BC CANCER

Provincial Health Services Authority

# Advances in Immunotherapy for Lymphoma

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Immunotherapy Research Fellow

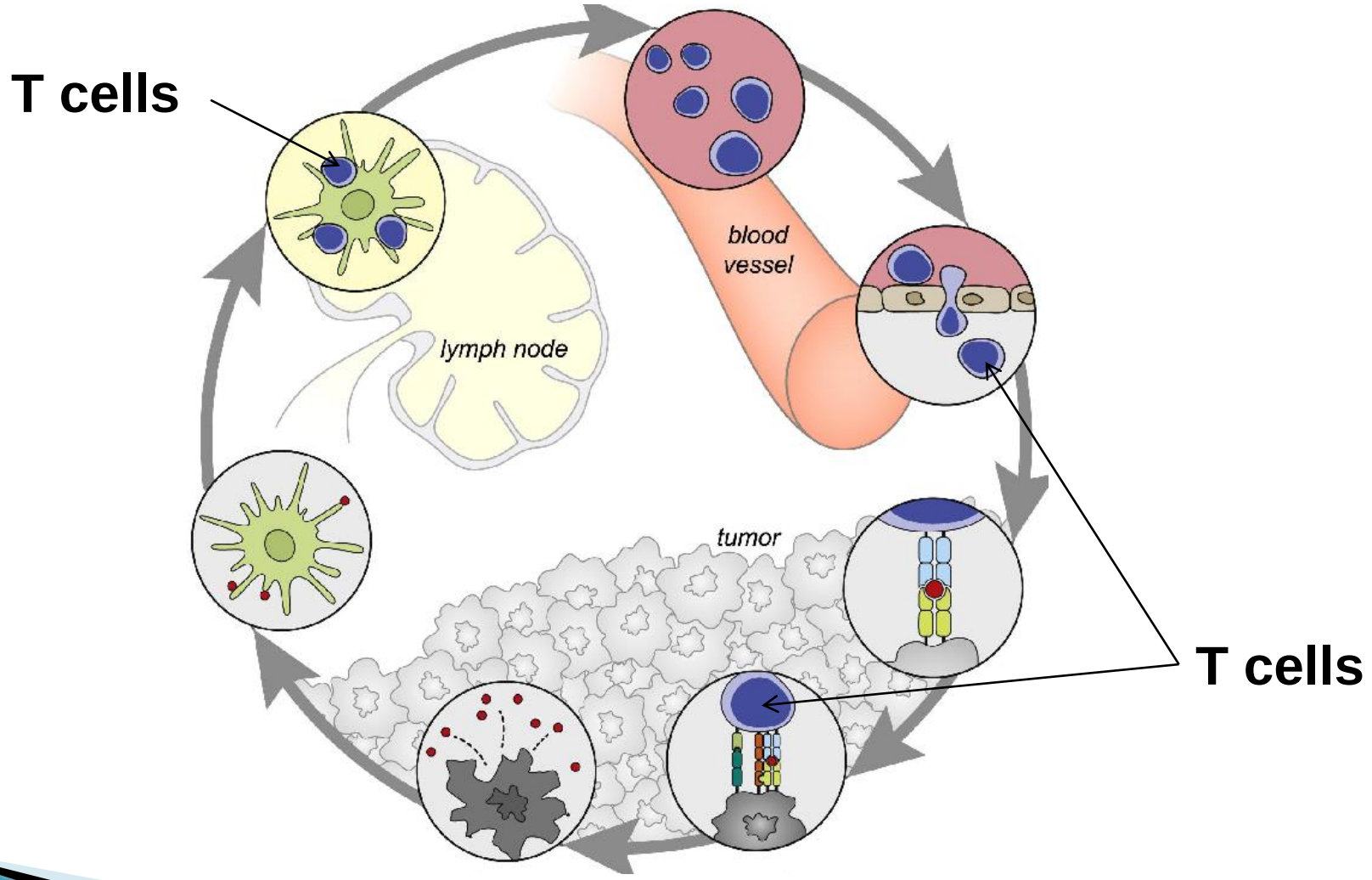
# Outline

- The immune system and cancer
- Immunotherapies available for lymphoma
- Upcoming immunotherapy clinical trials in BC
- The future of lymphoma immunotherapy

# What to remember today . . .

- The immune system is capable of recognizing and killing cancer cells, but cancer cells are good at hiding.
- “Immunotherapy” refers to different types of treatments with a collective aim to restore or enhance the immune system’s ability to kill cancer cells.
- Most new lymphoma immunotherapies are currently for relapsed disease or are still in clinical trials.
- Immunotherapy is a promising approach to cancer therapy, but we have much to learn.

# The immune system and cancer




Adapted from Chen & Mellman Immunity 2013;39:1-10

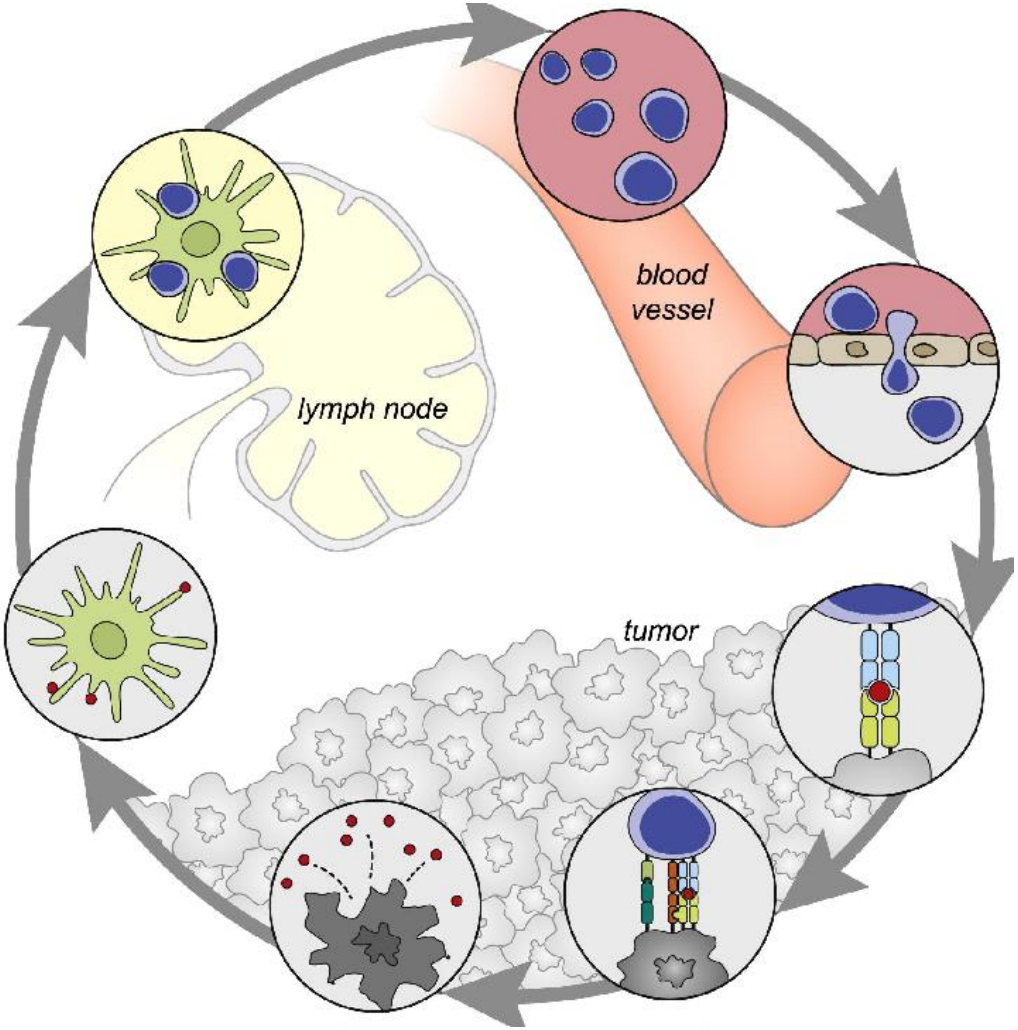
# The immune system and cancer

## 2

T cells (soldiers of the immune system) are alerted to the presence of abnormal proteins.

## 3

T cells travel to the site of the tumor.




## 1

Abnormal proteins sit on the surface or leak out of cancer cells.

## 4

T cells bind to the abnormal proteins on the cancer cell and kill it.

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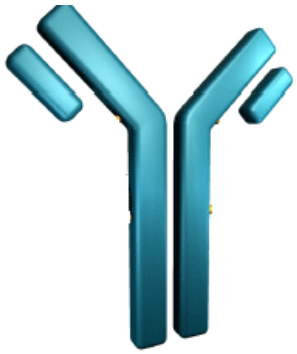
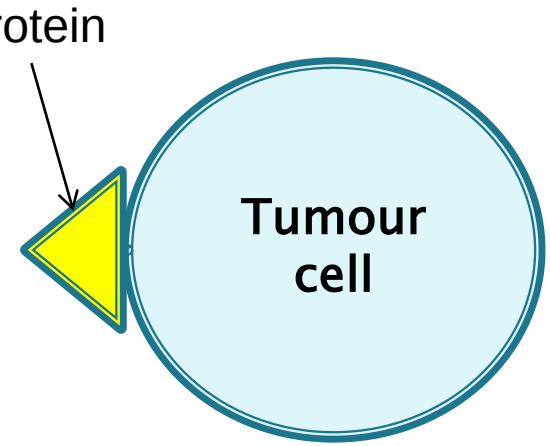
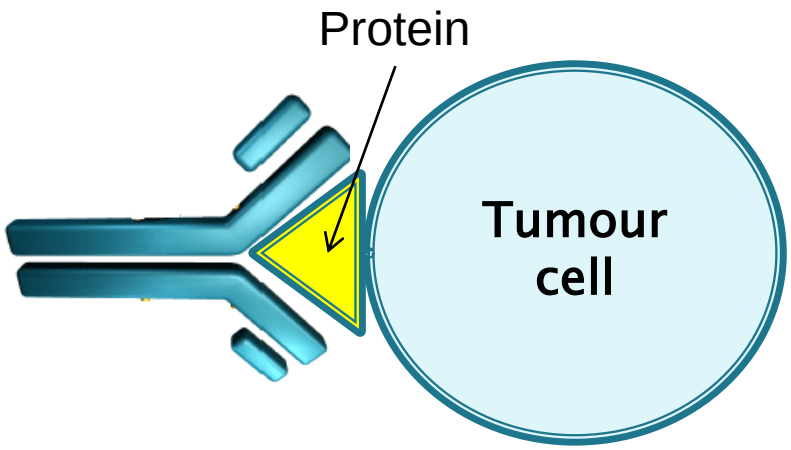
# Immunotherapies for lymphoma: Monoclonal antibodies



**Antibody**



# Immunotherapies for lymphoma: Monoclonal antibodies



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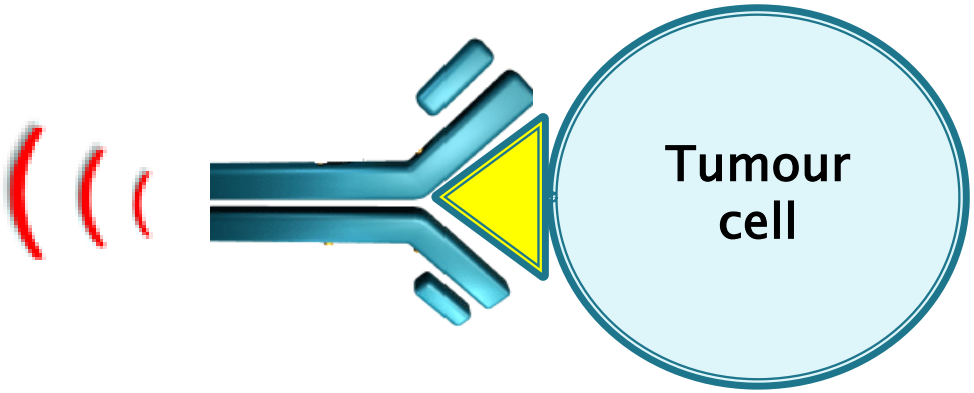

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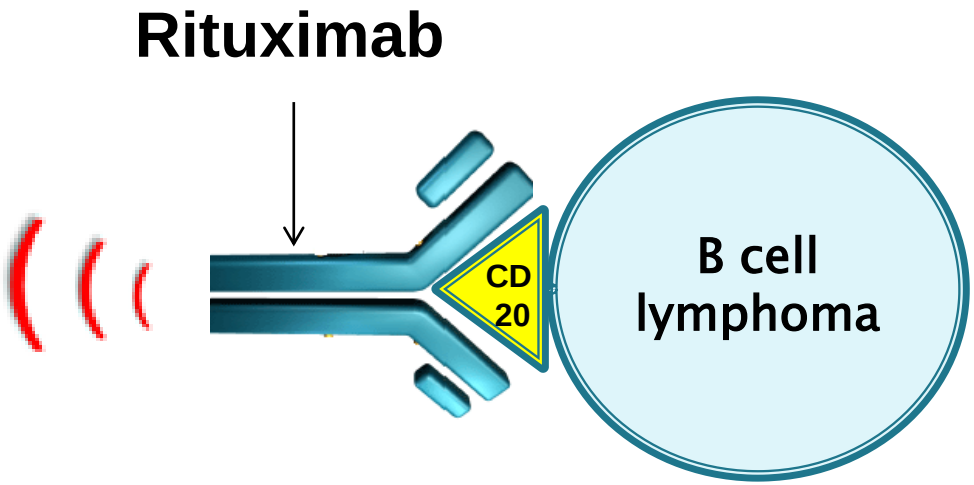
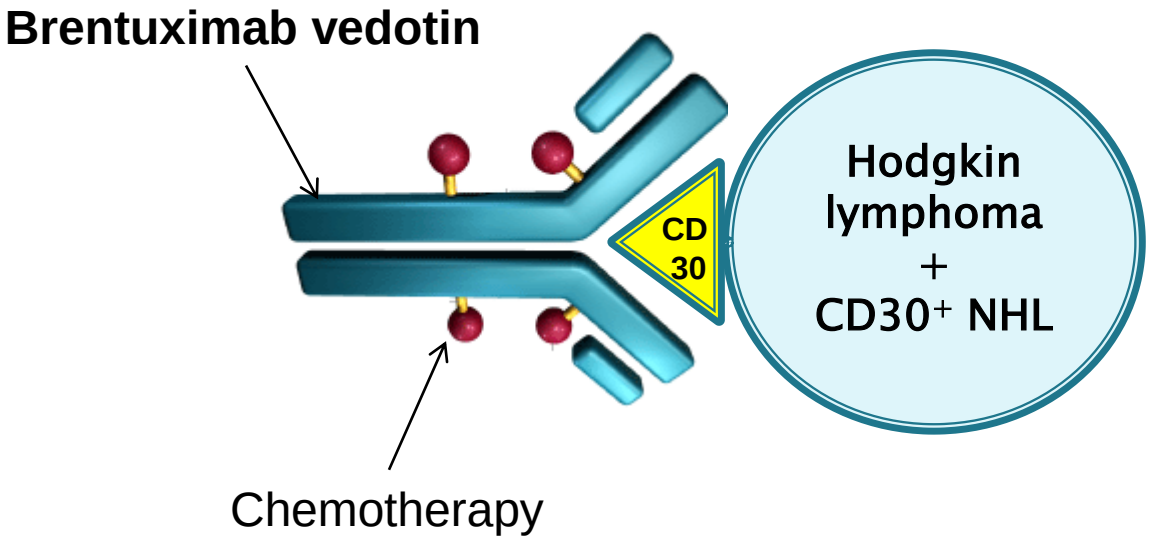


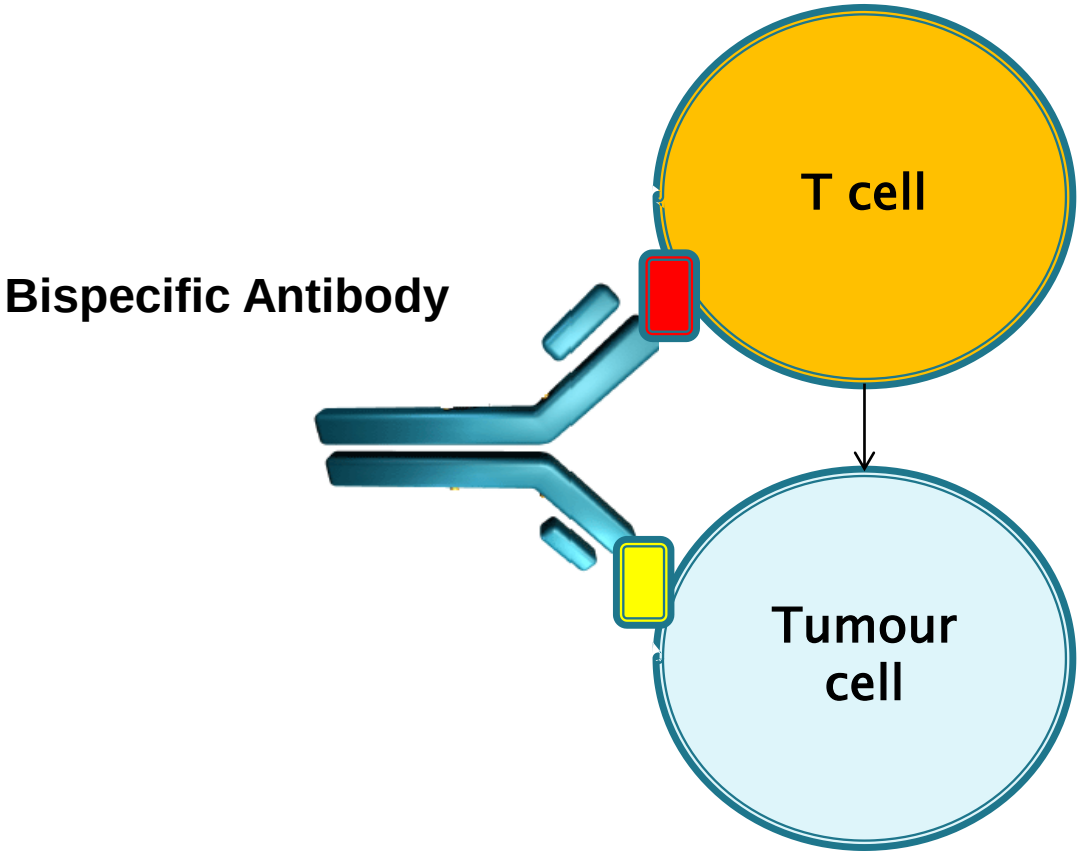

- First line therapy for all B-cell lymphomas

# Immunotherapies for lymphoma: Monoclonal antibodies



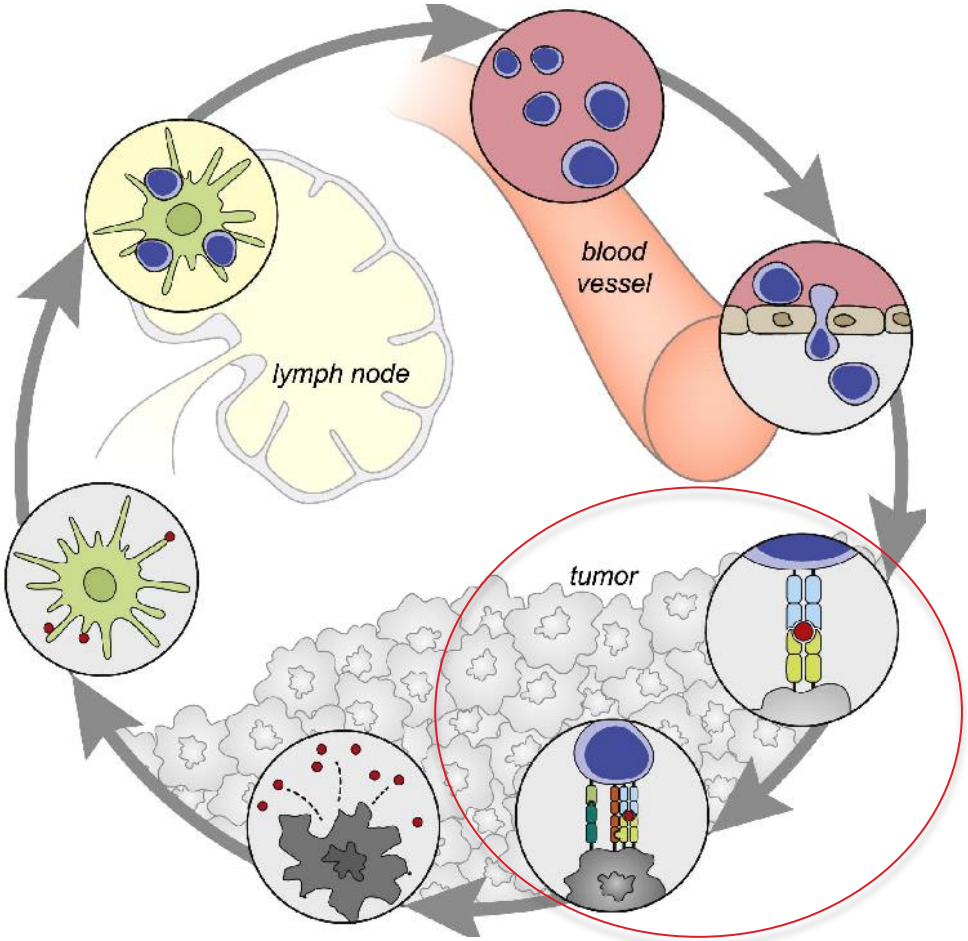

- Relapsed Hodgkin lymphoma
- Recently FDA-approved for first line therapy of Hodgkin lymphoma in combination with chemotherapy
- NHLs that express CD30

# Immunotherapies for lymphoma: Monoclonal antibodies



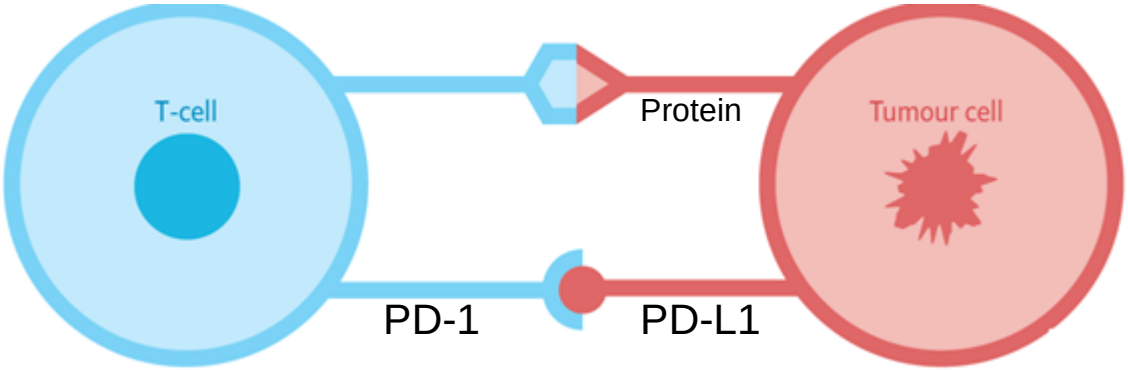

- No approved bispecific antibody therapies for lymphoma
- BC Cancer clinical trials open for relapsed B-cell NHL (DLBCL, FL, MCL)

# Immunotherapies for lymphoma: Checkpoint inhibitors



# Immunotherapies for lymphoma: Checkpoint inhibitors

T cell binds to abnormal protein on tumor cell




→ Tumor cell growth

If PD-1 binds PD-L1, T cell ignores tumor cell

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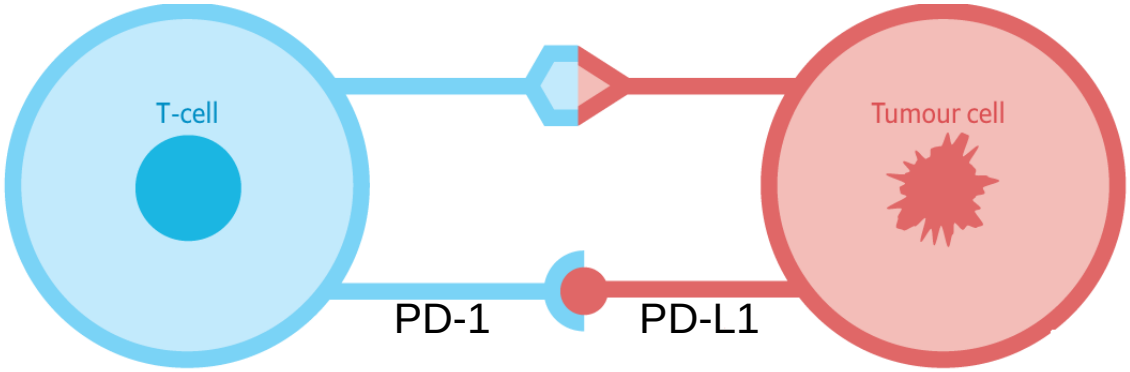


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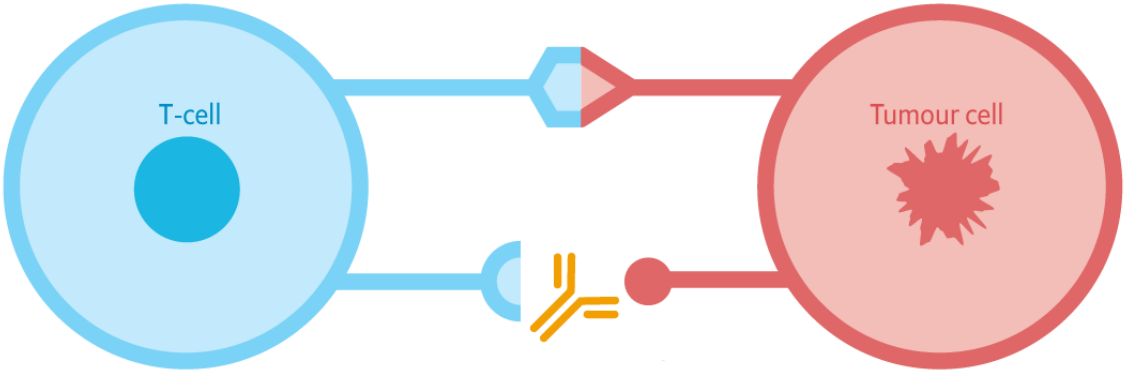
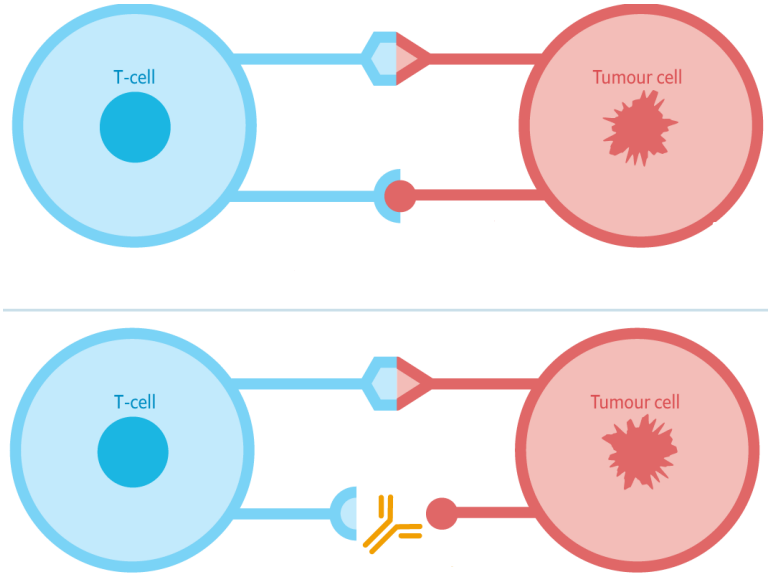



→ Tumor cell death

Checkpoint inhibitor prevents PD-1-PD-L1 binding

# Immunotherapies for lymphoma: Checkpoint inhibitors

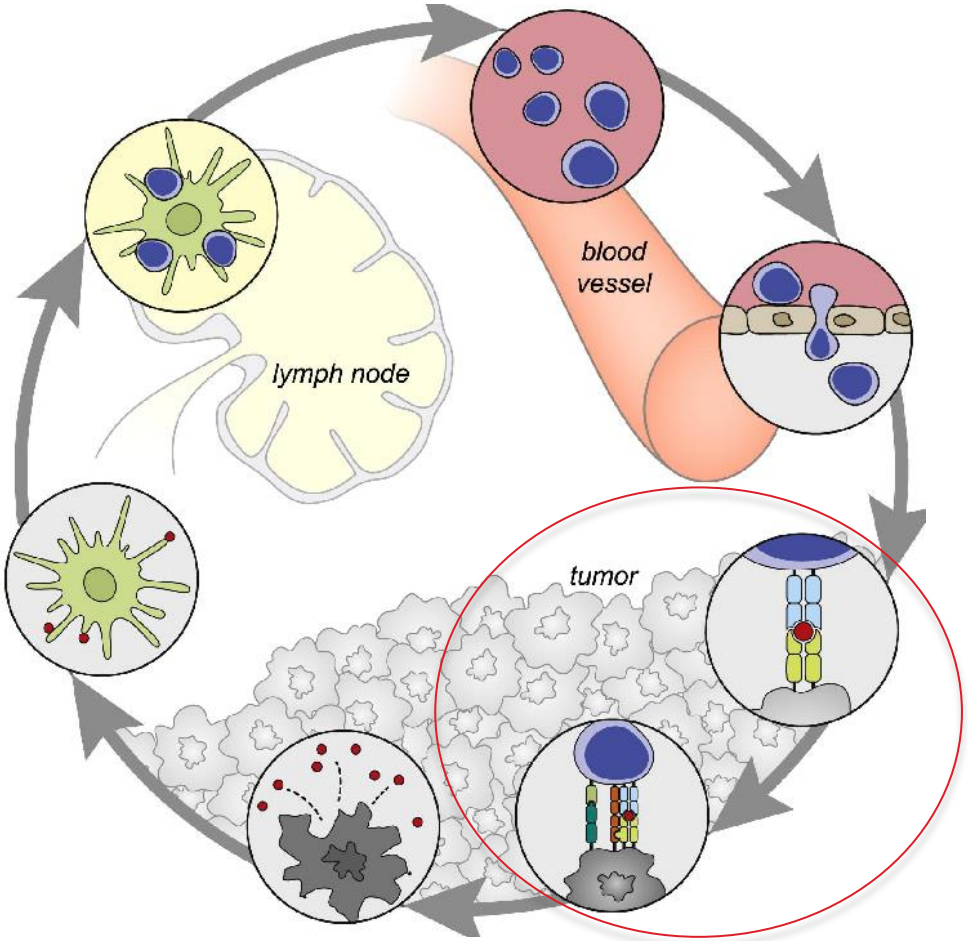



Tumor cell growth

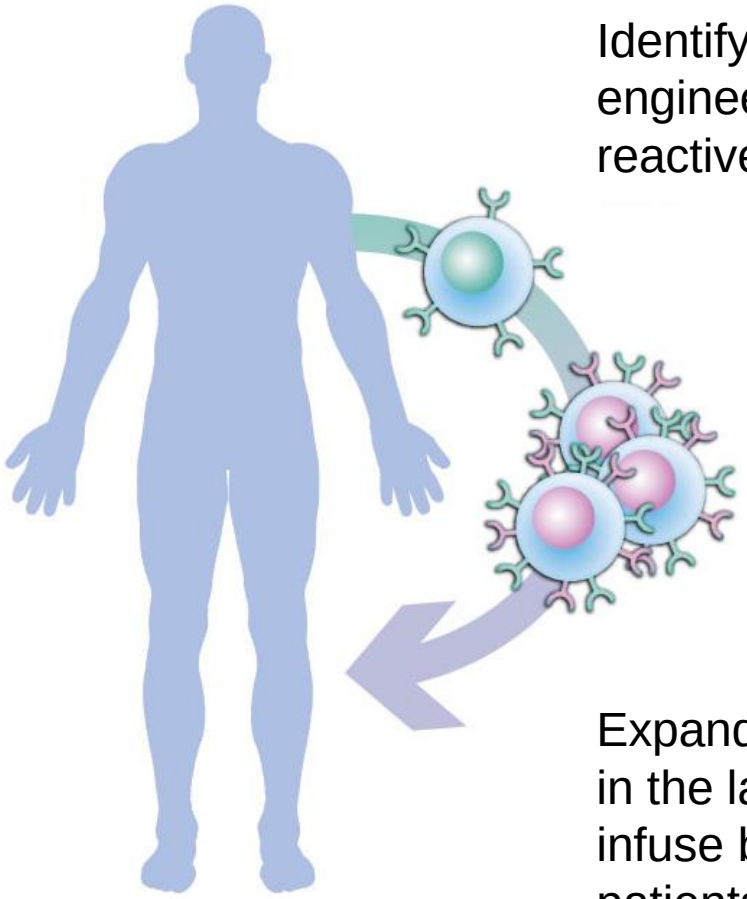
Tumor cell death

- Relapsed Hodgkin lymphoma
- BC Cancer clinical trials: indolent NHLs (eg FL, CLL), MCL, DLBCL, T cell lymphomas

# Immunotherapies for lymphoma: T cell therapies



# Immunotherapies for lymphoma: T cell therapy



Identify or genetically engineer tumour reactive T cells

Expand the T cells in the lab and infuse back into patients

# Immunotherapies for lymphoma: CAR T cells

- Chimeric Antigen Receptor T cells

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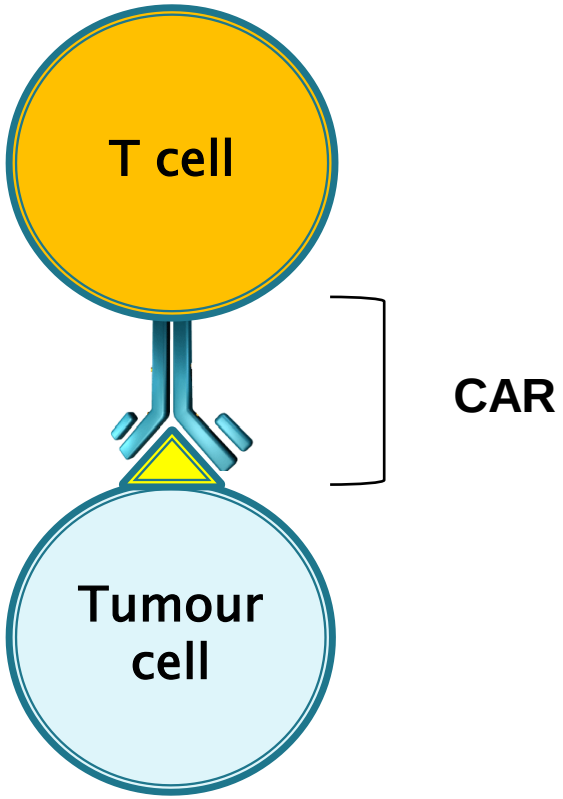
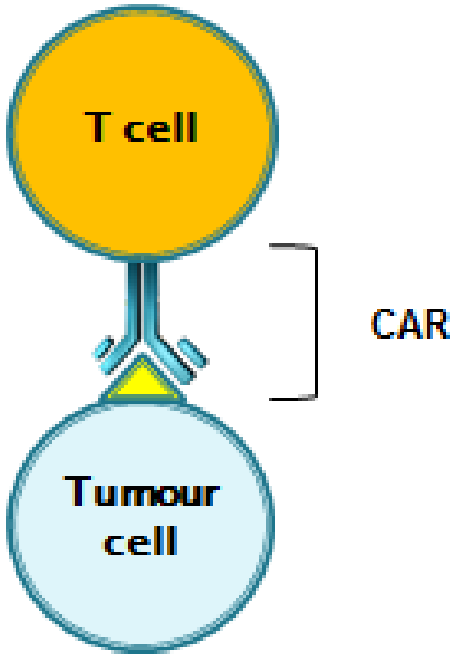


# Immunotherapies for lymphoma: CAR T cells

- FDA-approved in 2017 for relapsed, aggressive B cell lymphoma
  - ~50% of patients with complete response
  - Waiting for long term follow up

- Clinical trials in progress:
  - Hodgkin lymphoma
  - Chronic lymphocytic leukemia
  - Follicular lymphoma



# Immunotherapies for lymphoma: CAR T cells

- Challenges
  - Unclear why some patients do not respond
  - Unique and serious toxicities
  - Available at a limited number of specialized facilities in the US
  - Cost

# Immunotherapies for lymphoma: CAR T cells

- Building Canadian CAR T cell infrastructure
  - Multicenter initiative to produce Canadian CAR T cell products
  - Provide access for Canadian patients to CD19 directed CAR T cells ASAP
  - Create a cost-effective clinical and research platform for future CAR T cell development

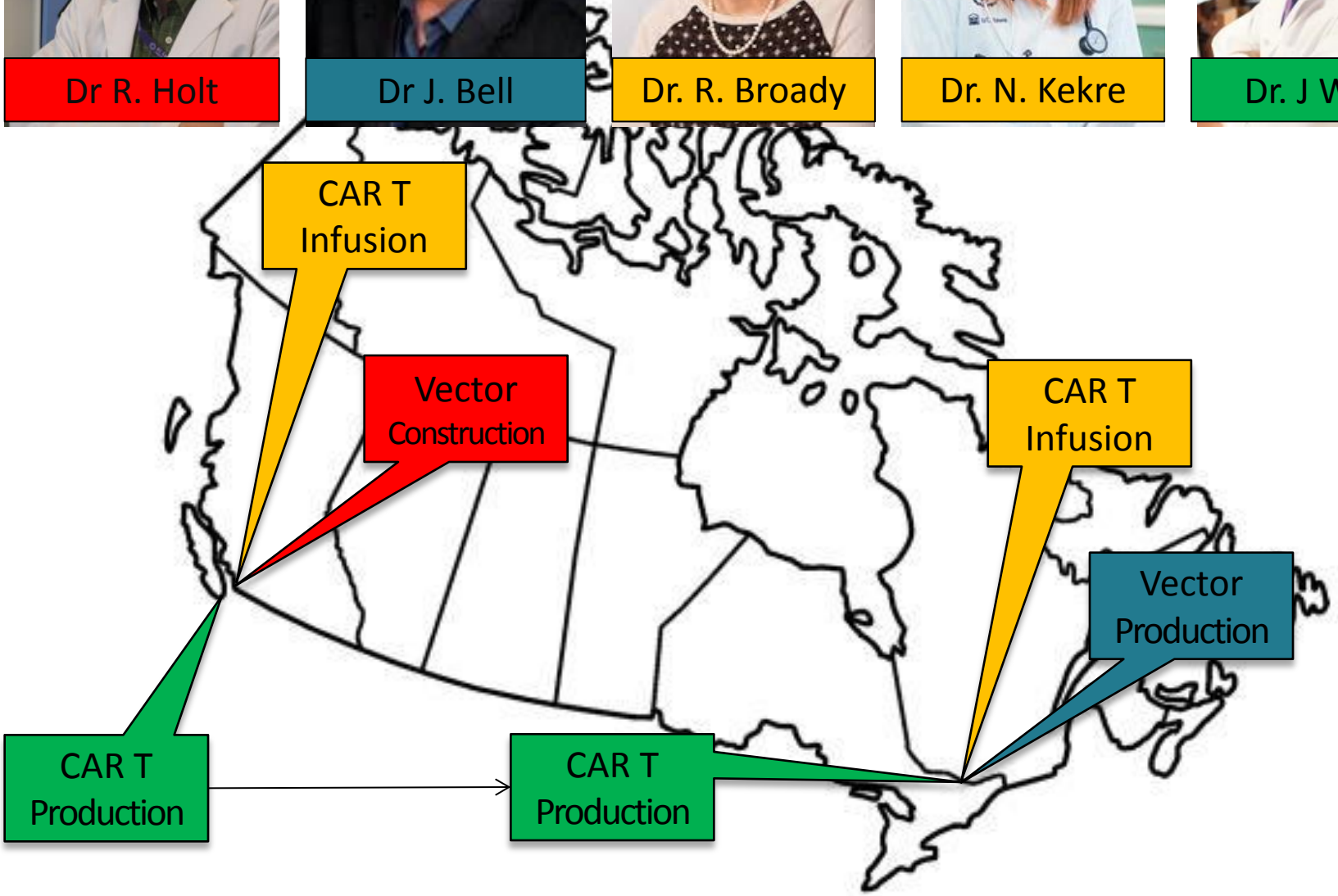
Dr R. Holt

Dr J. Bell

Dr. R. Broady

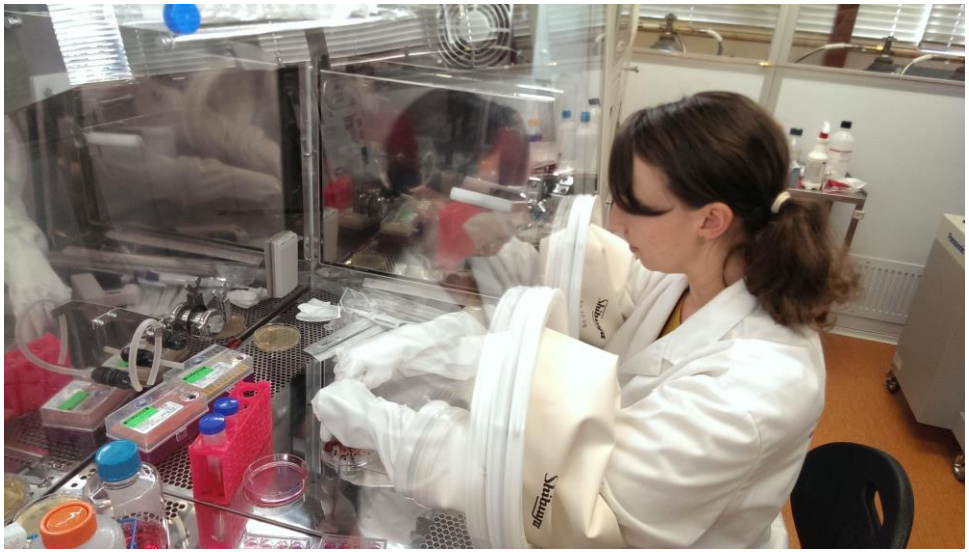
Dr. N. Kekre

Dr. J Webb



# Miltenyi CliniMACs Prodigy system for CAR-T cell production

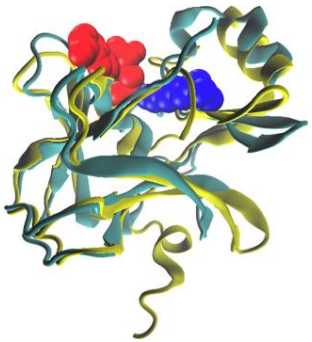
- Fully closed, automated system.
- 10-day T cell engineering and expansion protocol
- Deployable at point-of-use



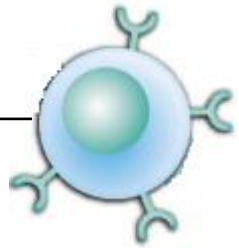
# Immunotherapies for lymphoma: Non-engineered T cell therapy

- Development of a non-engineered T cell trial in Victoria

Driver mutation in DNA

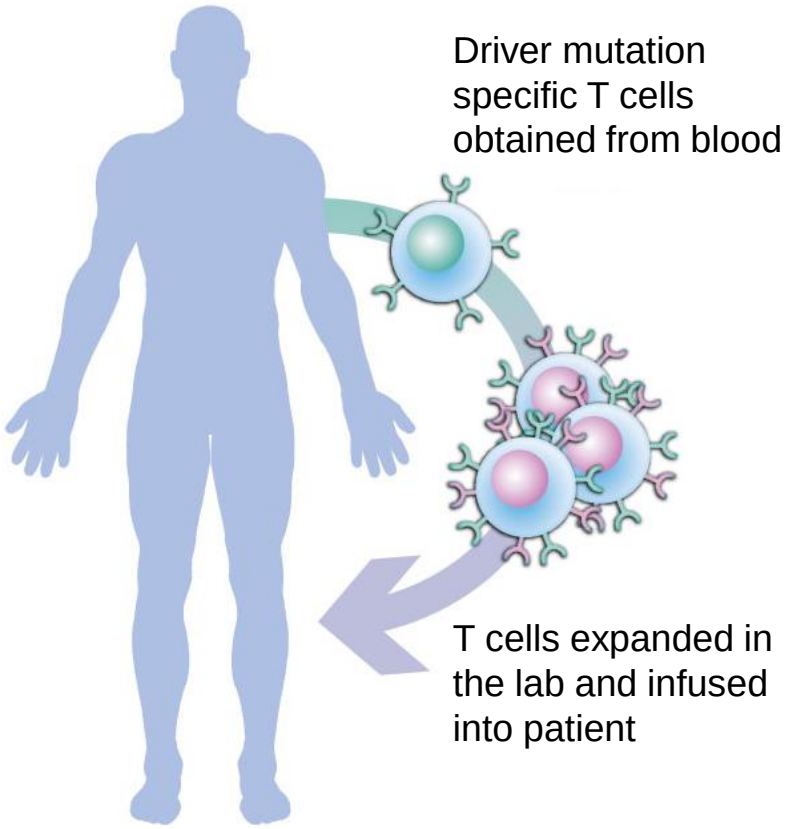


Protein that drives cancer cell growth



T cells recognize proteins

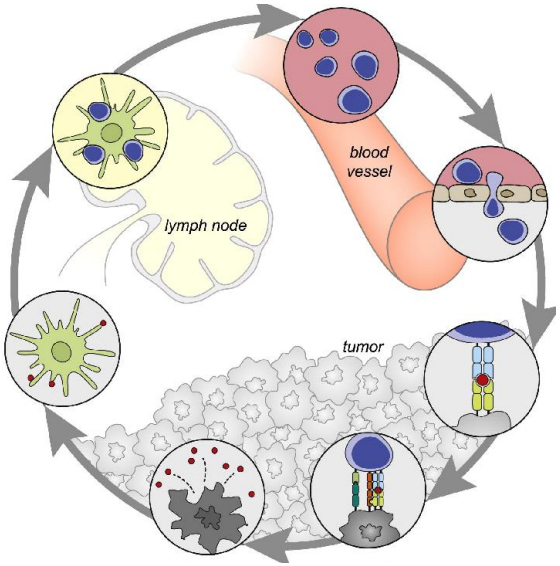
# Development of a non-engineered T cell trial in Victoria




- Phase I clinical trial for relapsed follicular and mantle cell lymphoma planned for 2019-2020
- Potential benefits over engineered T cell therapy
  - Safety
  - Personalization
  - Targeting multiple driver mutations simultaneously

# Future of lymphoma immunotherapy

- Identification of new checkpoints
- Better, safer CAR T cells
- Moving immunotherapies to earlier stages of treatment
- Combination therapies



# Summary

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# Acknowledgements


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Canadian Cancer Society

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