STUDY OF MODERN TREATMENTS IN CURING CHILDHOOD CANCER

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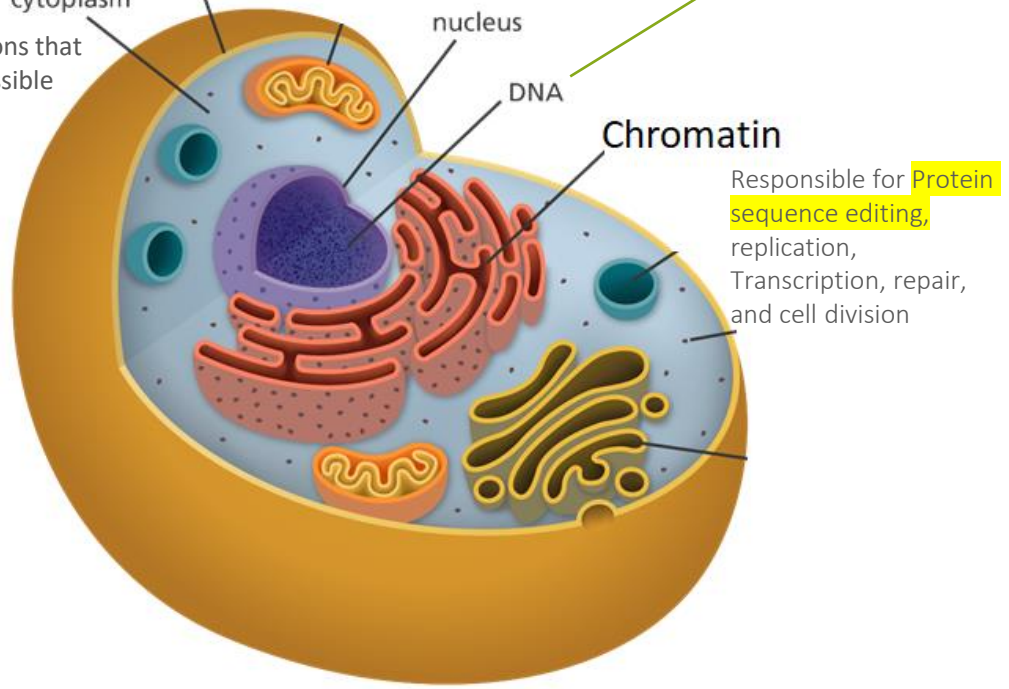
You are made of Trillions of cells that contain protein

Human body contains **trillions of cells**, the basic units of life. And every cell contains proteins.



Carries the Proteins and Instruction set (code) for cell creation

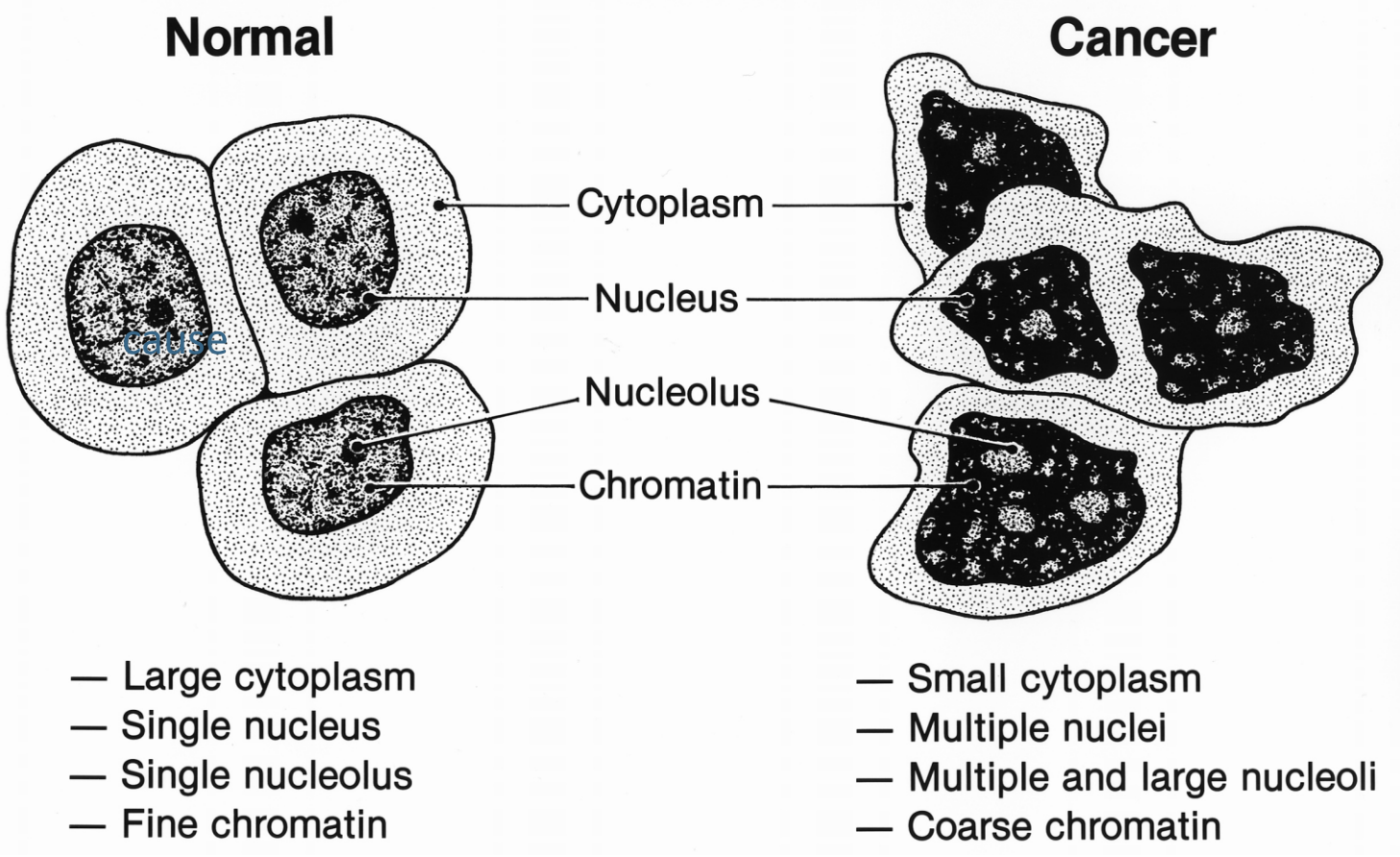
DNA contains four basic protein building blocks

- ✓ - Adenine (A)
- ✓ - Cytosine(C)
- ✓ - Guanine (G)
- ✓ - Thymine (T)

The sequence, of these protein bases form the instructions set to a cell to function.

Cancer cells under a microscope

When the body doesn't make the right amount or type of protein, it can cause conditions like **cancer or metabolic diseases** where the cells grow uncontrollably

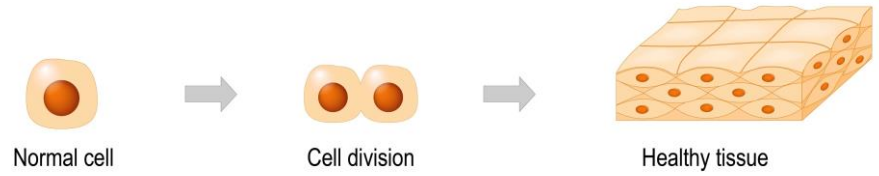


Defective Cancer cells multiplies uncontrolled

Cancer – Introduction

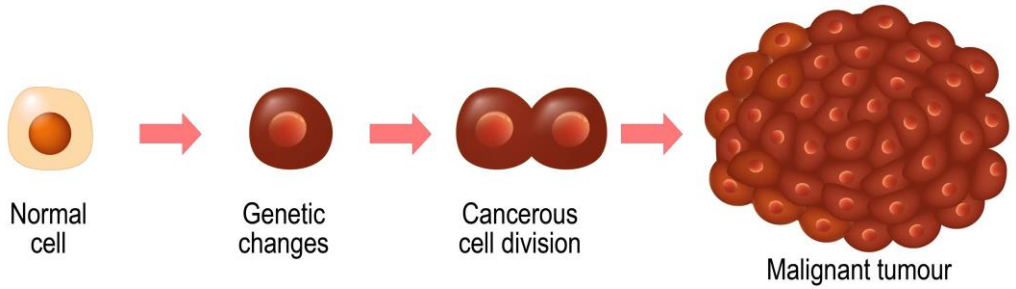
Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body.

Normal Cell Division and Growth



Cell Division is a process used by the body for growth and repair. **A parent cell divides to form two daughter cells** and stop. These daughter cells are used to build new tissue or to replace cells that have died because of aging or damage

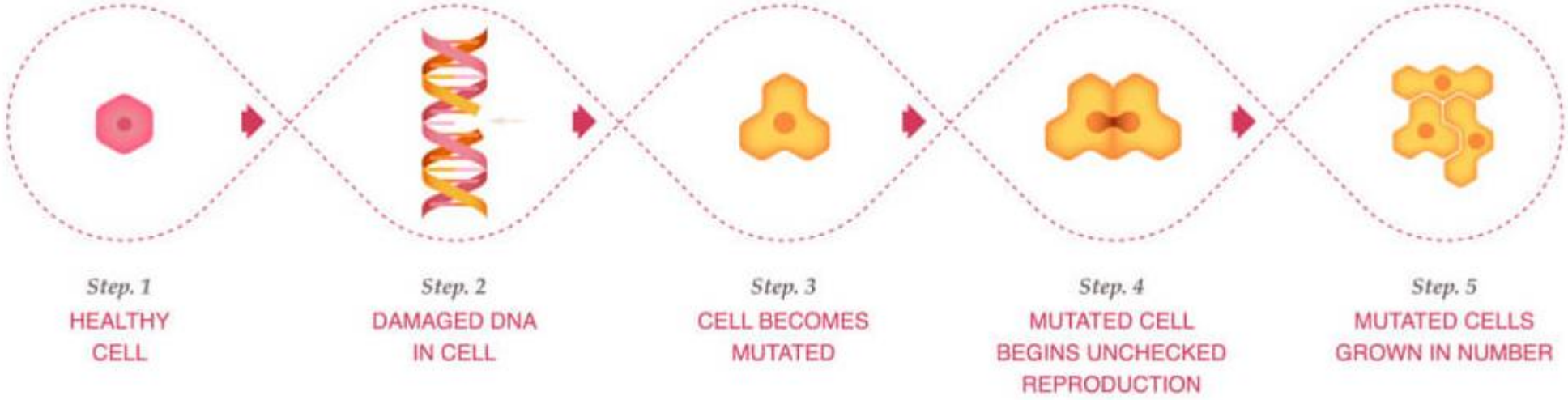
Cancer Cell Division and Growth (Tumors)



Healthy cells stop dividing when there is no longer a need for more daughter cells, **but Cancer cells continue to produce copies**. Cancer cells are unhealthy cells with altered DNA, that divide continually, forming solid tumors or flooding the blood or lymph with abnormal cells.

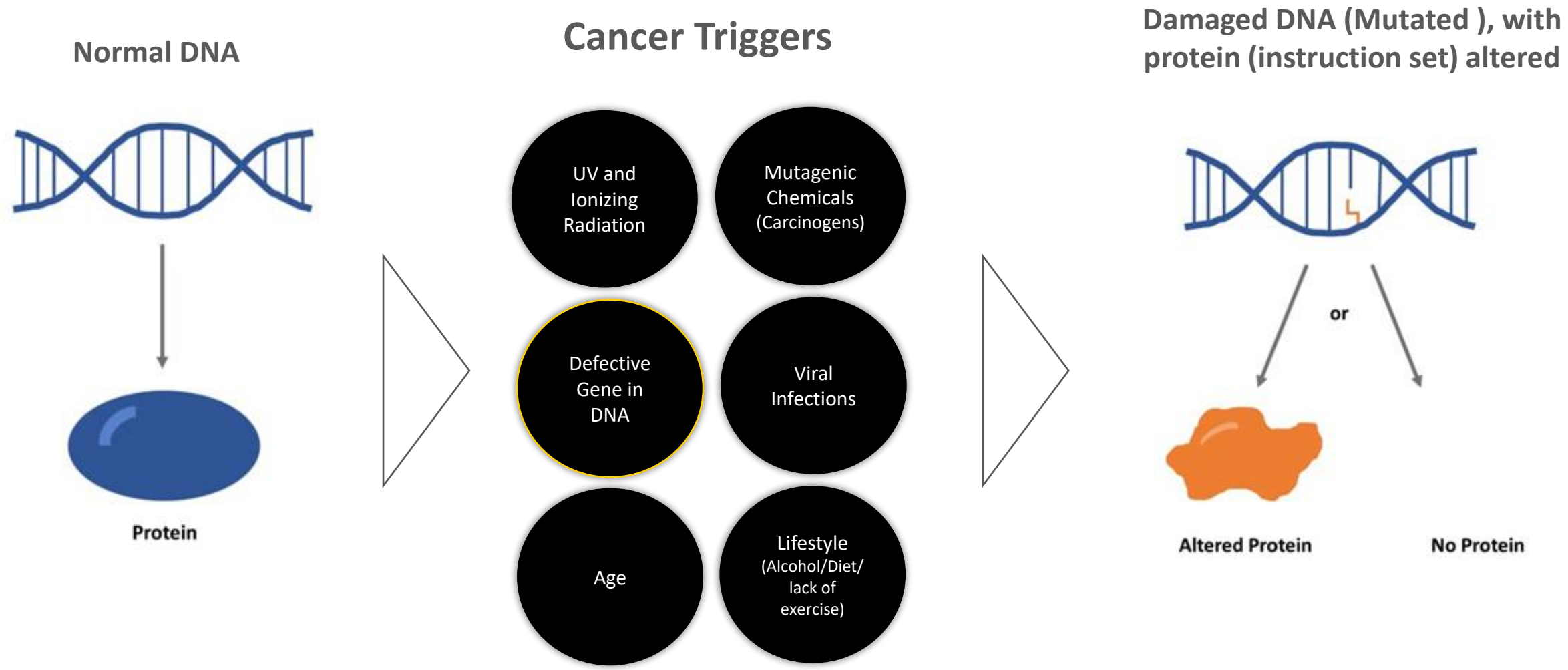
Cancer – How it starts

Cancer starts when the DNA becomes faulty, mutating the cell and making it cancerous



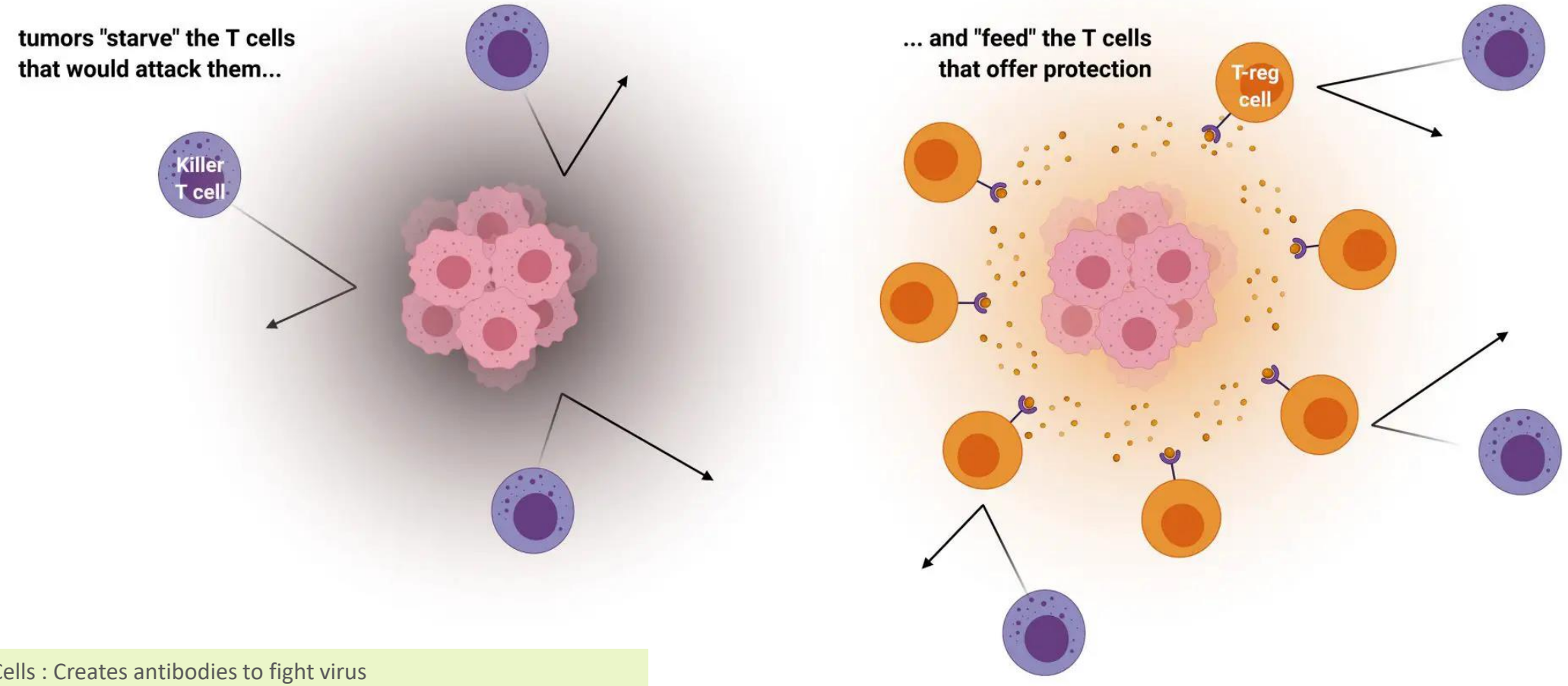
Cancer – How does DNA become faulty

Cancer starts when the DNA becomes faulty and mutated. Gene mutations in cancer cells interfere with the normal instructions in a cell and can cause it to grow out of control or not die when it should.



Why does our Immune system not kill cancer cells and cure cancer just like a Flu ?

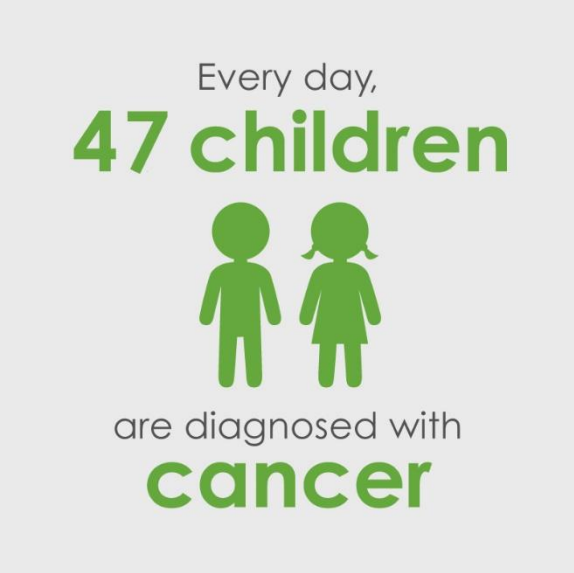
Our immune system DOES kill cancer cells in its initial stages. But, when the pace of cancer cell growth amplifies (Tumor) the cancer evades the immune system by “feeding” the T cells that protect the tumor and “starving” the T cells that would attack the tumor.



B – Cells : Creates antibodies to fight virus
T – Cells : Killer Cells to destroy mutations like cancer

CHILDHOOD CANCER

Cancer is the second-leading cause of death in youth ages 1 to 16. [Accidents (including road) are first].



Childhood cancer Facts

- Are not strongly linked to lifestyle or environmental risk
- Mostly due to genetic DNA mutations
- In USA : One in 285 children will be diagnosed with cancer before their 20th birthday. .

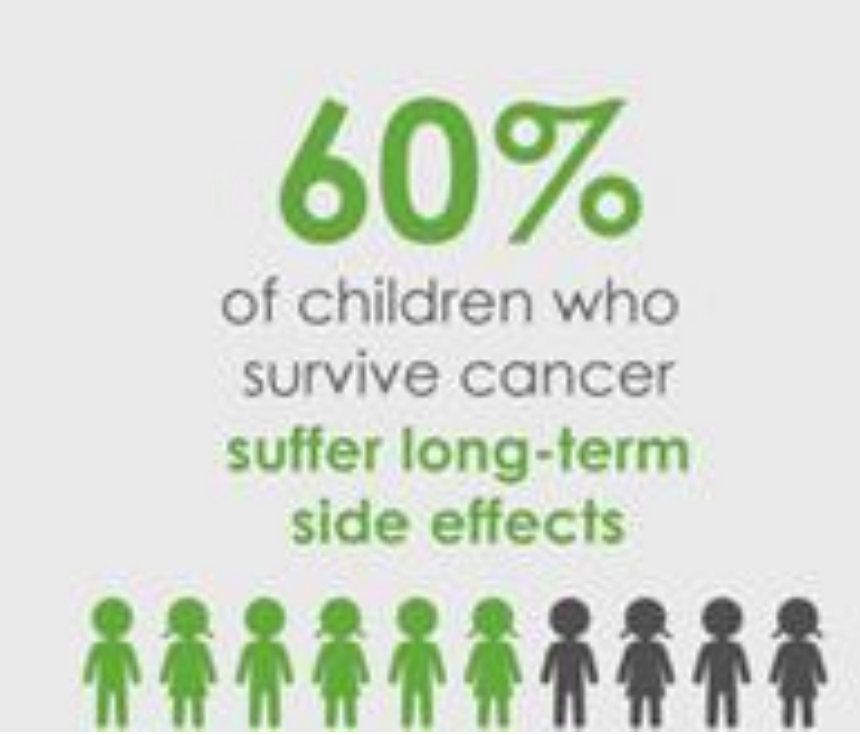
Mainstream treatments for childhood cancer

These **three** treatments enable up to **85% of children with cancer able to survive for 5 years or more**.

Overall, this is a huge increase since the mid-1970s, when the 5-year survival rate was about 58%.

Mainstream treatments side effects

Most childhood cancers are treated with **surgery, chemotherapy, radiation, or a combination of those therapies**. However, these treatments have various short term and long-term impacts.



Short term effects :

- Pain and fatigue
- Anemia
- Mouth problems
- Nausea/weight change/dietary issues, and hair, skin and nail problems

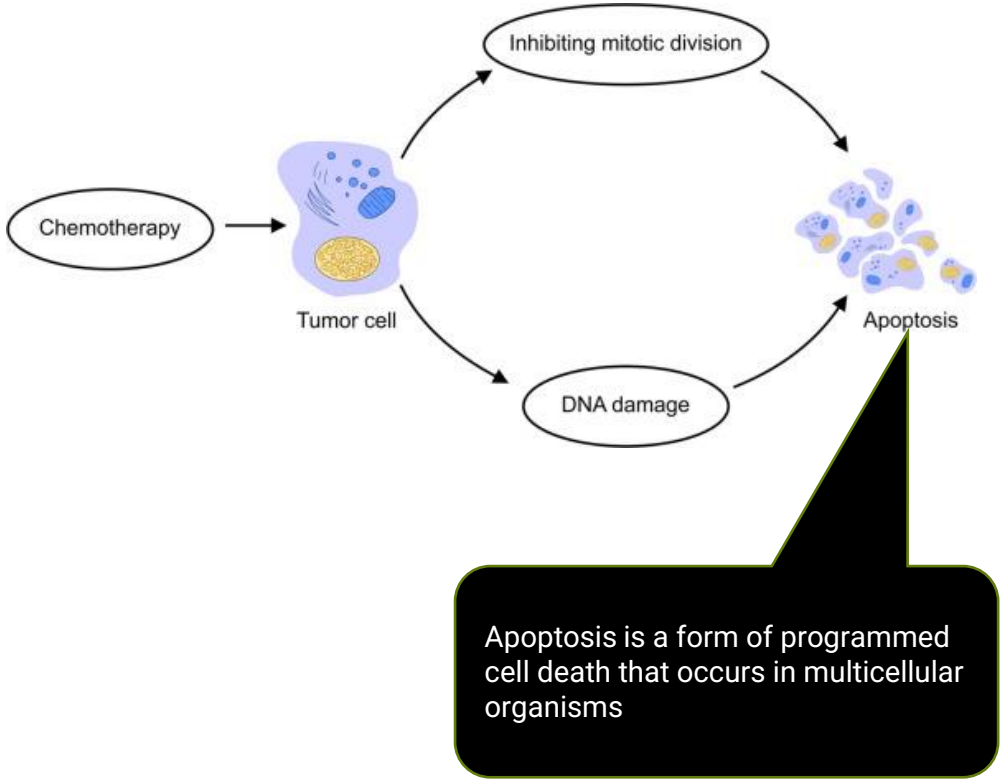
Long Term effects :

- Hearing loss from chemotherapy
- Increased risk of stroke from high doses of radiation to the brain.
- Impaired Nervous system damage due to the nerves outside the brain
- Spinal cord impair (called peripheral neuropathy).

Mainstream Treatment #1 : Chemotherapy

Chemotherapy is drug delivery treatment using cytotoxic medications to target the cancer cells across **the whole body** and **induce Apoptosis**

Sudden removal of the survival signals or disassociation from neighboring cells will cause a cell to initiate apoptosis.

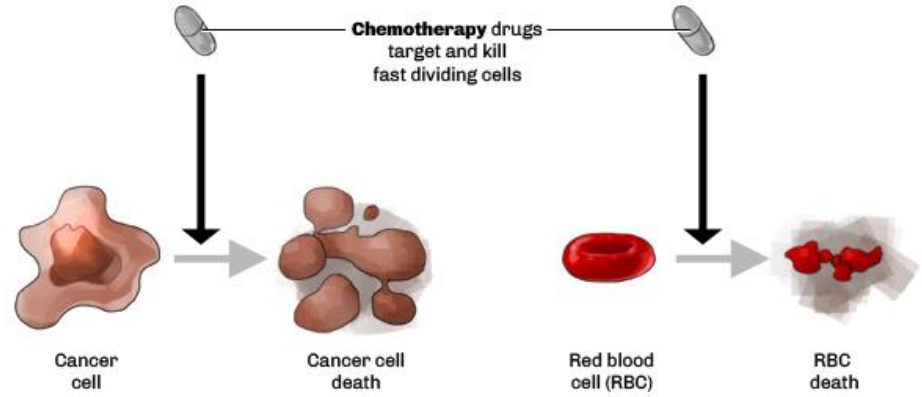


Chemo Side Effects

- Fatigue
- Hair Loss
- Decreased blood counts
- Nausea
- The possible development of secondary cancers

Common Issues :

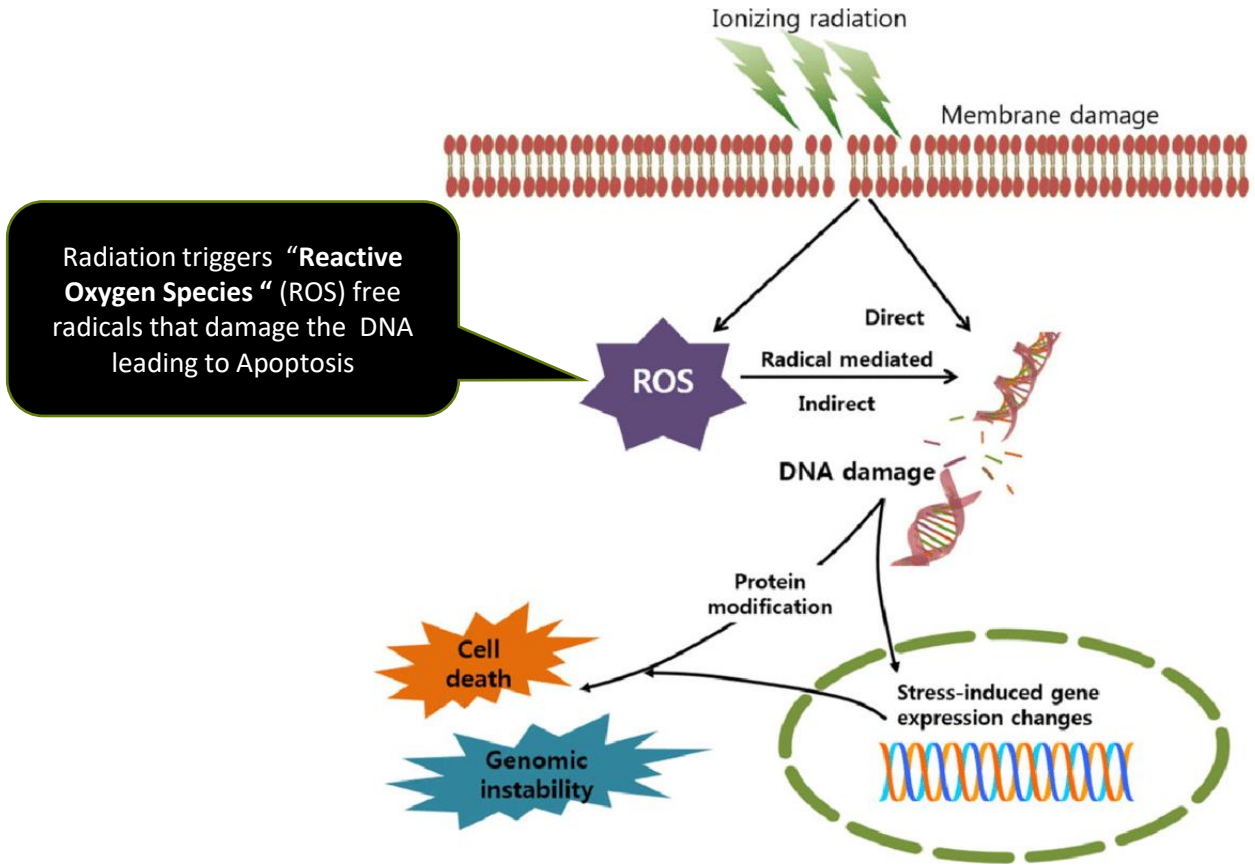
Chemo also targets RBC cells and kills it lowering immunity and causing life threatening scenarios esp. in children



Mainstream Treatment #2 : Radiotherapy

Radiation therapy uses ionizing energy, usually an invisible light beam, which targets a tumor or region specifically and destroys cancer cells in a localized manner.

Radiation works by making small breaks in the DNA inside cells. These breaks keep cancer cells from growing and dividing and cause them to die.



Side Effects

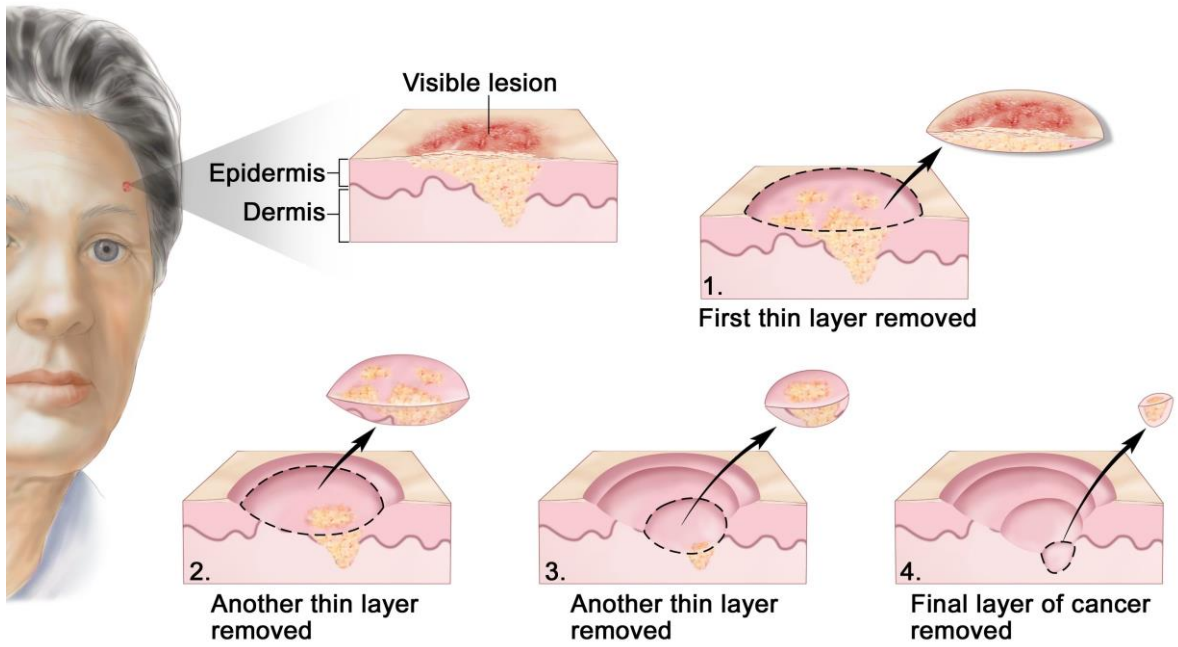
- Dry, inflamed skin
- Fatigue and stiffness Decreased blood counts
- Swelling (lymphedema)
- The possible development of secondary cancers

Common Issues :

Radiation can only be used in early stages of cancer and only if cancer is localized. Radiation treatment takes time to see results creating critical issues in young children.

Mainstream Treatment #3 : Surgery

Oldest Cancer treatment , surgery is an operation or procedure to take out a tumor and possibly some nearby tissue.



Precision surgery for removal of skin cancer

Side Effects

- Pain. .
- Infection.
- Loss of organ function.
- Fatigue.
- Bleeding.
- Blood clots.
- Altered bowel and bladder function.

Common Issues :

Will not apply to most internal cancers (Lukumania, Brain Cancer, Stomach etc) and highest chance of recurrence along with risk of loss of organ function

Research Question

Understand the new and alternative treatments to Surgery, Chemo and Radiation.

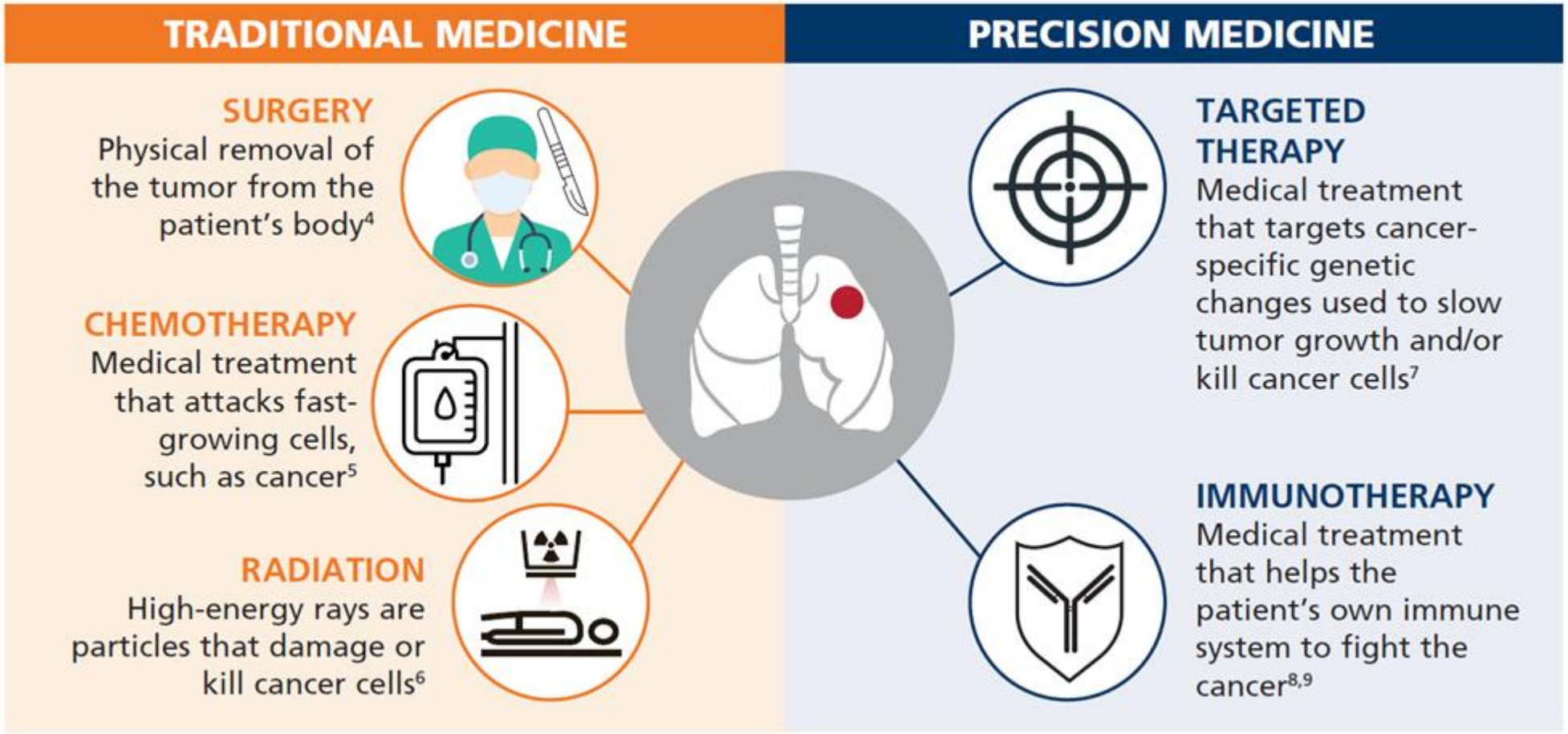
Thru independent research, discussion with medical researcher leaders and clinical study data, understand the efficacy (mortality), short term side effects and adult quality of life (long term side effects) for modern treatments.

Interview with Olena Nyzhnykevych

Vice President of Development, Pediatric Cancer at Seattle Children's

Modern Childhood Cancer Treatments

Advances in Radiotherapy and Immunotherapy are the future as they score higher in long term quality of life for survivours.

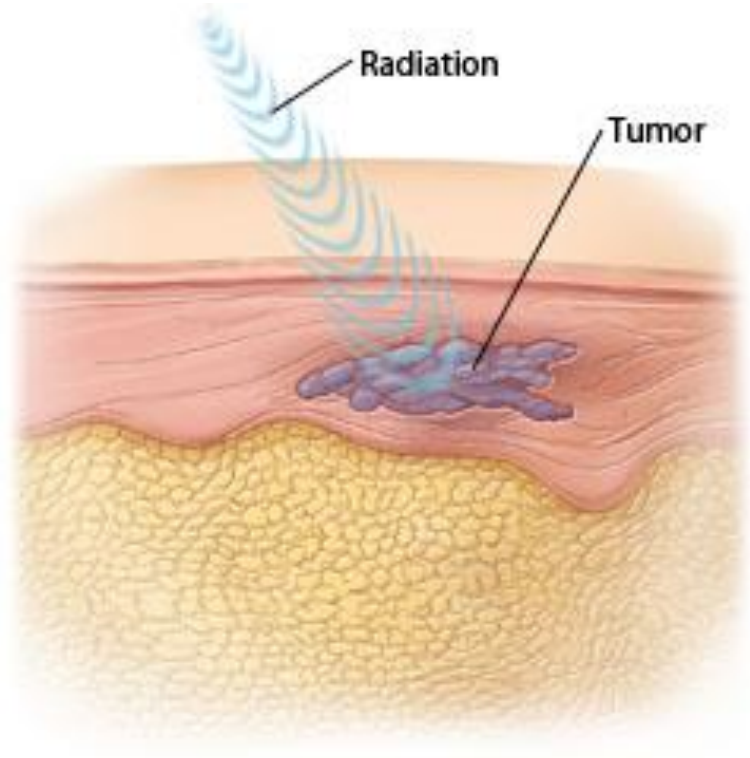


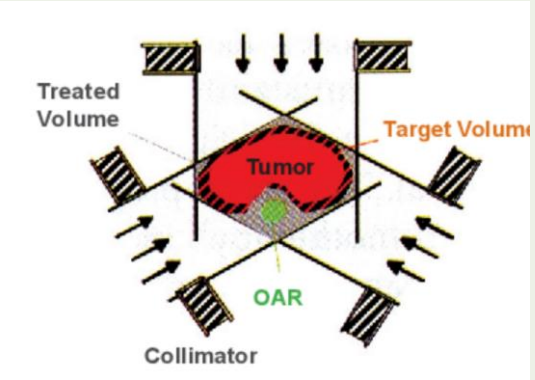
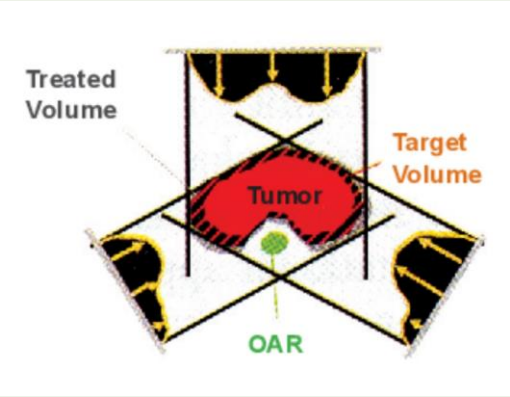
MODERN TREATMENT #1:TARGETED THERAPY-RADIOTHERAPY:IMRT

Intensity-modulated radiation therapy (IMRT) is **an advanced type of radiation therapy used to treat cancer and noncancerous tumors**. IMRT uses advanced technology to manipulate photon and proton beams of radiation to conform to the shape of a tumor

Effectively Treats

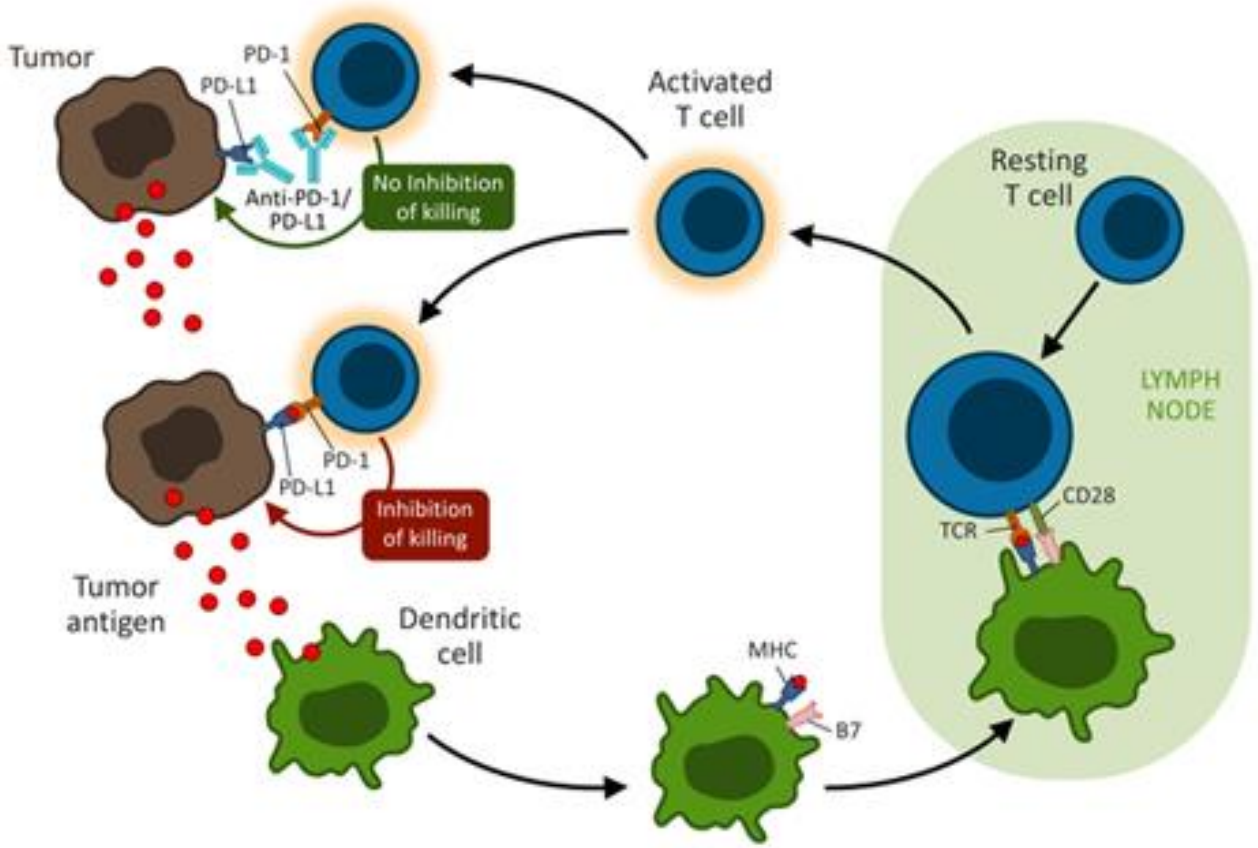
- Breast cancer.
- Cervical cancer.
- Colon cancer.
- Lung cancer.
- Prostate cancer.
- Stomach cancer.
- Uterine cancer.
- Other cancer types.

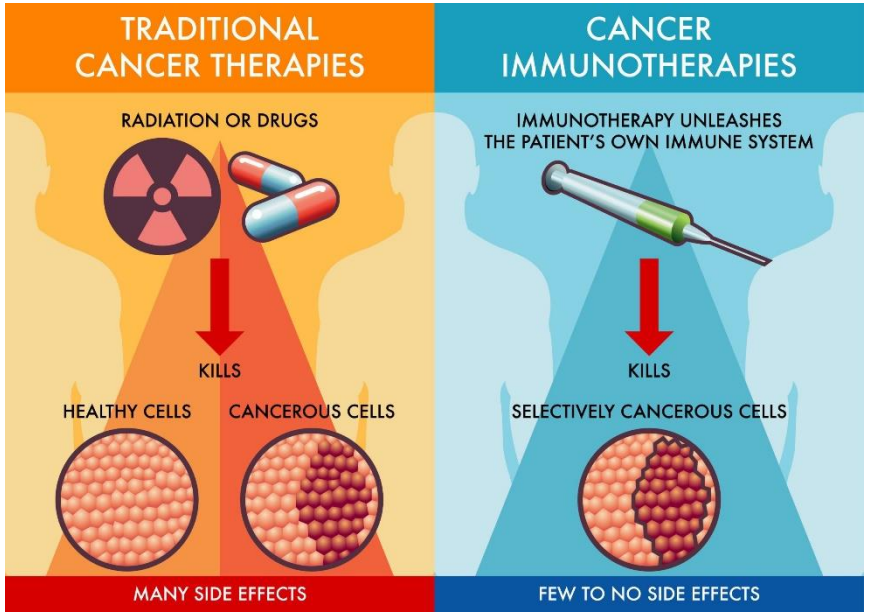


Why is IMRT a very successful treatment compared to other radiations	
All Radiation Methods Radiation is equally sent to Tumor and organ at risk	IMRT Notice the avoidance of radiation to OAR **(Organ at Risk)**
	

Modern Treatment : Immunotherapy

Immunotherapy unleashes patient's own immune system to cure cancer

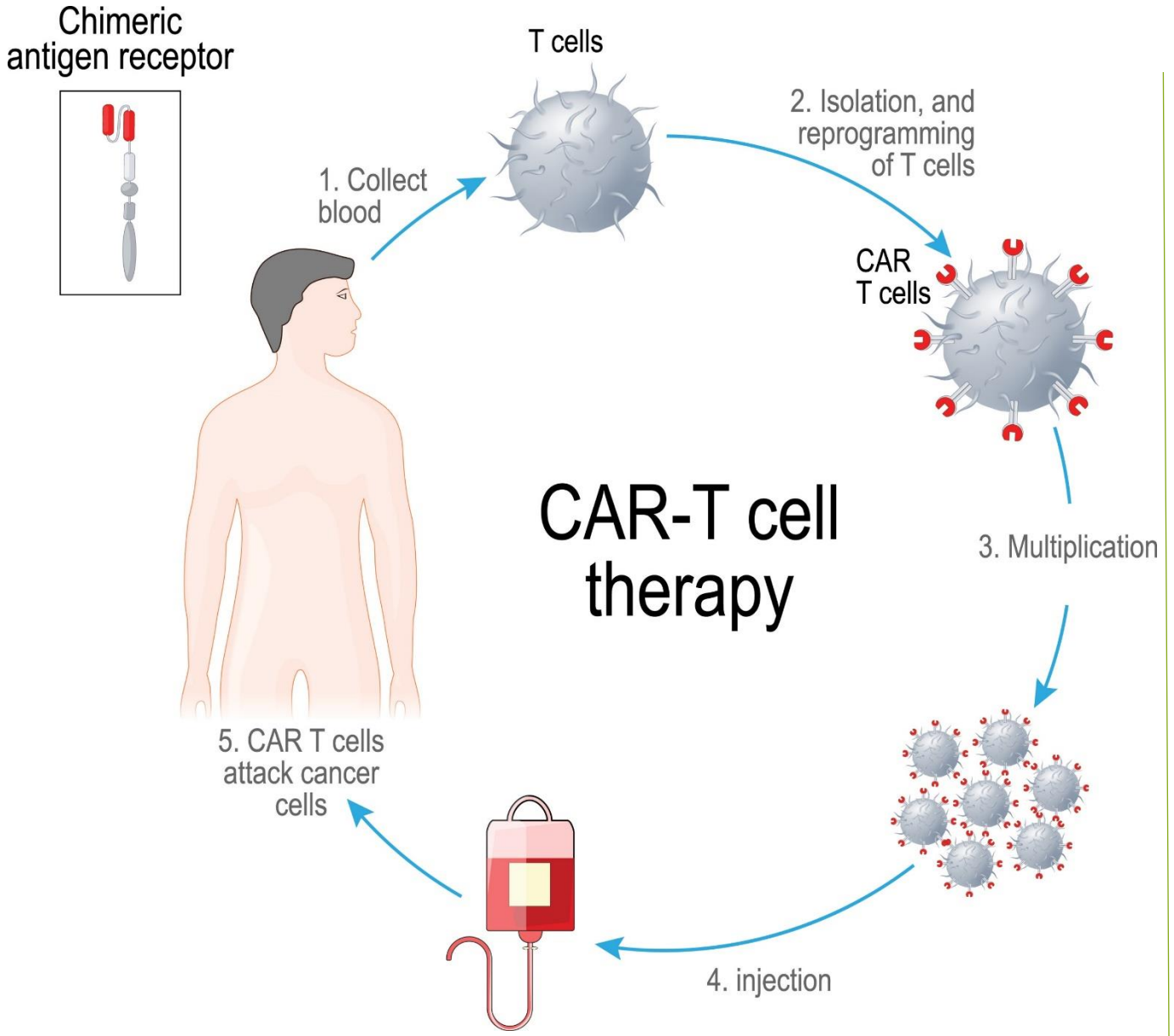




Common Issues :

Most patients use this in conjunction with other treatments. Body's T-Cells take time to respond, and for higher stage and rapidly spreading cancers it will not apply

MODERN TREATMENT #1 : IMMUNOTHERAPY : CAR T-CELLS



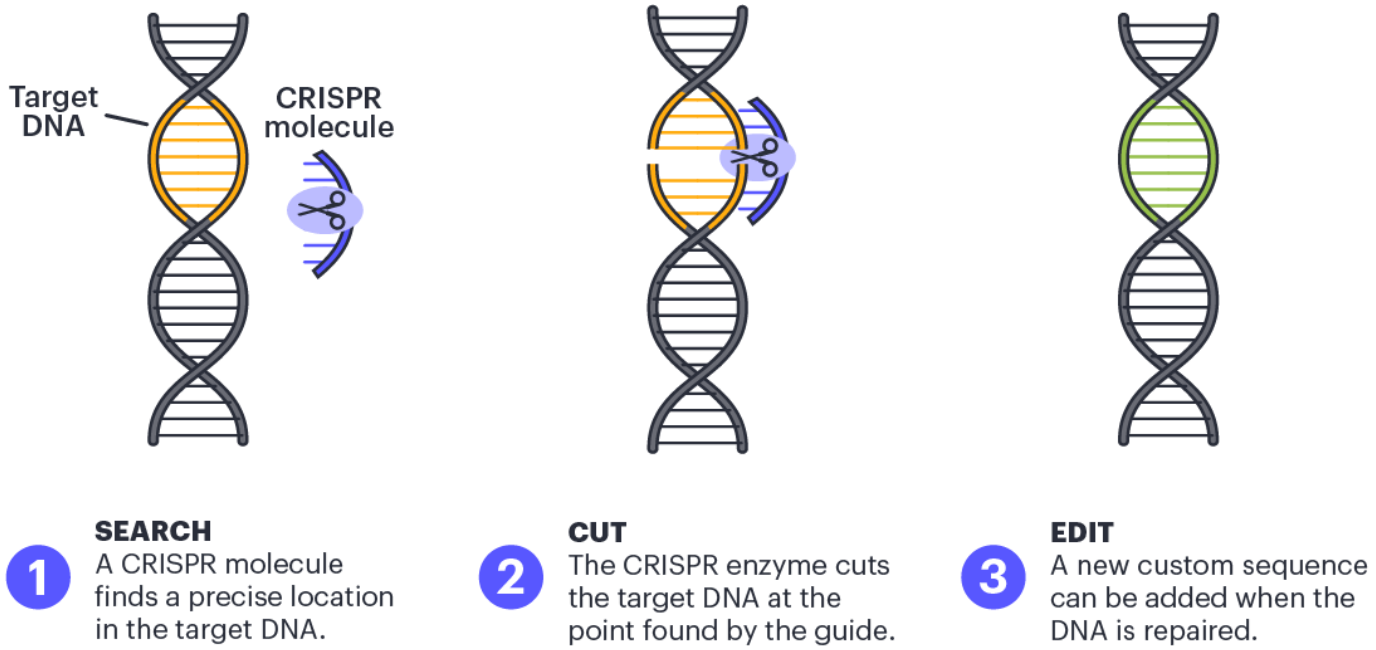
Empower patient's immune system to fight cancer organically

T-Cells : T cells help organize the immune response in the body and kill cells infected by pathogens. Doctors extract and genetically modify T cells to produce antigen receptors, which teach them to recognize and attach to a specific protein (antigen) on targeted tumor cells. Once infused back into your body, these engineered cells get to work destroying tumors.

Editing T- Cells : Ex vivo gene transfer:
T-Cells are removed from the patient and sent to a lab. In the lab, these cells are altered. Often, new DNA is added to the cells that help fight tumor. Once the newly altered cells are prepared, they're delivered back to patient, usually by an intravenous (IV) infusion

Curing Cancer : Edited T cells contain a receptor to specifically recognize a tumour-associated antigen and thereby selectively kill tumour cells, just like healing a common cold or flu.

MODERN TREATMENT #2 : IMMUNOTHERAPY : GENE EDITING USING CRISPER



Gene Editing using CRISPER

DNA REPAIR : *Not only cancer, but CRISPR-Cas9 DNA REPAIR therapy is used for curing a wide range of diseases, including Genetic blindness, Alzheimer's , Huntington's disorders, and HIV.*

CRISPR technology : **Finds a specific bit of DNA inside a cell and** alters that piece of DNA.

GENE EDITING : A small clinical trial has shown that researchers can use CRISPR gene editing to **alter immune cells so that they will recognize mutated proteins specific to a person's tumors**. Those cells can then be safely set loose in the body to find and destroy their target

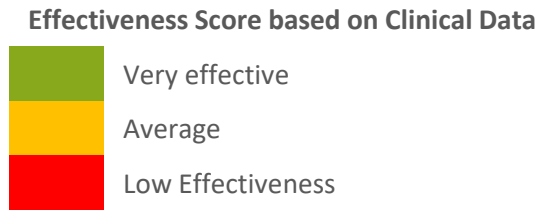
Once CRISPR cuts the target DNA, it gets repaired or replaced with a different sequence. Scientists use this method to knock out human genes in cancer cells and identify which of those genes are essential for the growth of tumor cells without harming normal cells.

SUMMARY

RESEAFCH RESULTS

Answering our research question, CART-T Cell immunotherapy and IMRT Radiation therapy are better options for childhood cancer. However cancer is complex and in most cases the patients need a combination of therapies based on the stage of detection

	Chemotherapy	Radiotherapy	Surgery	Stem Cell Immunotherapy	CAR T Cell Immunotherapy	IMRT Radiation Therapy	Gene editing
Child Mortality							
Short term side effects							NA
Adult quality of life (long term side effects)							NA
Average Recovery timeline							NA



FOOTNOTES

Topic	Footnote
Cell Anatomy	**National Library of Medicine** **The Molecular Composition of Cells** https://www.ncbi.nlm.nih.gov/books/NBK9879/
How cancer arises	Scientific American **How Cancer Arises** Robert A. Weinberg https://www.jstor.org/stable/24993349
Killing cancer cells and cell death	**Escaping Cell Death: Survival Proteins in Cancer** **Science Direct** **https://www.sciencedirect.com/science/article/abs/pii/S0014482799944555**
Impact of Immune system on Cancer	Cancer research, UK **The immune system and cancer** https://www.cancerresearchuk.org/about-cancer/what-is-cancer/body-systems-and-cancer/the-immune-system-and-cancer
Childhood Cancer Statistics	American Cancer Society **Key Statistics for Childhood Cancers** https://www.cancer.org/cancer/cancer-in-children/key-statistics.html National Cancer Institute **Cancer in Children and Adolescents** https://www.cancer.gov/types/childhood-cancers/child-adolescent-cancers-fact-sheet

FOOTNOTES.. CONT

Topic	Footnote
Childhood Cancer Study	**Childhood cancer** Authors : Robert W. Miller M.D., Dr. John L Young Jr. P.H., Biljana Novakovic M.D. https://acsjournals.onlinelibrary.wiley.com/doi/abs/10.1002/1097-0142(19950101)75:1+%3C395::AID-CNCR2820751321%3E3.0.CO;2-W
IMRT	Book : Photophysics and Nanophysics in Therapeutics https://www.sciencedirect.com/book/9780323898393/photophysics-and-nanophysics-in-therapeutics Authors : Nilesh M. Mahajan, Avneet Saini, ... Sanjay J. Dhoble
CART- Therapy	**Neurological updates: neurological complications of CAR-T therapy** https://www.researchgate.net/figure/Schematic-diagram-illustrating-the-process-of-CAR-T-cell-therapy-C-2017-Terese-Winslow_fig1_346490966
CRISPER Gene Editing using CAS9	**Precision cancer mouse models through genome editing with CRISPR-Cas9** Authors : Haiwei Mou, Zachary Kennedy, Daniel G. Anderson, Hao Yin & Wen Xue https://genomemedicine.biomedcentral.com/articles/10.1186/s13073-015-0178-7
What does the future hold ?	**The Future of Cancer Research: Five Reasons for Optimism** Memorial Sloan Kettering cancer center **https://www.mskcc.org/news/future-five-reasons-optimism**

APPENDIX

Terminology and Definitions

Terms	Definitions
Nucleolus	By **housing the cell's genome**, the nucleus **serves both as the repository of genetic information and as the cell's control center**. **DNA replication, transcription, and RNA processing** all take place within the nucleus, with only the final stage of gene expression (translation) localized to the cytoplasm.
DNA	**Deoxyribonucleic Acid**. Like a recipe book it holds the instructions for making all the proteins in our bodies DNA contains four basic building blocks - Adenine (A) - Cytosine(C) - Guanine (G) - Thymine (T) The order, or sequence, of these bases form the instructions set to a cell to function properly.
RNA	**Ribonucleic acid**, or RNA is one of the three major biological macromolecules that are essential for all known forms of life (along with DNA and proteins)
mRNA	**mRNA carries the instructions set**, to make a specific protein. mRNA carries these instructions from the DNA in a cell's nucleus to the cell's **cytoplasm** (watery interior), where the protein-making machinery reads the mRNA sequence and cells put the protein together.
Cell Division	Cell Division is a process used by the body for growth and repair. **A parent cell divides to form two daughter cells**, and these daughter cells are used to build new tissue or to replace cells that have died because of aging or damage.
Cancer Cells	Healthy cells stop dividing when there is no longer a need for more daughter cells, **but Cancer cells continue to produce copies**. Cancer cells are unhealthy cells with altered DNA, that divide continually, forming solid tumors or flooding the blood or lymph with abnormal cells.
Metastasis	**Metastasis** is a disease agent's (Germ/Pathogen) spread from an initial or primary site to a different or secondary site within the host's body. When tumor cells metastasize, the new tumor is called a secondary or metastatic tumor, and its cells are similar to those in the original tumour.