WHAT IS IMMUNOTHERAPY?

COLORECTAL CANCER CANADA

Overview

Immunotherapy is a treatment that helps your body's own immune system find and destroy cancer cells.

- It works by helping the immune system recognize cancer as a threat.
- Unlike chemotherapy, it doesn't kill cancer cells directly. It helps your body fight them.
- Some people with certain types of colorectal cancer (CRC) may benefit from this treatment.
- Immune checkpoint inhibitors are type of immunotherapy that "release the brakes" on T-cells so they can attack cancer cells

💡 *Think of it like training your immune system to become a cancer-fighting team.*

How Does Immunotherapy Work?

Cancer cells sometimes send out **"off" signals that hide them** from the immune system. These signals tell your immune cells to leave the cancer alone.

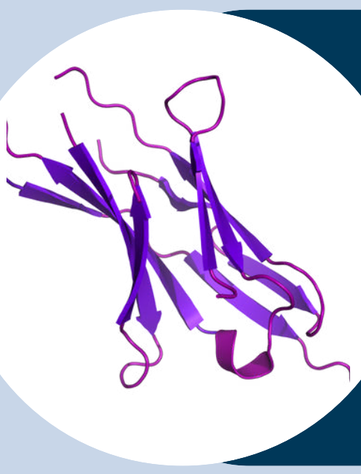
Immunotherapy uses drugs called **checkpoint inhibitors** to block those signals. Blocking these turns the immune system "back on" to fight the cancer.

Once the signals are blocked, immune cells like T-cells can **recognize cancer cells, attack them**, and slow down or stop cancer growth.

Checkpoint Inhibitors

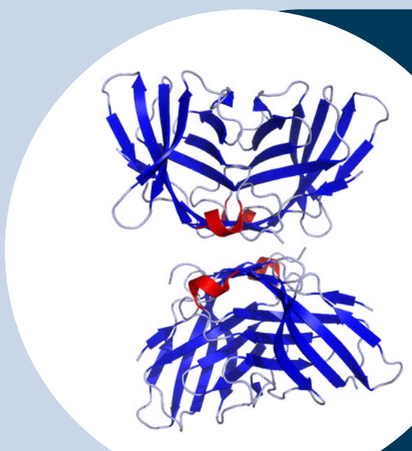
Checkpoint inhibitors are a type of immunotherapy drug that help the immune system fight cancer. There are **different types** of these drugs, and each one targets a **specific protein** that cancer cells use to avoid being attacked. These proteins act like "brakes" on the immune system. When they're blocked, immune cells, especially **T-cells**, can stay active and attack the cancer more effectively.

Checkpoint inhibitors target proteins like:



PD-1 and PD-L1

- PD-1 inhibitors block a protein on T-cells that tells them to slow down.
- Blocking PD-1 helps T-cells stay active and attack cancer.



CTLA-4

- CTLA-4 inhibitors block a "brake" on T-cells called CTLA-4 that slows immune responses
- Blocking it starts a stronger attack against cancer.

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What is Biomarker Testing?

Before starting immunotherapy, your doctor may test your tumor for biomarkers. These are signals in your cells (known as tumour markers) that help predict how well immunotherapy might work for you.

For colorectal cancer, two key biomarkers are:

- MSI-H (Microsatellite Instability-High)
- dMMR (Deficient Mismatch Repair)

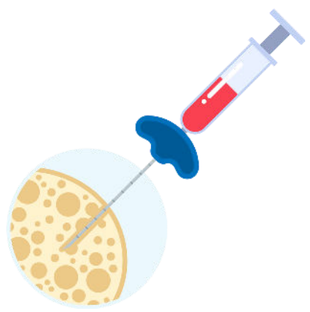
💡 MSI-H is a type of mismatch repair deficiency. dMMR and MSH-H usually describe the same thing. Tumours that are mismatch repair (MMR) proficient are usually microsatellite stable (MSS).

If your cancer is MSI-H or dMMR, it may respond better to immunotherapy

How Does Biomarker Testing Work?

1

A small piece of the tumor is carefully removed either through **surgery or a biopsy**, where a doctor uses a thin needle to take a sample.



2

In the lab, specialists examine the tumor under a microscope and run tests on its DNA and proteins to look for **biomarkers like MSI-H or dMMR**.

3

Results show whether your tumor has genetic changes, proteins, or other biological signs, called **biomarkers** that could make immunotherapy more effective.

WHY GENES MATTER

Your genes help control how your cells grow and repair themselves. When certain genes change (mutate), they can affect how well treatments work.

Common gene mutations in colorectal cancer include:

- KRAS – Often linked to lower response to some treatments
- BRAF – May cause cancer to grow faster
- NRAS and APC – Can affect treatment planning

Doctors may test your tumor for these mutations to help choose the best treatment for you. **Even if you don't qualify for immunotherapy now, biomarker testing can help guide other options.**

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Immunotherapy Drugs for Colorectal Cancer

	Pembrolizumab (Keytruda)	Nivolumab and Ipilimumab
Type	PD-1 inhibitor	PD-1 inhibitor
How it works	Blocks PD-1 to keep T-cells active against cancer	Blocks PD-1 to keep T-cells active against cancer
Who it's for	MSI-H or dMMR CRC	MSI-H or dMMR CRC
When it's used	For advanced/metastatic or inoperable CRC	When other treatments haven’t worked (i.e. surgery)
How it's given	IV infusion every 3–6 weeks	IV infusion every 2–4 weeks
Infusion time	About 30 minutes	30-60 minutes
Used alone or with	Usually given alone	Alone or with ipilimumab (Yervoy – a CTLA-4 blocker)
Common side effects	Fatigue, rash, diarrhea, thyroid changes	Tiredness, joint pain, skin rash
Serious risks	Inflammation of lungs, liver, intestines (rare)	Inflammation of lungs, liver, intestines (rare)

Both drugs are approved by Health Canada for MSI-H/dMMR CRC and help boost your immune system’s ability to fight cancer.

- Pembrolizumab is covered by public drug plans, while Nivolumab and Iilimumab are approved for advanced CRC but are not currently available through public drug plans.
- Access usually requires biomarker testing to confirm MSI-H or dMMR status.
- In some cases, they may be covered through public health plans, private insurance, clinical trials or special access programs.

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References

1. Adebayo AS, Agbaje K, Adesina SK, Olajubutu O. Colorectal Cancer: Disease Process, Current Treatment Options, and Future Perspectives. Pharmaceutics. 2023 Nov 12;15(11):2620. doi: 10.3390/pharmaceutics15112620. PMID: 38004598; PMCID: PMC10674471.
2. Canadian Cancer Society / Société canadienne du cancer. Immunotherapy [Internet]. [cited 2025 Jun 12]. Available from: https://cancer.ca/en/treatments/treatment-types/immunotherapy
3. Cornista AM, Giolito MV, Baker K, Hazime H, Dufait I, Datta J, Khumukcham SS, De Ridder M, Roper J, Abreu MT, Breckpot K, Van der Jeught K. Colorectal Cancer Immunotherapy: State of the Art and Future Directions. Gastro Hep Adv. 2023;2(8):1103-1119. doi: 10.1016/j.gastha.2023.09.007. Epub 2023 Sep 19. PMID: 38098742; PMCID: PMC10721132.
4. Johdi NA, Sukor NF. Colorectal Cancer Immunotherapy: Options and Strategies. Front Immunol. 2020 Sep 18;11:1624. doi: 10.3389/fimmu.2020.01624. PMID: 33042104; PMCID: PMC7530194.
5. The Canadian Agency for Drugs and Technologies n Health (CADTH) Reimbursement Recommendation: Pembrolizumab (Keytruda). Indication: For the treatment of adult patients with high-risk early-stage triple-negative breast cancer in combination with chemotherapy as neoadjuvant treatment and then continued as monotherapy as adjuvant treatment after surgery [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2022 Sep [cited 2025 Jun 12]. PMID: 38696625. Available from: https://www.cda-amc.ca/sites/default/files/DRR/2022/PC0279%20Keytruda%20TNBC%20-%20Final%20CADTH%20Recommendation%20Final.pdf
6. Zhao P, Li L, Jiang X, Li Q. Mismatch repair deficiency/microsatellite instability-high as a predictor for anti-PD-1/PD-L1 immunotherapy efficacy. J Hematol Oncol. 2019 May 31;12(1):54. doi: 10.1186/s13045-019-0738-1. PMID: 31151482; PMCID: PMC6544911.