

# Immunotherapy in breast cancer

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Immune recognition of s...Immune recognition of s...美乳癌免疫療法 末期端

Secure | https://topick.hket.com/article/2088388/美乳癌免疫療法%E3%80%80末期端癌細胞消失?mtc=40001&srkw=pembrolizumab

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美國一名末期乳癌患者接受免疫療法後，癌細胞完全消失。專家表示，如長遠證明治療成效及安全性，本港有望引入。(資料圖片)

乳癌是香港女性頭號癌症，美國國家癌症研究所最新研究發現，一名末期乳癌患者接受混合版免疫療法後，癌細胞完全消失，兩年沒有復發，屬全球首宗個案。研究人員相信，有關療法將來可適用於治療更多癌症患者。

有本港腫瘤科教授認為，新療法可給予末期癌症患者新希望，但他估計費用逾100萬元，香港亦未掌握有關技術。

今年52歲、兩子之母的末期乳癌患者Judy Perkins兩年多前被美國國家癌症研究所選中，配合免疫治療藥物pembrolizumab，接受免疫療法T細胞輸入療法 (ACT)。她憶述，接受治療前，醫生指她只能多活3個月，因化療已無法阻止癌細胞擴散。治療後42周，Judy Perkins體內癌細胞完全消失，兩年後的今天亦無出現復發迹象。她形容：「專家可能只說是延長康復，但我會稱為治癒。」

Shhh...we won't tell anyone.

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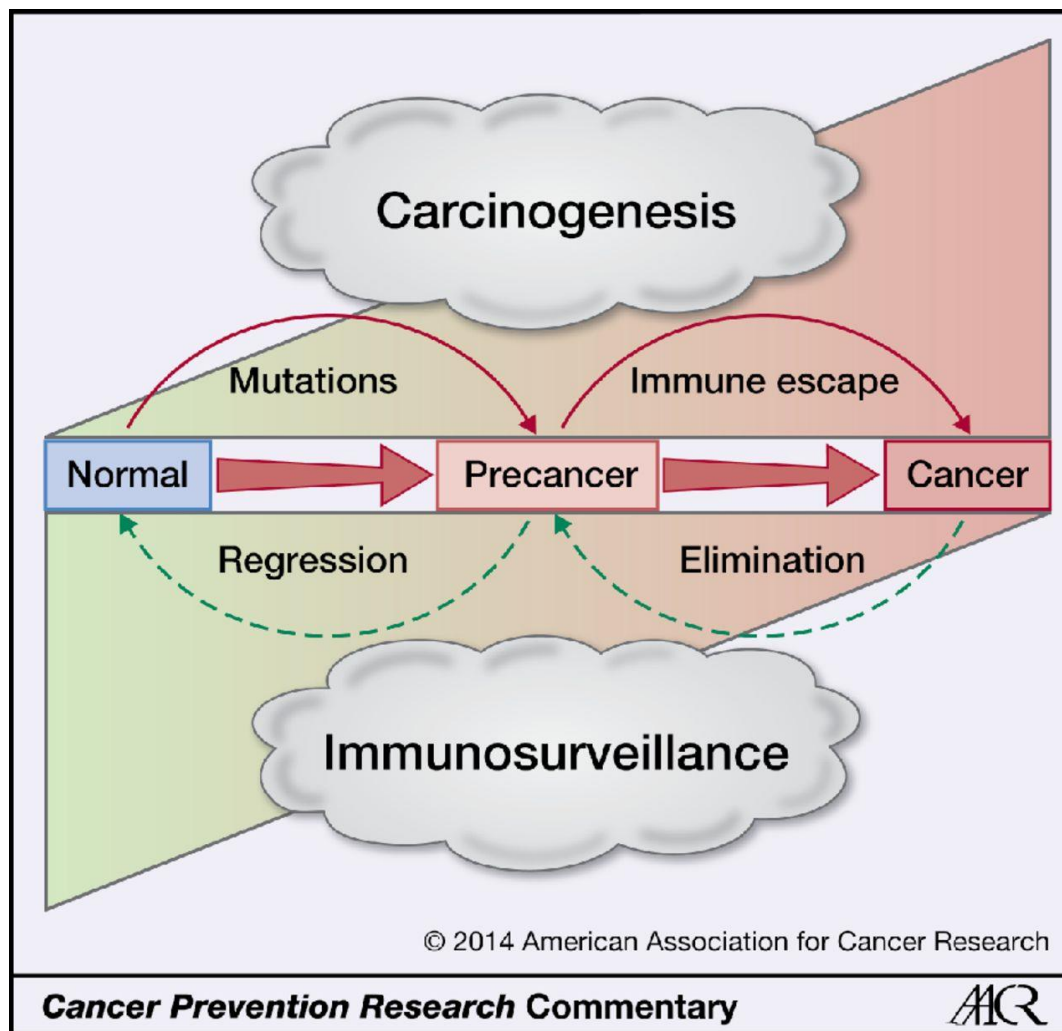
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# Case sharing by Dr. Kwan

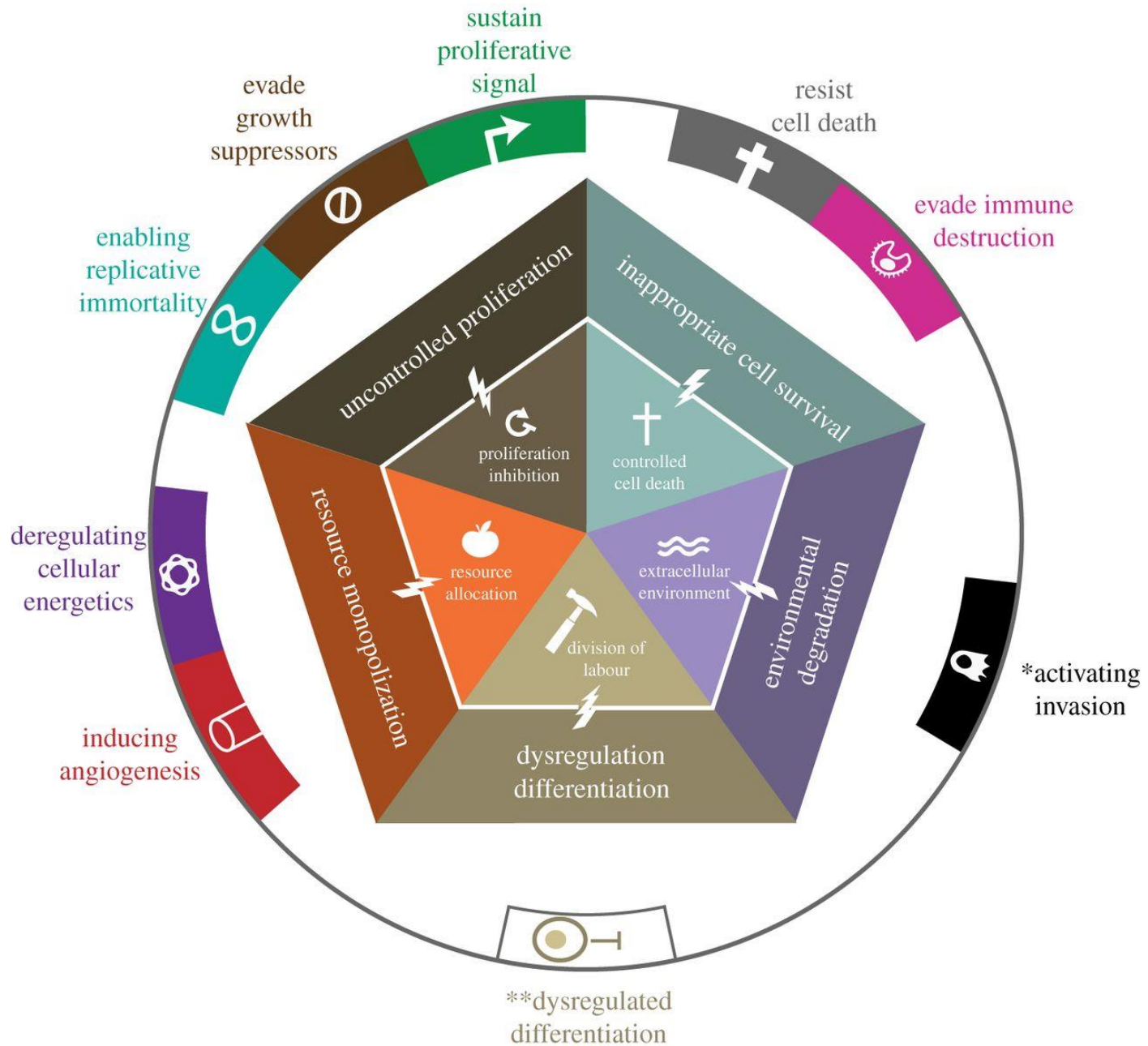
# Outline

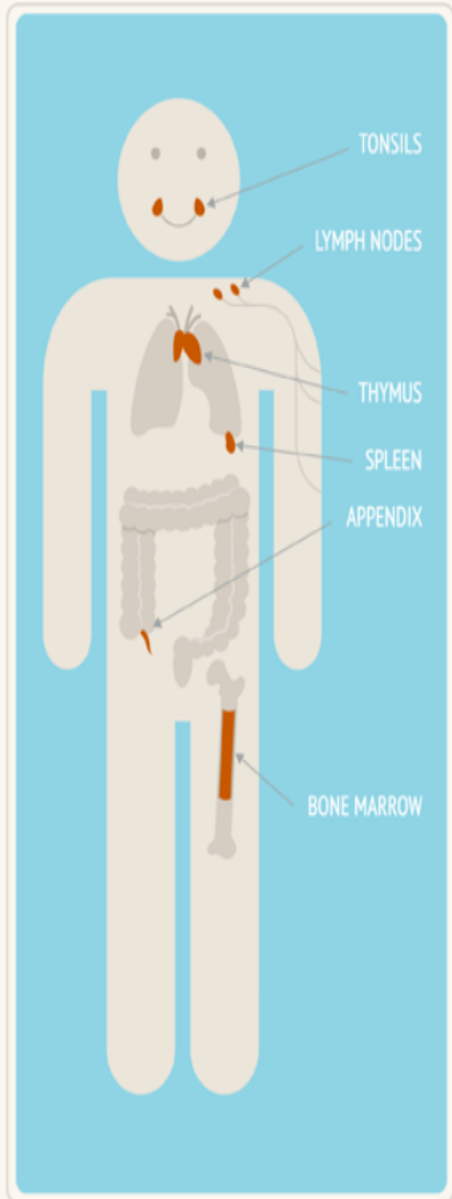
- Discuss how immune system is central to the formation of the tumor
- How are the current approaches to use the new generation of immune therapy to fight cancer
- What can we look forward to?

During progression from normal to precancer and cancer mutations may provide immune response to continuously survey and eliminate these mutated cells.



Asad Umar Cancer Prev Res 2014;7:1067-1071





## THE IMMUNE Army



### DENDRITIC CELLS

INTELLIGENCE AGENTS

情報人員

These cells take in available information about threats throughout the body, regroup at headquarters (secondary lymphoid organs), and alert other cells to the danger and give them clues about how to strategize an attack.



### CD4+ HELPER T CELLS

COMMANDANTS

指揮官

These cells provide specialized orders and support to other cells, including B cells and CD8+ killer T cells, and help direct and coordinate their responses against enemies.



### B CELLS

彈藥工廠／庫

MUNITIONS FACTORIES

When activated, B cells turn into plasma cells—factories that can churn out thousands of highly targeted antibodies every second.



### CD8+ KILLER T CELLS

NAVY SEALS/TRAINED ASSASSINS

追擊手

CD8+ T cells are the ruthless killers of the immune system. Each one can kill thousands of harmful cells, including cancer cells. They can seek out and destroy cells that have dangerous forces inside them, such as viruses and proteins that are being aberrantly expressed in cancer cells.



### CYTOKINES

通訊／密碼

COMMUNICATIONS/CODES

These molecules help immune cells talk to each other and coordinate the right attack.



### ANTIBODIES

彈藥

AMMUNITION

These are the bullets that can seek out and bind to proteins on cancer cells, cutting off vital signaling pathways or marking the cells for attack by other immune cells.

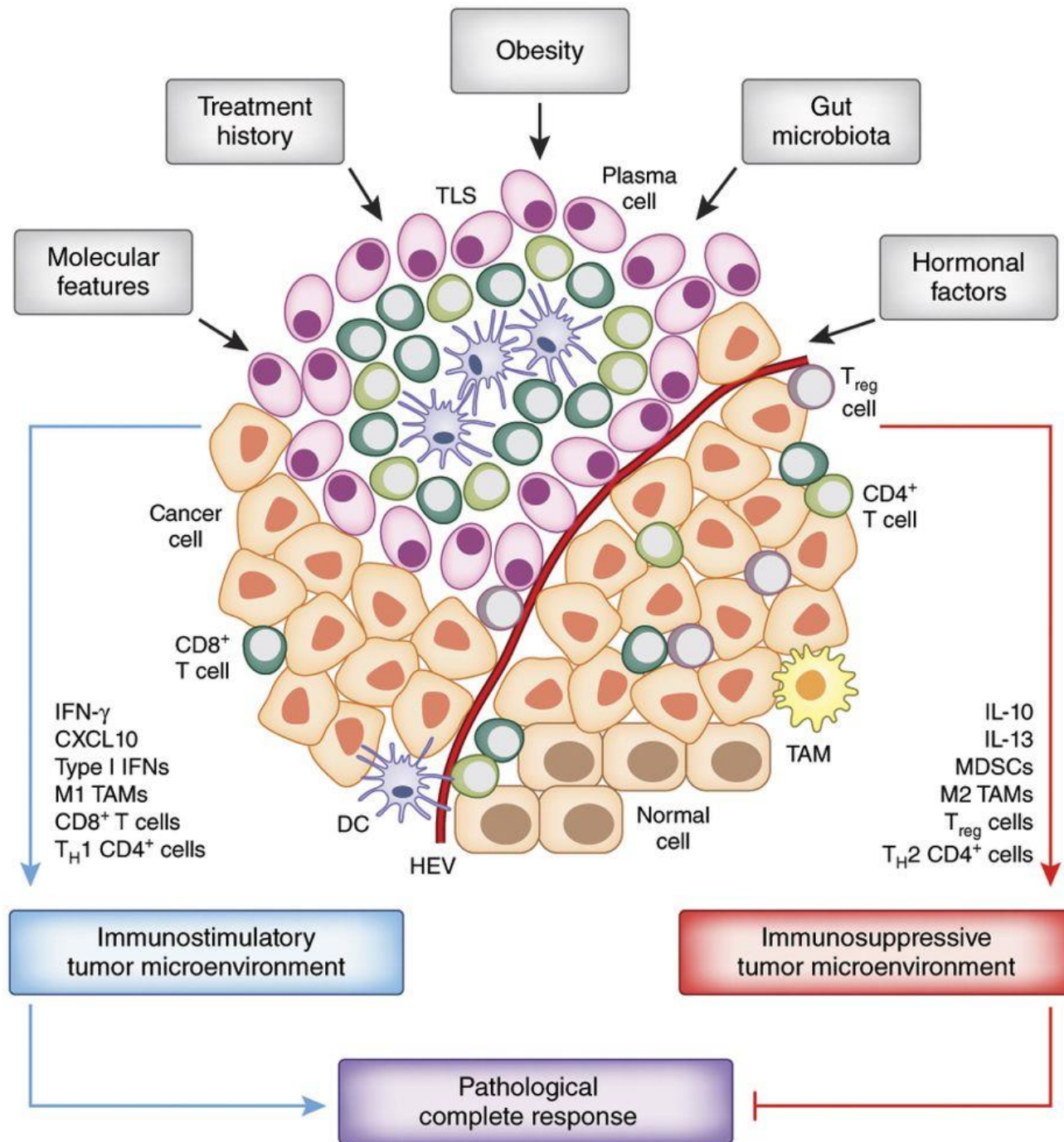


### REGULATORY T CELLS

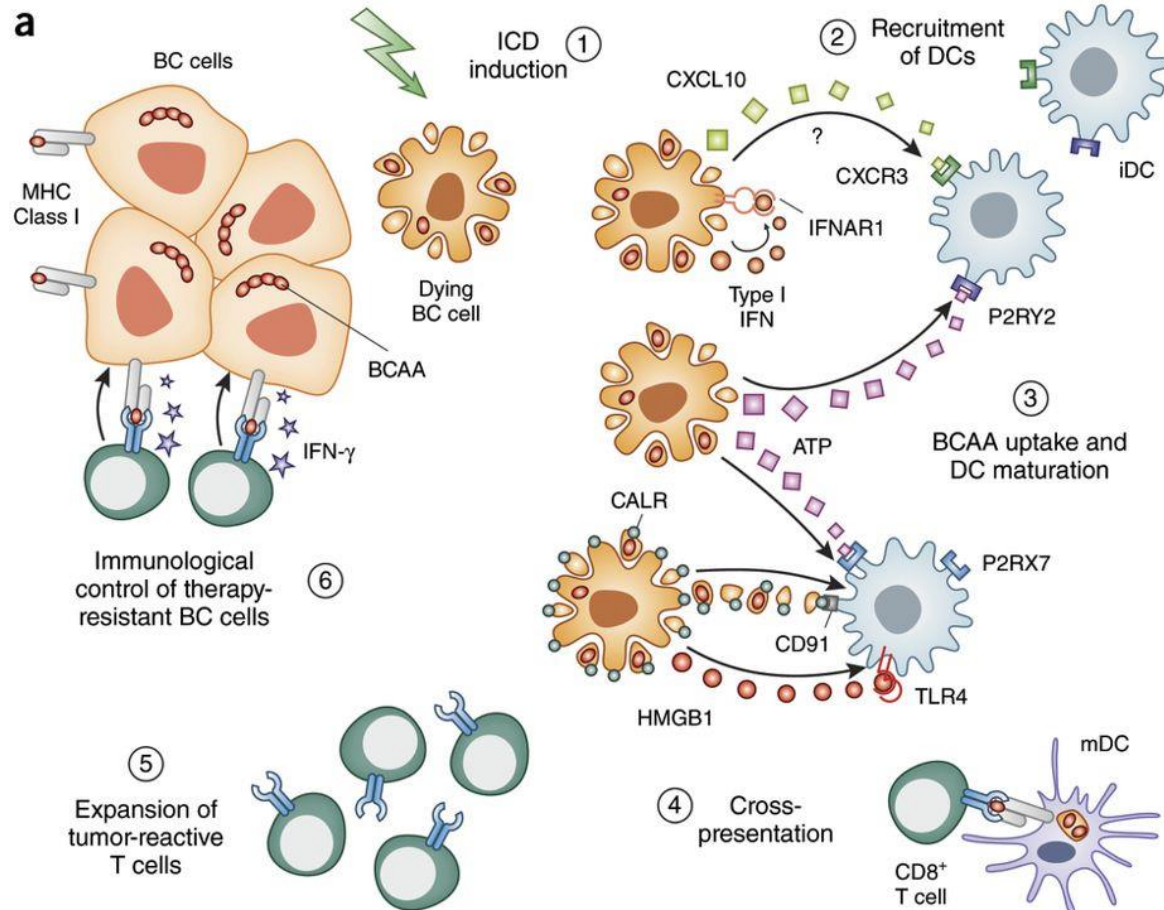
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監管





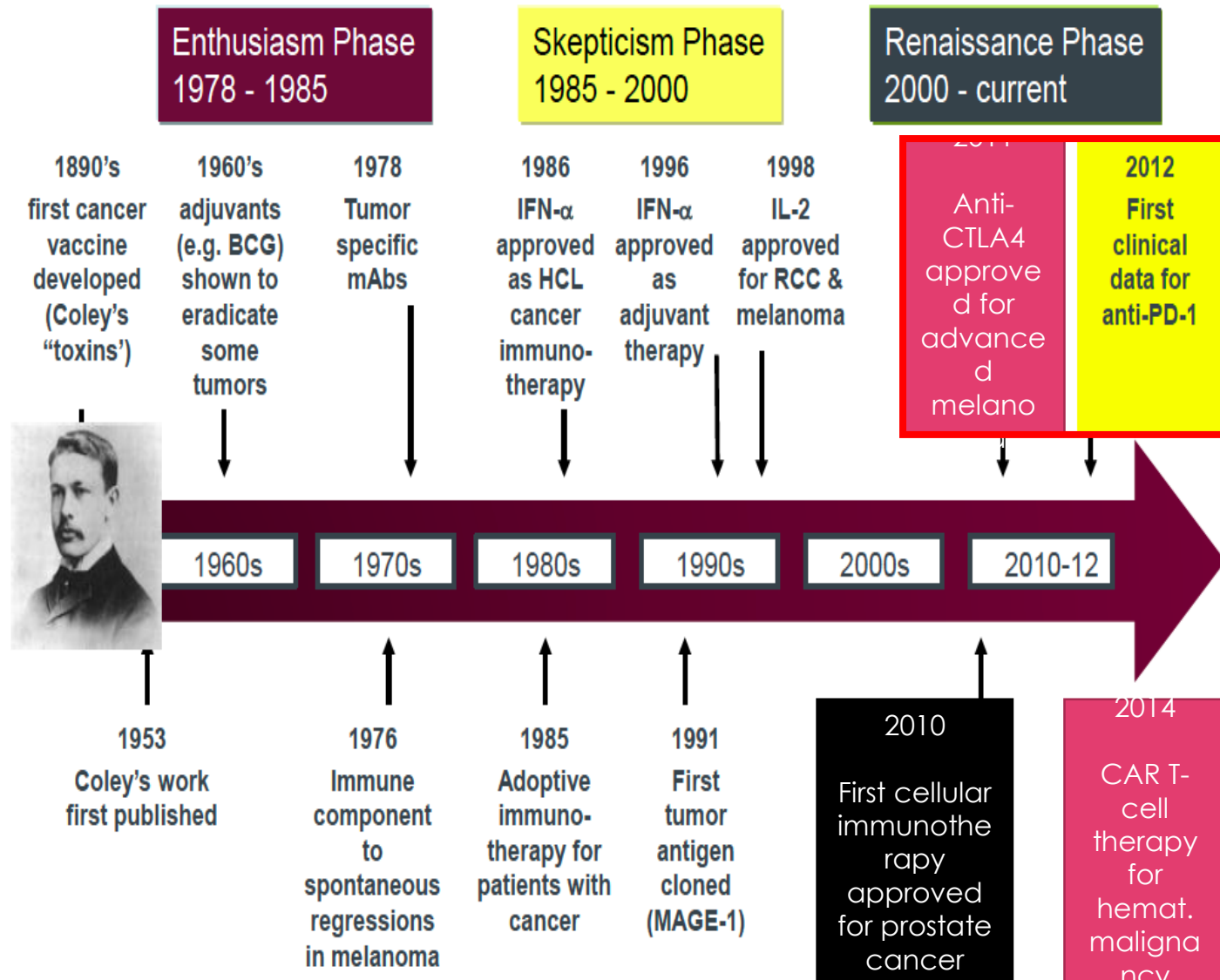





**b**

Therapy	Cancer cells		Immune system		
ICD inducers	Stress	Ligands	Receptors	Effects	Subversion
Anthracyclines	ER stress	→ CALR	CD91	→ BCAA uptake	⊥ CD47 expression
Taxanes	Autophagy	→ ATP	P2RY2 P2RX7	→ DC recruitment IL-1β secretion	⊥ P2RX7 SNPs CD39/CD73 Autophagy defects
Cyclophosphamide	Viral mimicry	→ Type I IFN	IFNAR1	→ T-cell recruitment	⊥ IFR7 deficiency
Radiotherapy	Cell death	→ HMGB1	TLR4	→ BCAA processing	⊥ TLR4 SNPs HMGB1 loss

# History of Cancer Immunotherapy

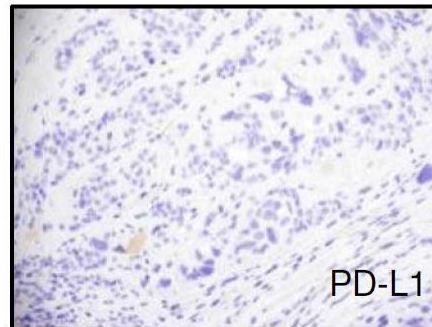
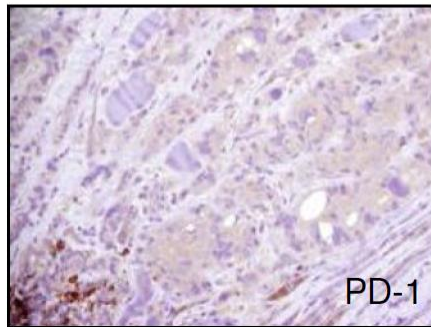
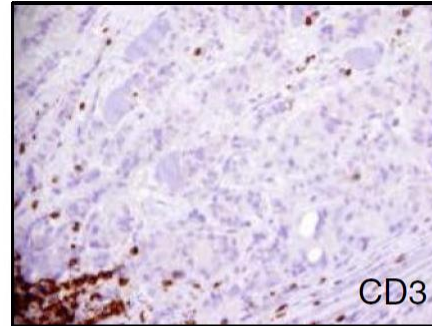
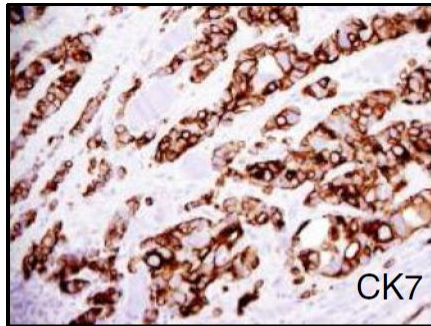


# Immune recognition of somatic mutations leading to complete durable regression in metastatic breast cancer

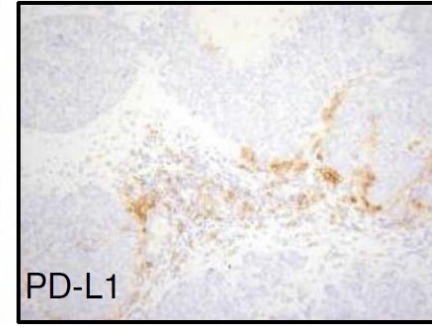
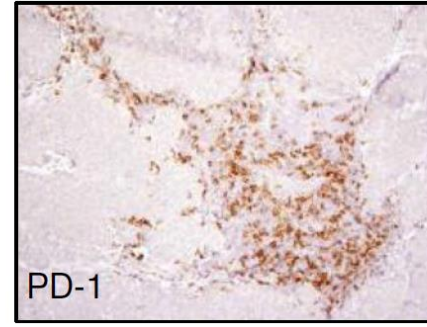
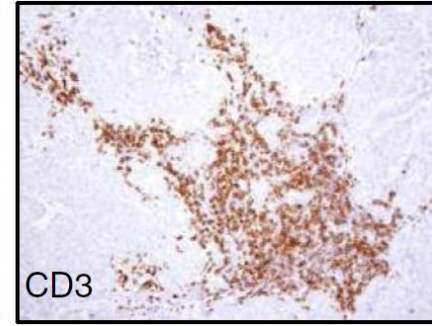
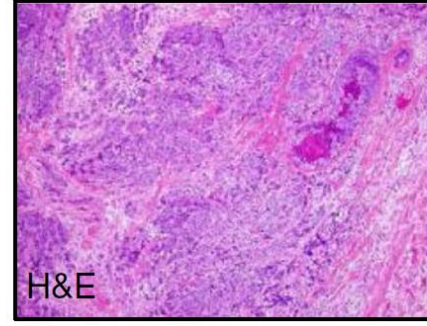
Nikolaos Zacharakis<sup>1</sup>, Harshini Chinnasamy<sup>1</sup>, Mary Black<sup>1</sup>, Hui Xu<sup>1</sup>, Yong-Chen Lu<sup>1</sup> <sup>1</sup>, Zhili Zheng<sup>1</sup>, Anna Pasetto<sup>1</sup>, Michelle Langhan<sup>1</sup>, Thomas Shelton<sup>1</sup>, Todd Prickett<sup>1</sup>, Jared Gartner<sup>1</sup>, Li Jia<sup>1</sup>, Katarzyna Trebska-McGowan<sup>2</sup>, Robert P. Somerville<sup>1</sup>, Paul F. Robbins<sup>1</sup>, Steven A. Rosenberg<sup>1\*</sup>, Stephanie L. Goff<sup>1</sup> and Steven A. Feldman<sup>1</sup>

# Immune infiltration is heterogeneous

Left chest wall core biopsy



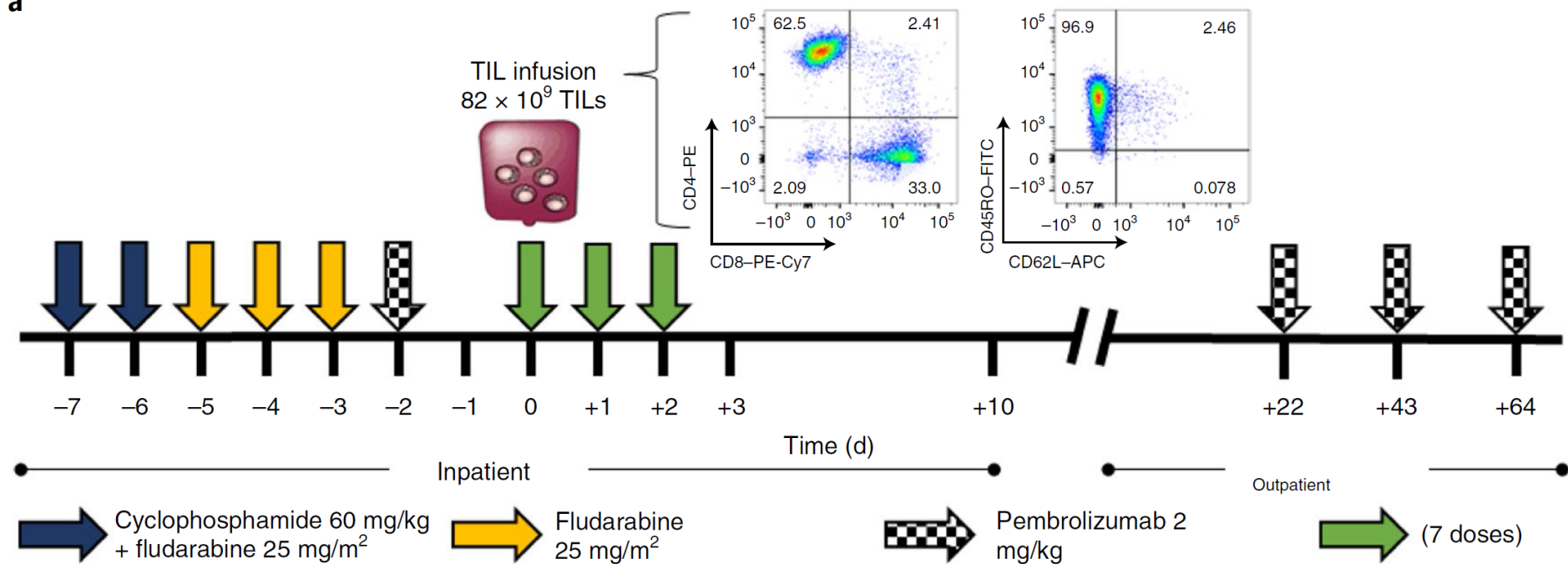
Right breast subcutaneous resected mass



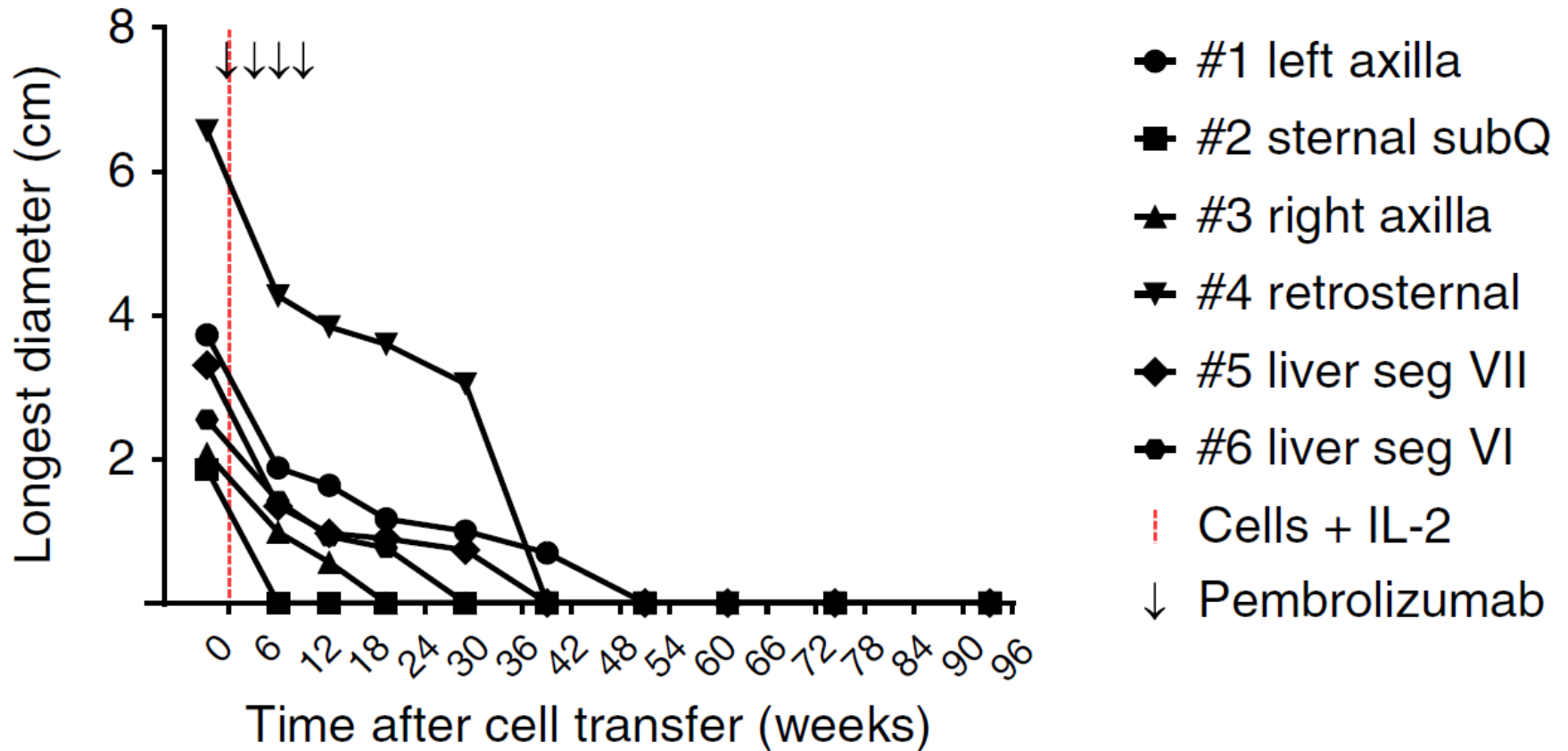


# How they did it

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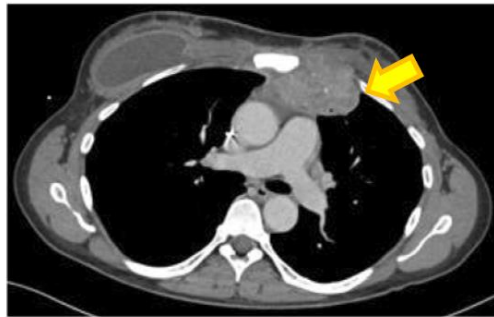


# Response is gradual

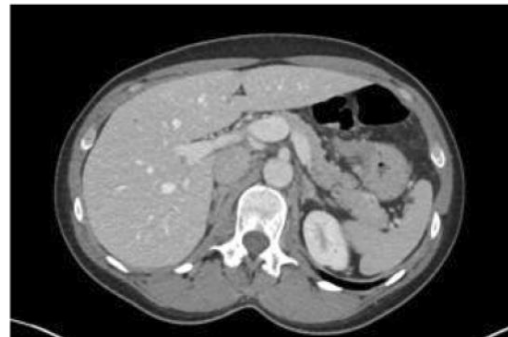
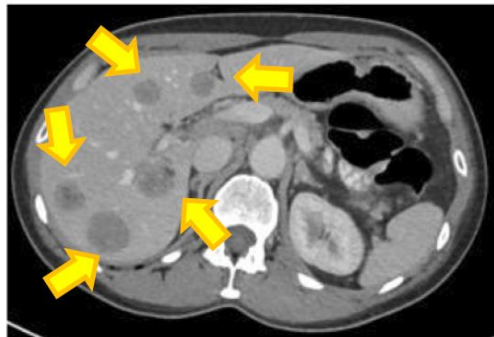
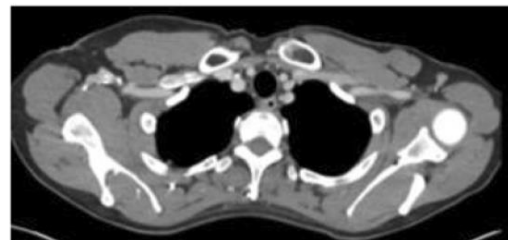
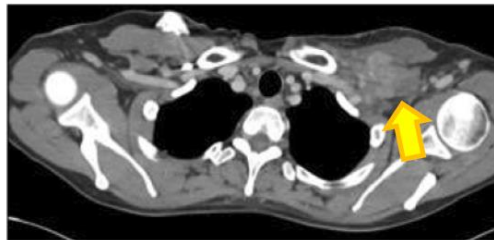
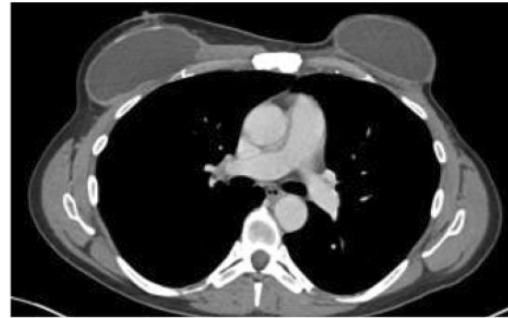




Pre-treatment



22 months  
post-treatment



# Looking ahead

- ▶ IO pathway is a universal anti-tumor pathway.
- ▶ In order to harness it, we are only learning again how to think about tumor and host interaction
- ▶ It is not a simple break and accelerator paradigm
- ▶ The host immune system can be tweaked internally and externally to recognise tumors which had been fooling the system. Perhaps it is a matter of balance of numbers
- ▶ Therapies that we have considered standard of care can be used to stimulate the immune system but we have yet to come up with the winning recipe

# Immune response cycle Check Point Inhibitors

