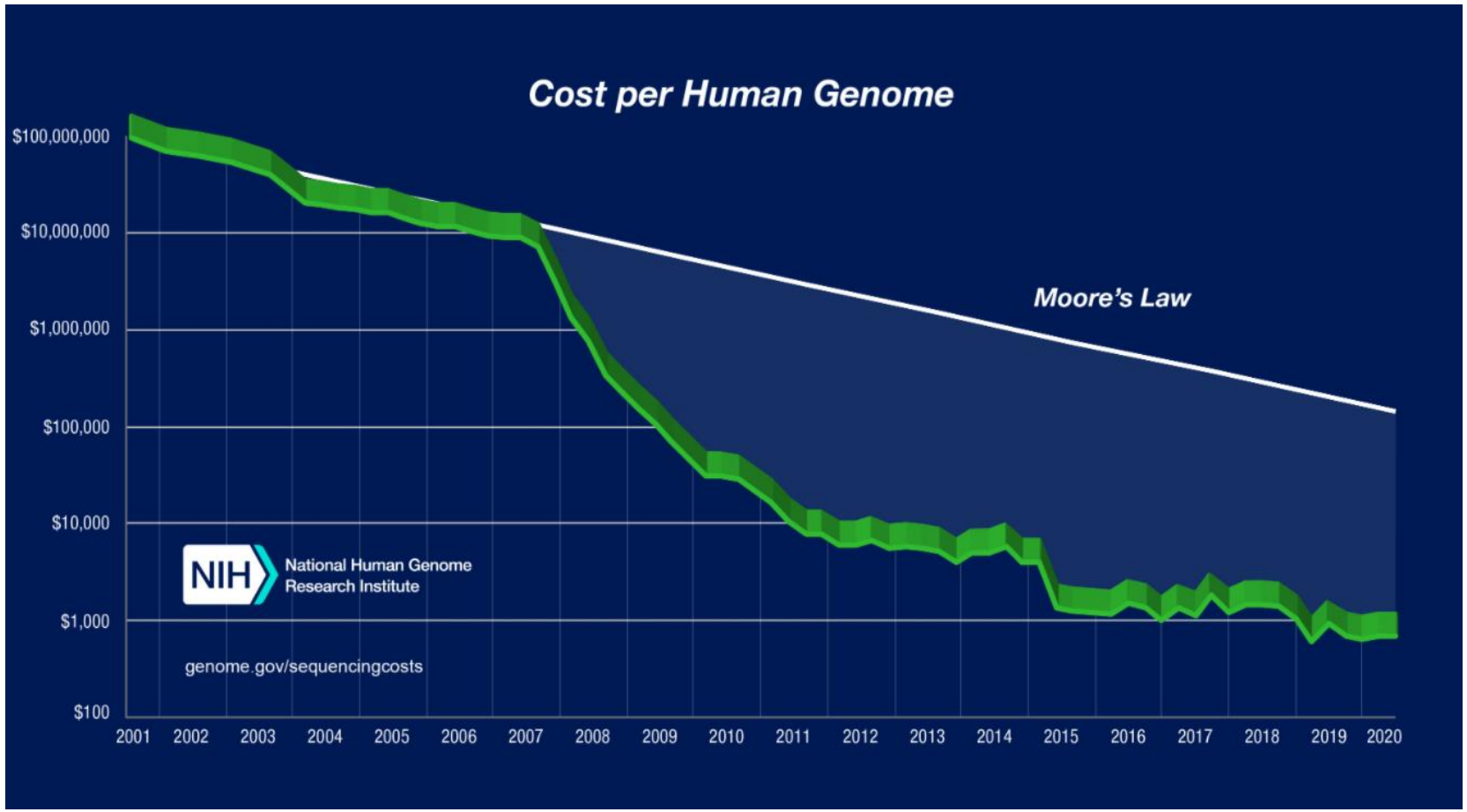
Far



Far

- Everyone with a sequenced genome.

- Everyone with proteomic evaluation.



Genome efforts across the globe

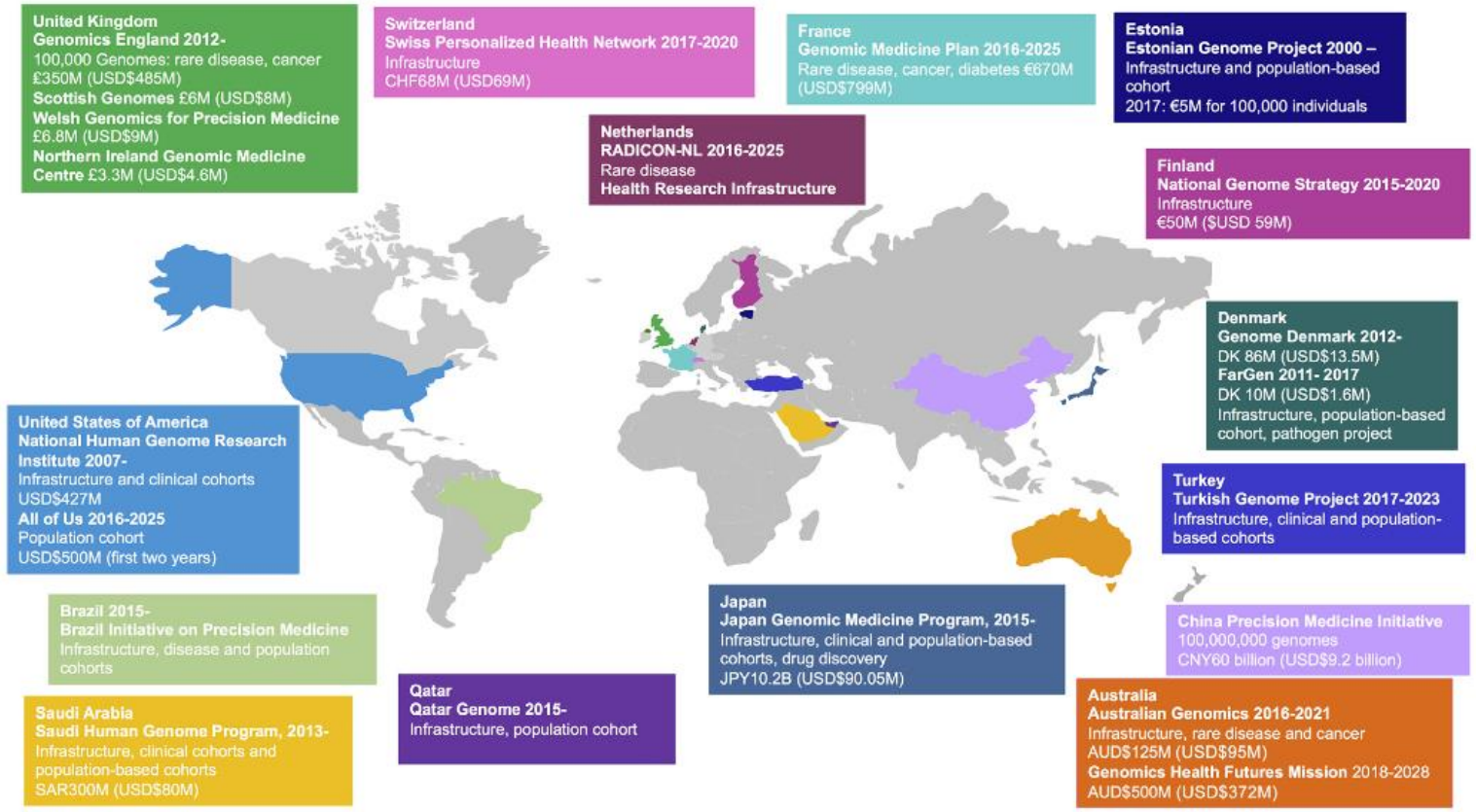
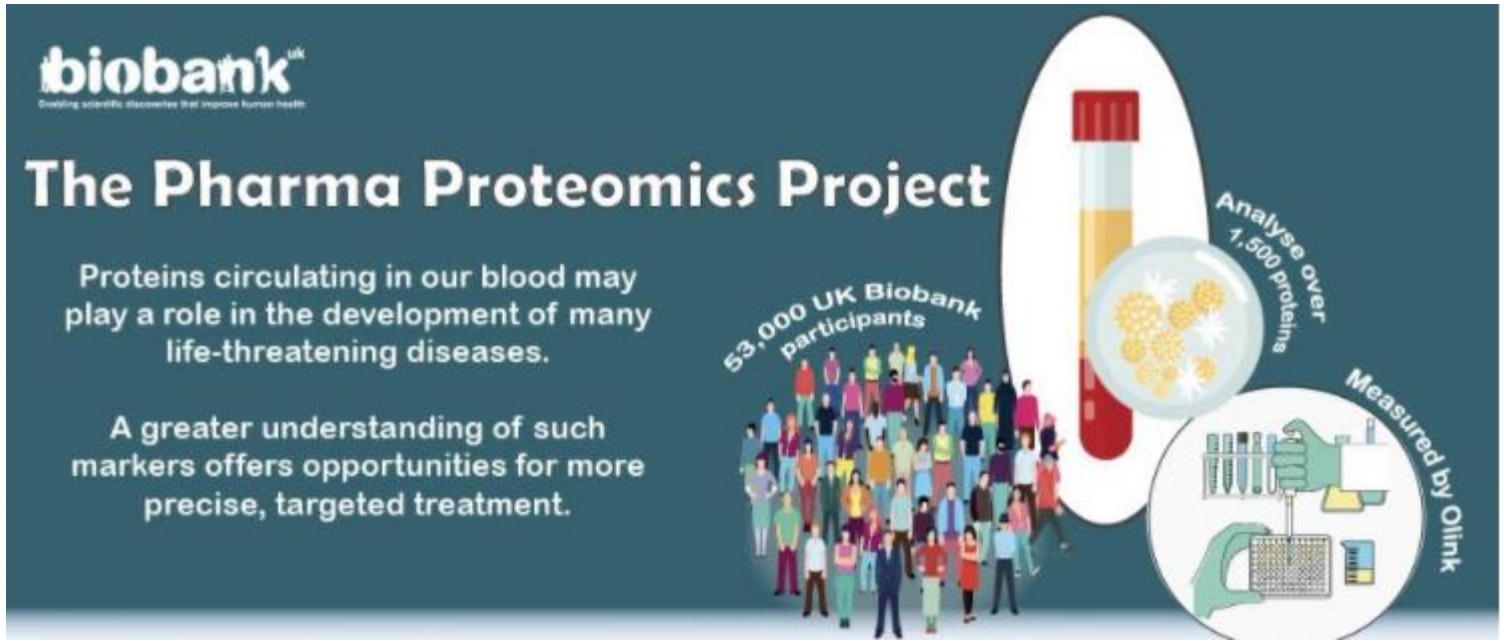


Figure 1. Map of Currently Active Government-Funded National Genomic-Medicine Initiatives

The American Journal of Human Genetics *104*, 13–20, January 3, 2019

Intermountain's effort to improve population health

Intermountain Healthcare and deCODE genetics Launch Groundbreaking DNA Study of 500,000 People to Find New Links Between Genetics and Disease

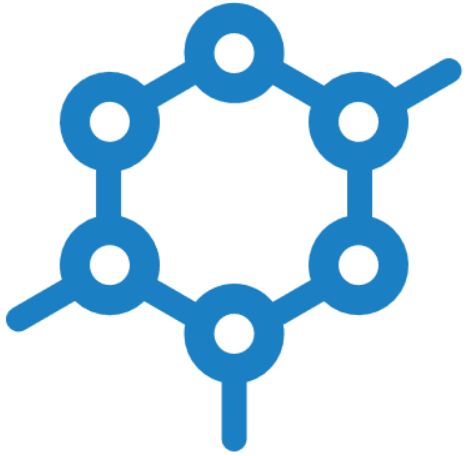


The next –omics, proteomics

https://www.ukbiobank.ac.uk/learn-more-about-uk-biobank/news/uk-biobank-launches-one-of-the-largest-scientific-studies

Genomics/Proteomics

Potential of disease



Manifestation of disease

Summary

- Near
  - CAR-T, TILs, Cancer vaccines, Oncolytic viruses, Combination x plus immunotherapy, Enhanced clinical response to toxicity
- Not too far
  - Enhanced Biomarkers for response, Enhanced Biomarkers to monitor toxicity
- Far
  - Everyone with a sequenced genome, Everyone with proteomic evaluation.

Society for Immunotherapy of Cancer
ADVANCES IN Cancer IMMUNOTHERAPY™

Thank you