

Checkpoint Inhibition: The New Cancer Treatment Revolution

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Presenter Disclosure

- **Faculty:** Joel Gingerich
- **Relationships with commercial interests:**
N/A

Mitigating Potential Bias

- N/A

Learning Objectives

- Identify the role of immune checkpoint inhibition in cancer treatment
- Describe how checkpoint inhibition works
- Recognize the unique toxicities associated with immune checkpoint inhibition and how to treat them

Promising New Cancer Treatment Uses Immune Cells
–TIME 11/2014

“This is it” the cancer treatment that has doctors talking about
a cure – globalnews.ca 3/2016

Harnessing the Immune System to Fight Cancer
– New York Times 7/2016



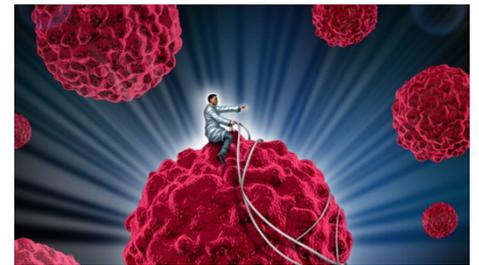
Setting the Body’s “Serial Killers” Loose on Cancer
– New York Times 8/2016

Background

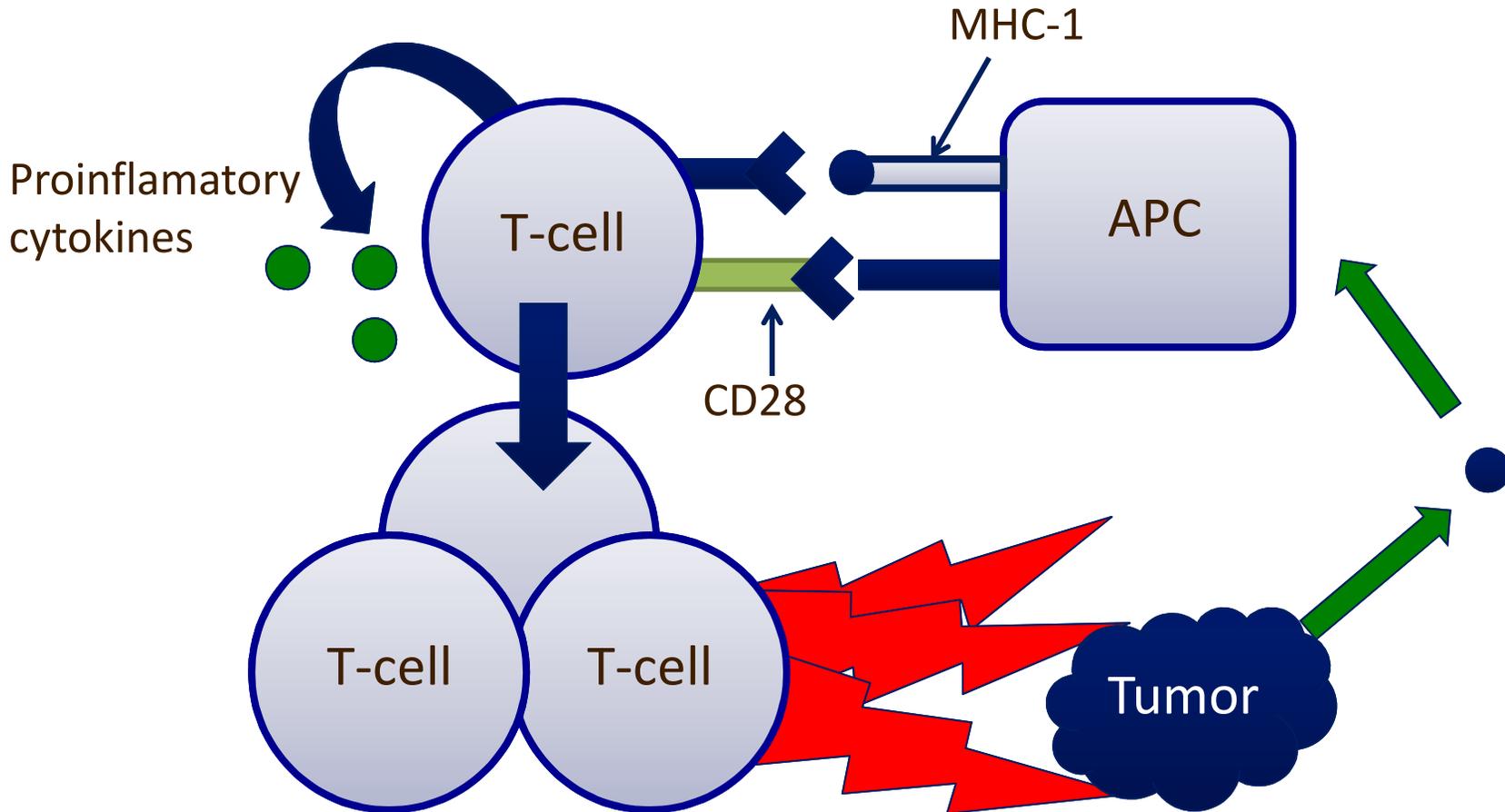
- The role of immunotherapy in cancer treatment is not new:
 - 1st described 100+ years ago
 - Used in metastatic melanoma/renal cell carcinoma for many years (IL-2, IFN- α)
- Limited by toxicity and limited benefit

Advantages of immunotherapy

- Develops long-term immune memory
 - The effects last much longer than the actual tx
 - Chance for long term control/ cure
- Utilizes the bodies own immune system
 - Resistant to cancer mutations



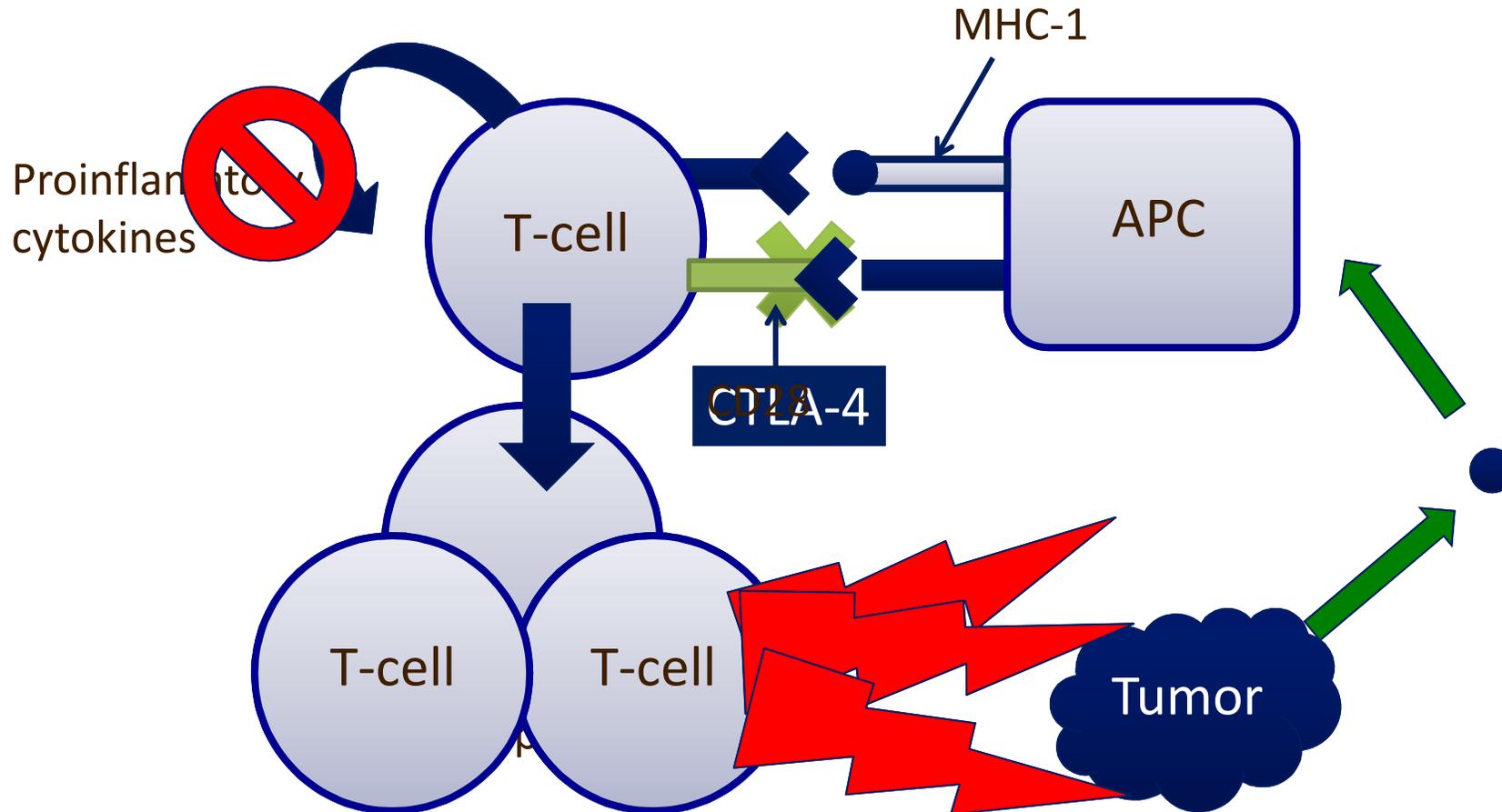
Normal immune response to tumors



T cells proliferate and differentiate into effector and memory cells

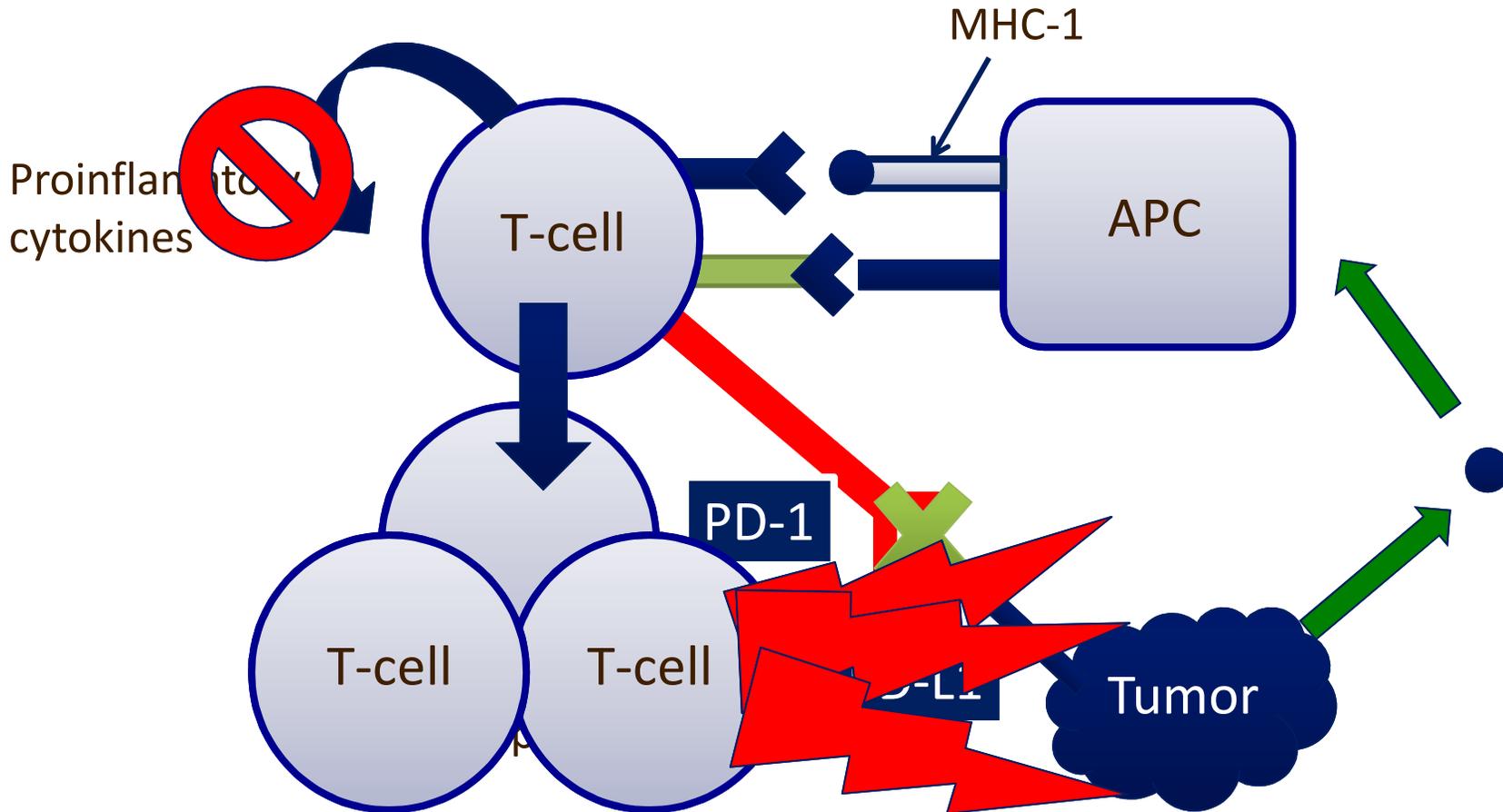
Immune checkpoints (“breaks”):

CTLA-4



T cells proliferate and differentiate into effector and memory cells

Immune checkpoints: Programmed death-1 (PD-1)



T cells proliferate and differentiate into effector and memory cells

Immune checkpoint inhibitors: (+) Phase III randomized clinical trials

Cancer	Drug	Mechanism	Line	OS Δ
Melanoma	ipilimumab	CTLA-4	1 st line	2.1 mo
	ipilimumab	CTLA-4	2 nd line	3.6 mo
	Nivolumab	PD-1	1 st line	↑ 30.8% (1 year)
	Pembrolizumab*	PD-1	1 st or 2 nd line	↑ 15.9% (1 year)
Lung cancer	Nivolumab	PD-1	2 nd line	2.8 mo
	Nivolumab	PD-1	2 nd line	3.2 mo
	Pembrolizumab	PD-1	2 nd line	4.2 mo
RCC	Nivolumab	PD-1	2 nd line	5.4 mo

Some pts may be line term survivors:
i.e. 20% of met. melanoma pts alive at 5 years

Promising results from clinical trials

- Melanoma:
 - Adjuvant therapy (i.e. after surgery)
 - Combination therapy (Nivolumab/ipilimumab)
- Bladder cancer
- Prostate cancer
- Pancreatic cancer
- Head and neck cancer
- Breast cancer
- Hematologic malignancies



Cost

- \$8,200/ month
- Pembrolizumab currently funded for treatment in Manitoba
- Others will be soon



Adverse events associated with immune-checkpoint inhibitors

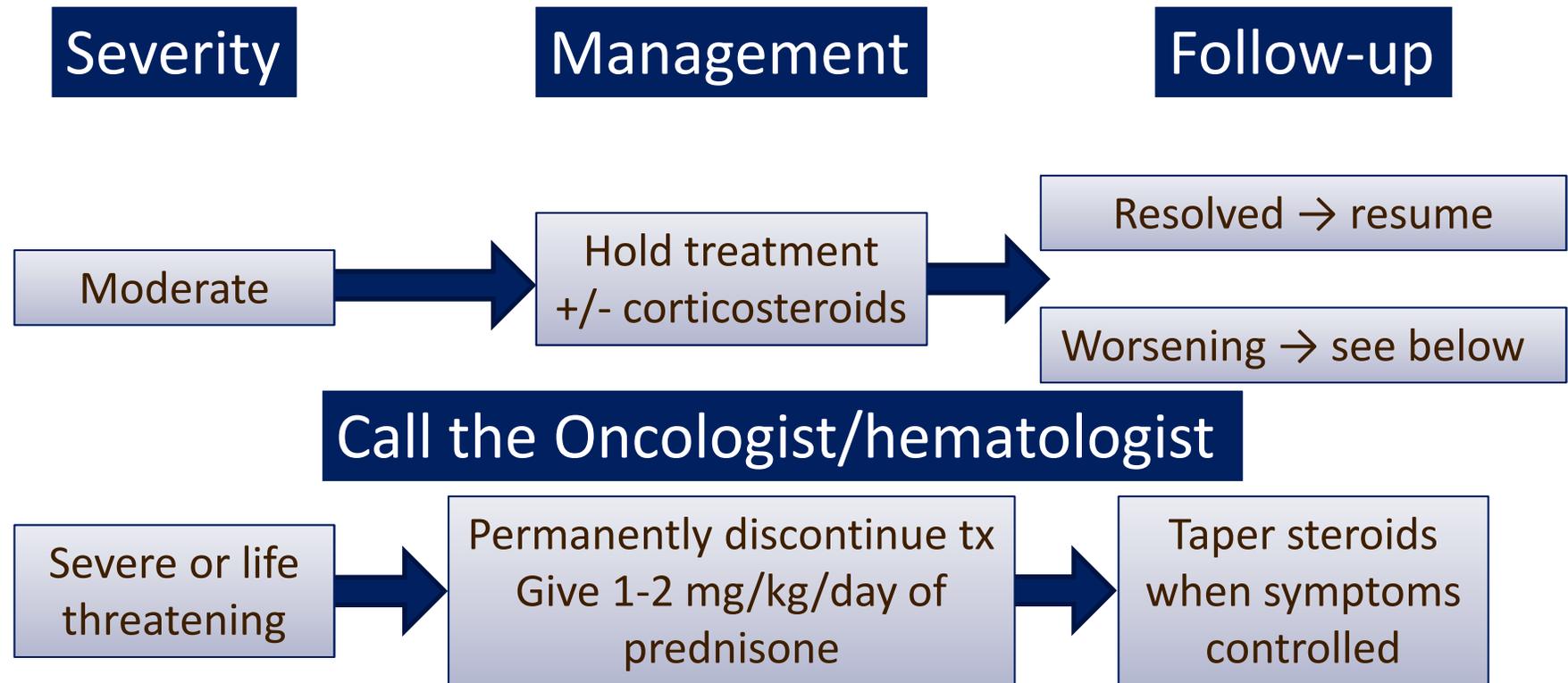
Immune-mediated adverse reactions	
Rash (50%): pruritis, vitiligo	Diarrhea/colitis (35%)
Pneumonitis (5%)	Hepatotoxicity (5%)
Endocrinopathies (6%): hypophysitis, thyroid, adrenal insufficiency	Neurologic (rare): Guillain-Barre, aseptic meningitis, encephalopathy, myasthenia

Toxicities: CTLA-4 > PD-1

Can be life threatening if not managed correctly

Death due to treatment (1%)

How to manage toxicity



http://www.accessdata.fda.gov/drugsatfda_docs/remis/Yervoy_2012-02-16_Full.pdf

Immune checkpoint inhibitor conclusions

- Rapidly changing the landscape of cancer treatment
- Seem to have benefits in many types of cancers
 - May improve long term outcome in a subset of pts
- Have unique immune related toxicities
 - Can be life threatening if not identified and treated properly



Selected bibliography

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