50 ways to kill your Cancer

New Anticancer Therapies and Technology: Innovations Shaping the Future of Cancer Treatment

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Disclosures

Honoraria from:
Astra Zeneca, Esai, Pfizer, Menarini Stemline, Novartis
Conference expenses from:
Novartis, Lilly

Introduction

- **Introduction to Cancer Treatment**
  - Cancer is one of the leading causes of death worldwide
  - Traditional treatments: Surgery, chemotherapy, radiation therapy
  - While these methods have been effective, they come with significant limitations, such as side effects, resistance, and incomplete targeting of cancer cells

- **Objective of the Presentation:**
  - Explore (50?!) emerging anticancer therapies and technologies that are transforming cancer treatment
  - Discuss their potential to increase effectiveness and reduce side effects

Overview of current cancer therapies

- **Surgical Treatments**: Removal of tumours
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- **What is Precision Medicine?**
  - A personalized approach based on genetic, environmental, and lifestyle factors
- **Why Precision Medicine Matters in Cancer Treatment:**
  - Helps tailor treatment based on individual genetic makeup of cancer
  - Enables more effective targeting of cancer cells while sparing healthy tissue

Innovative Approaches in Cancer Therapy- Precision Medicine

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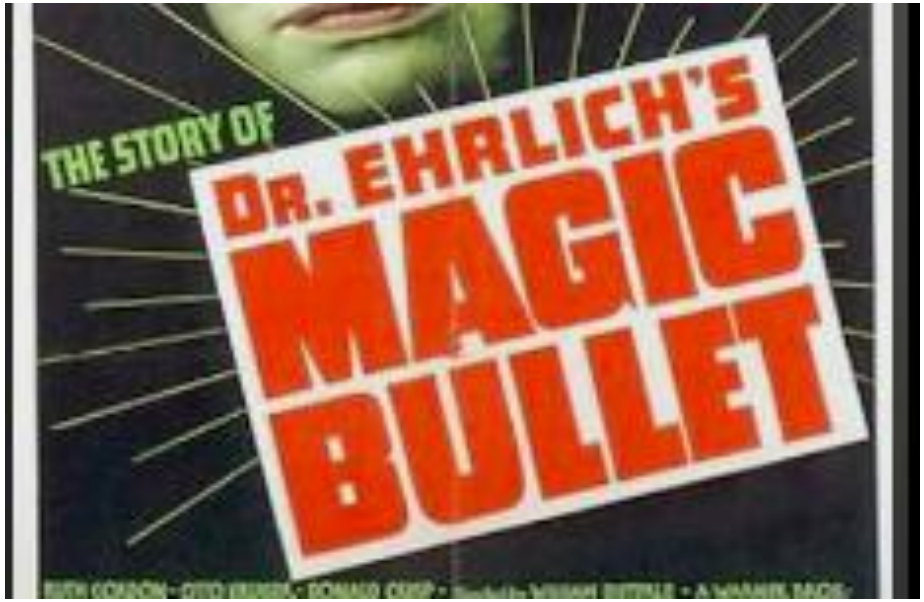

Hallmarks of Cancer

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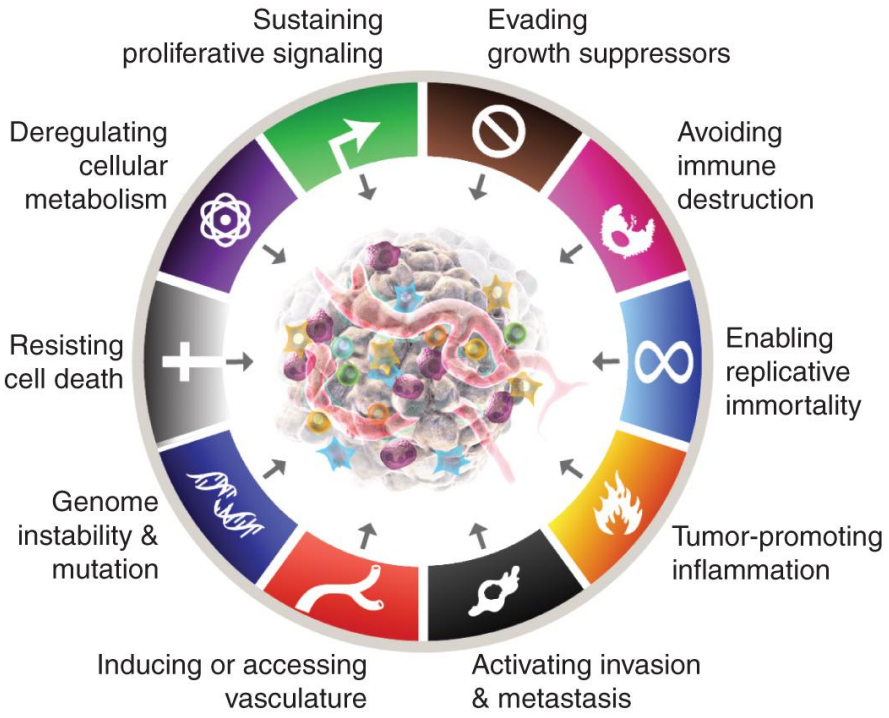

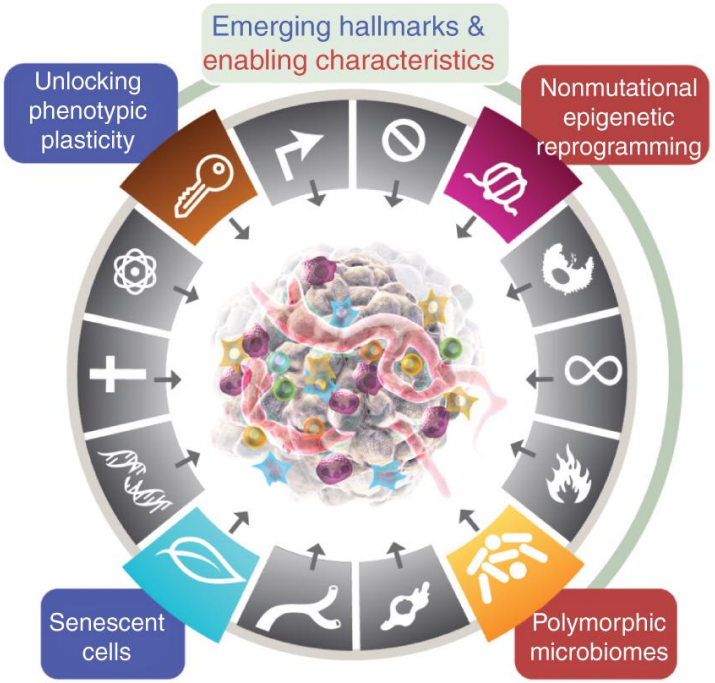

Hanahan; PMID 35022204

Innovative Approaches in Cancer Therapy- Immunotherapy

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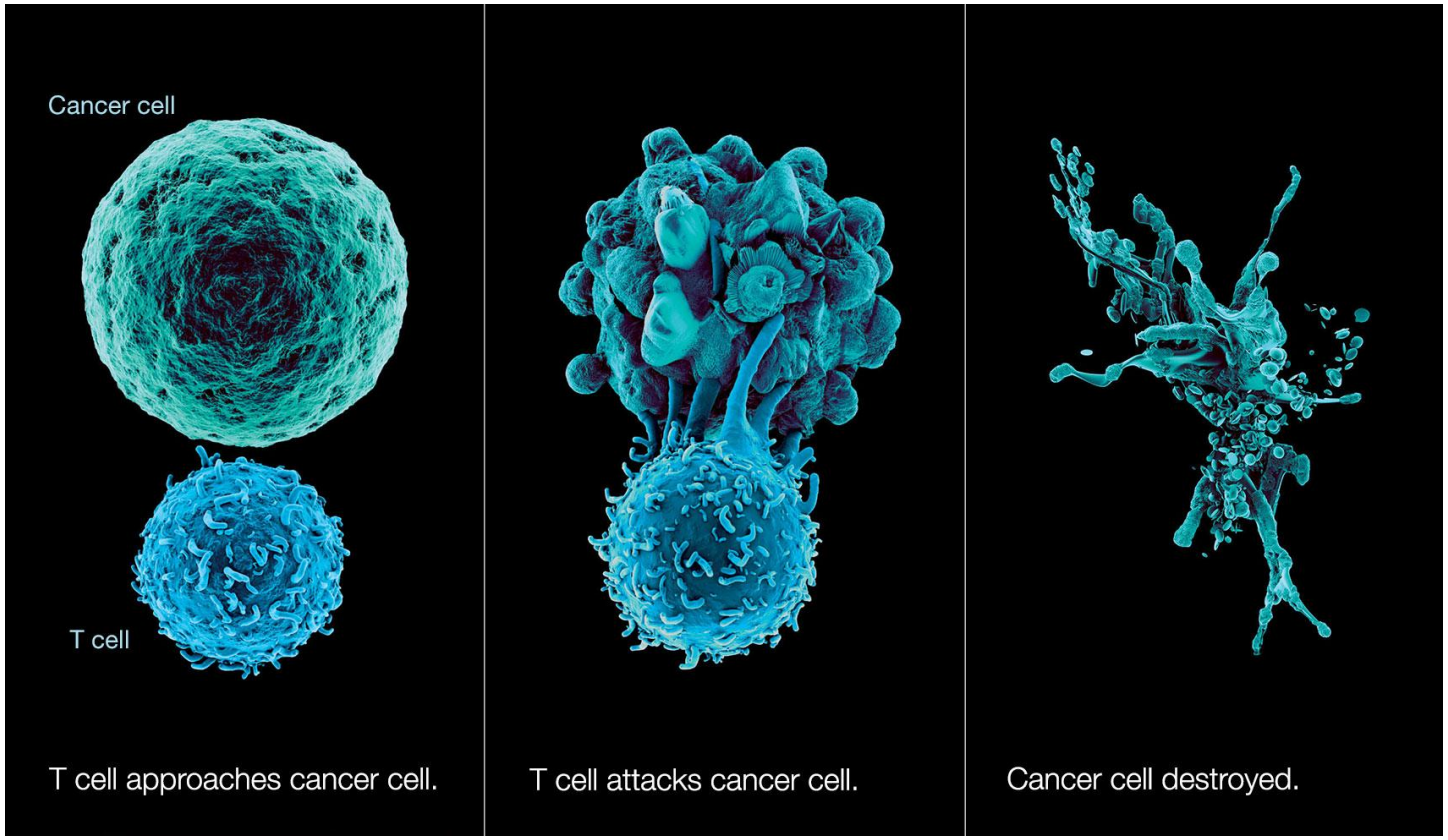

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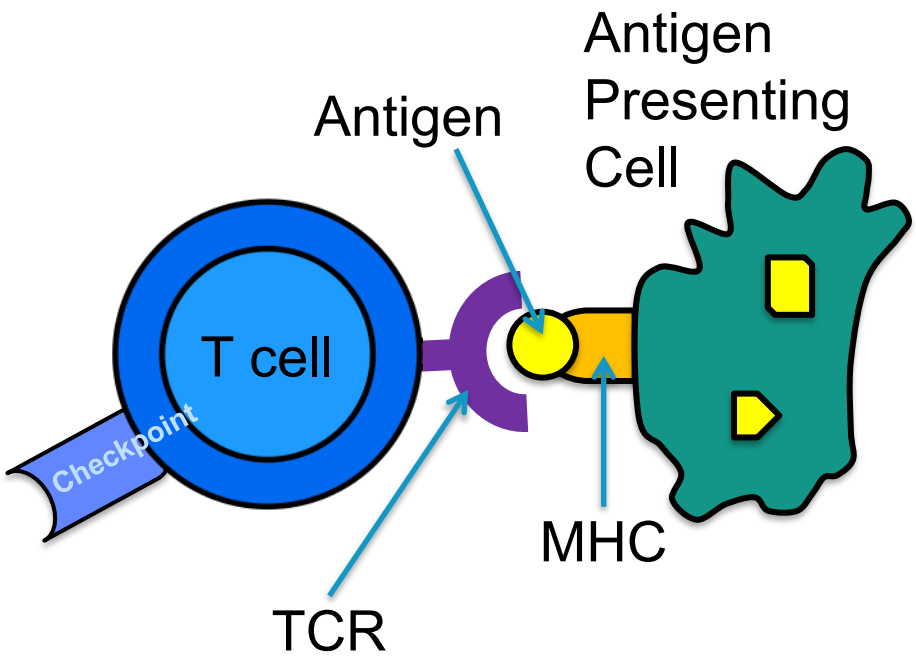
Normal T cell Function



- Regulatory mechanisms to control T cell function (e.g. stop autommunity) = CHECKPOINTS

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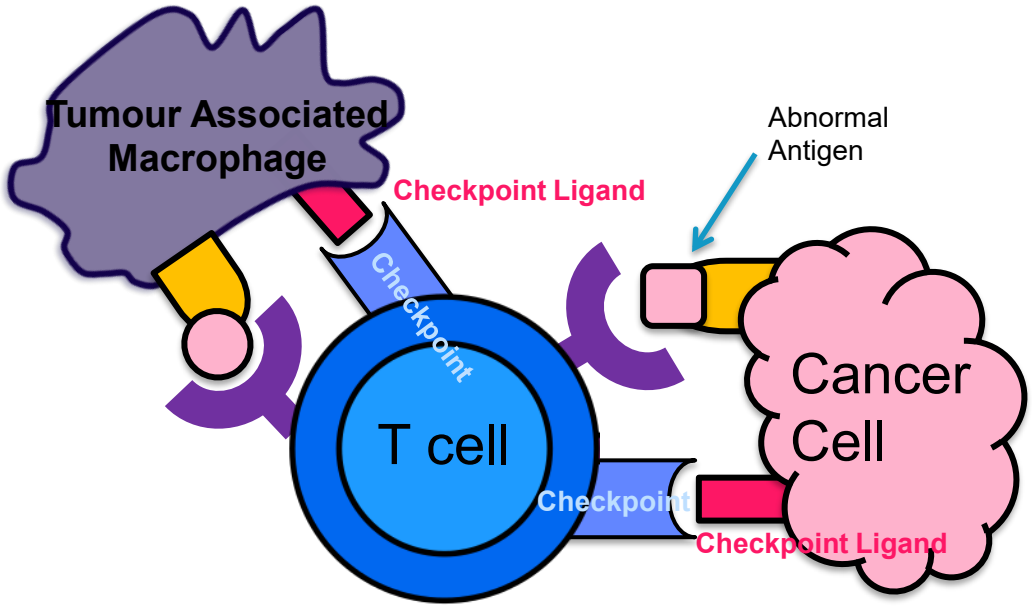
What happens in Cancer?

- Some cancer cells and non-cancer cells within tumour
- Express inhibitory receptors (e.g. PDL1)
- Which bind to '**checkpoints**' on outside of T cells



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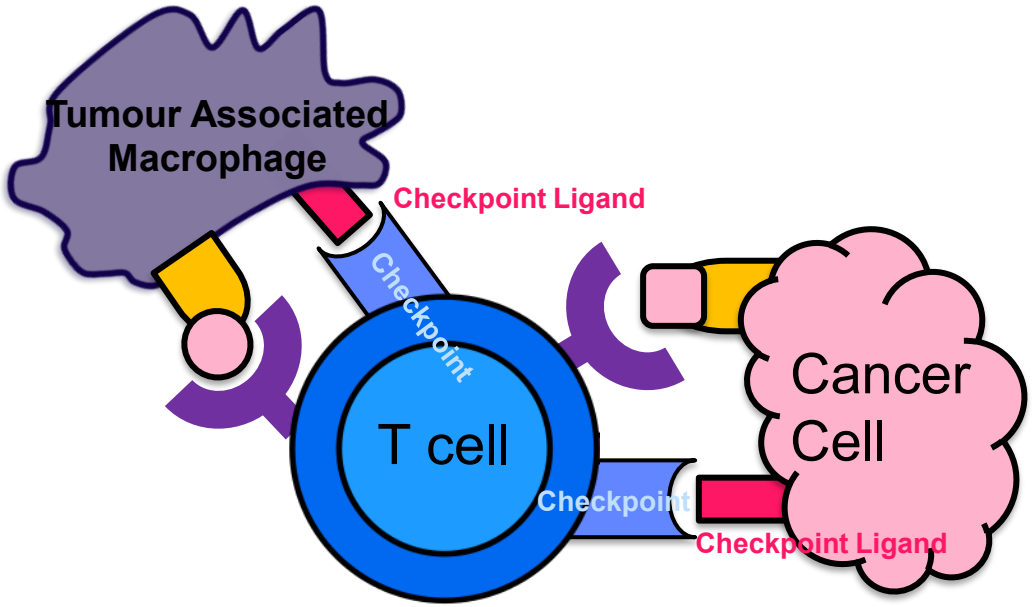
What happens in Cancer?

- Some cancer cells and non-cancer cells within tumour
- Express inhibitory receptors (e.g. PDL1)…
- Which bind to **'checkpoints'** on outside of T cells
- That cause T cell anergy



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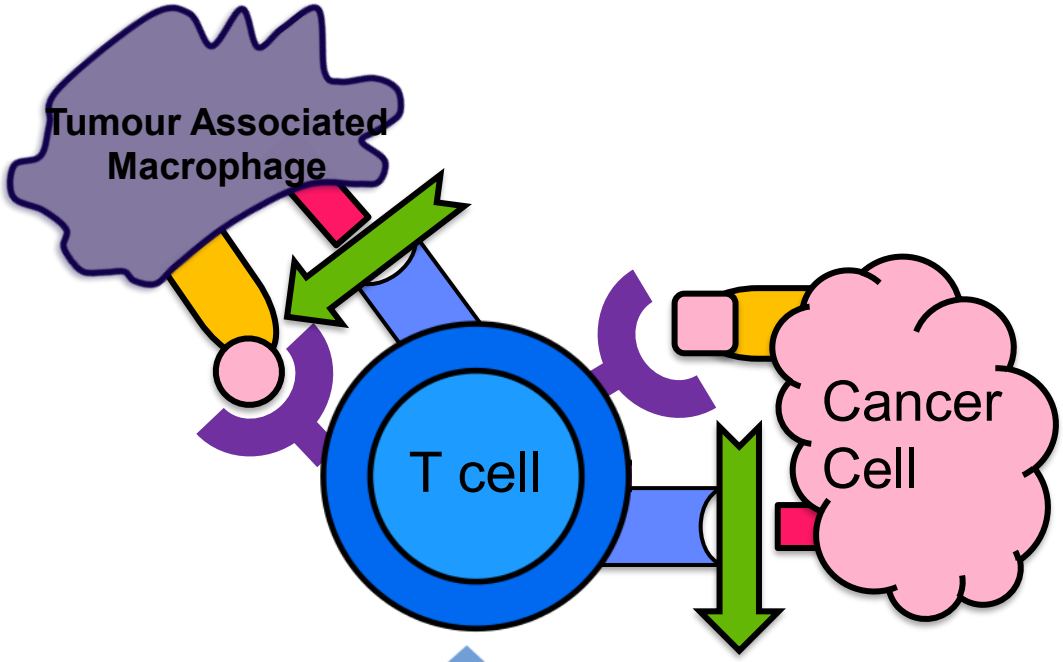
How do checkpoint inhibitors work?

- Antibodies
- Prevent binding of checkpoints!



Biology of Immunotherapy Checkpoint Inhibitors

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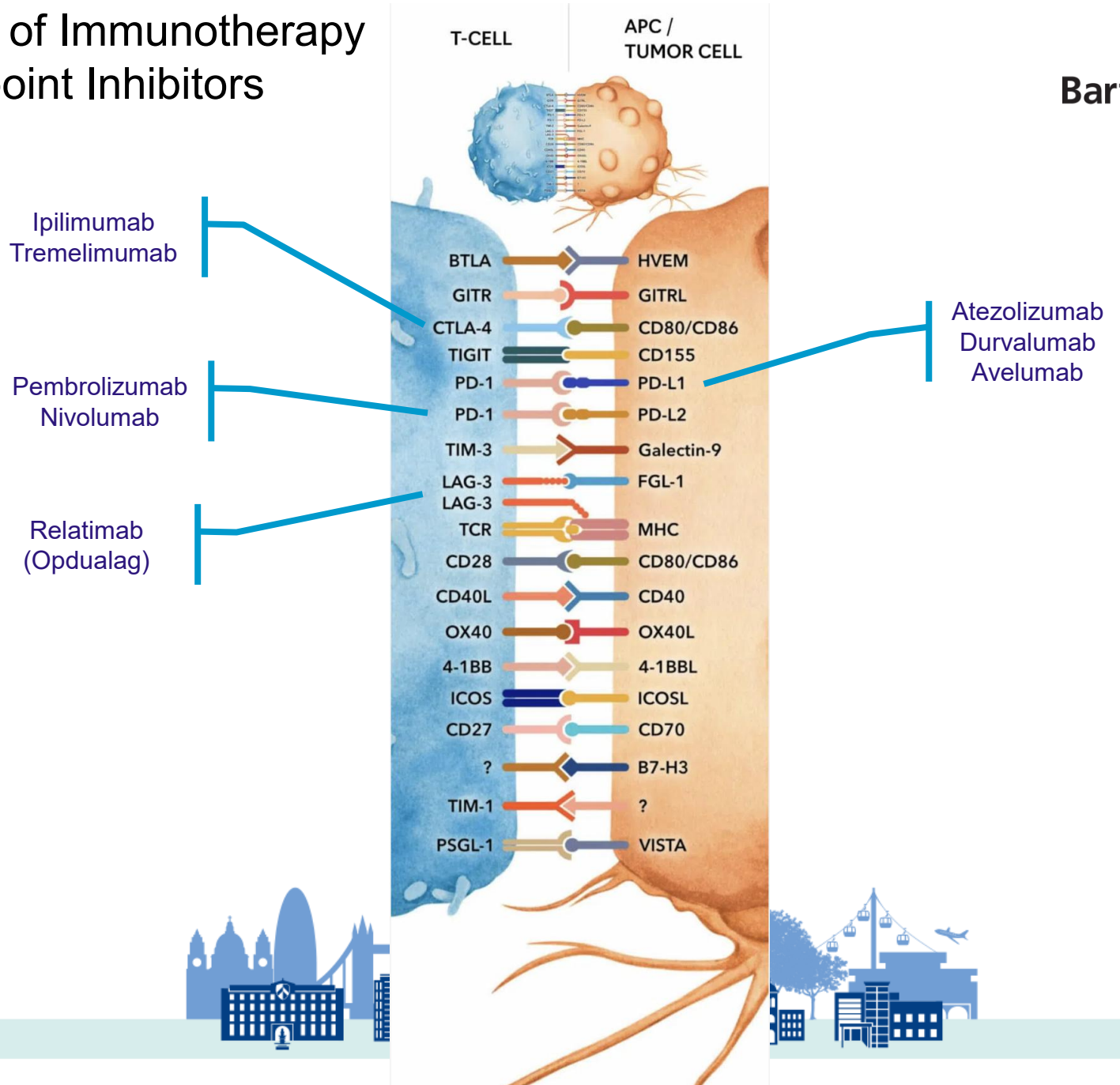
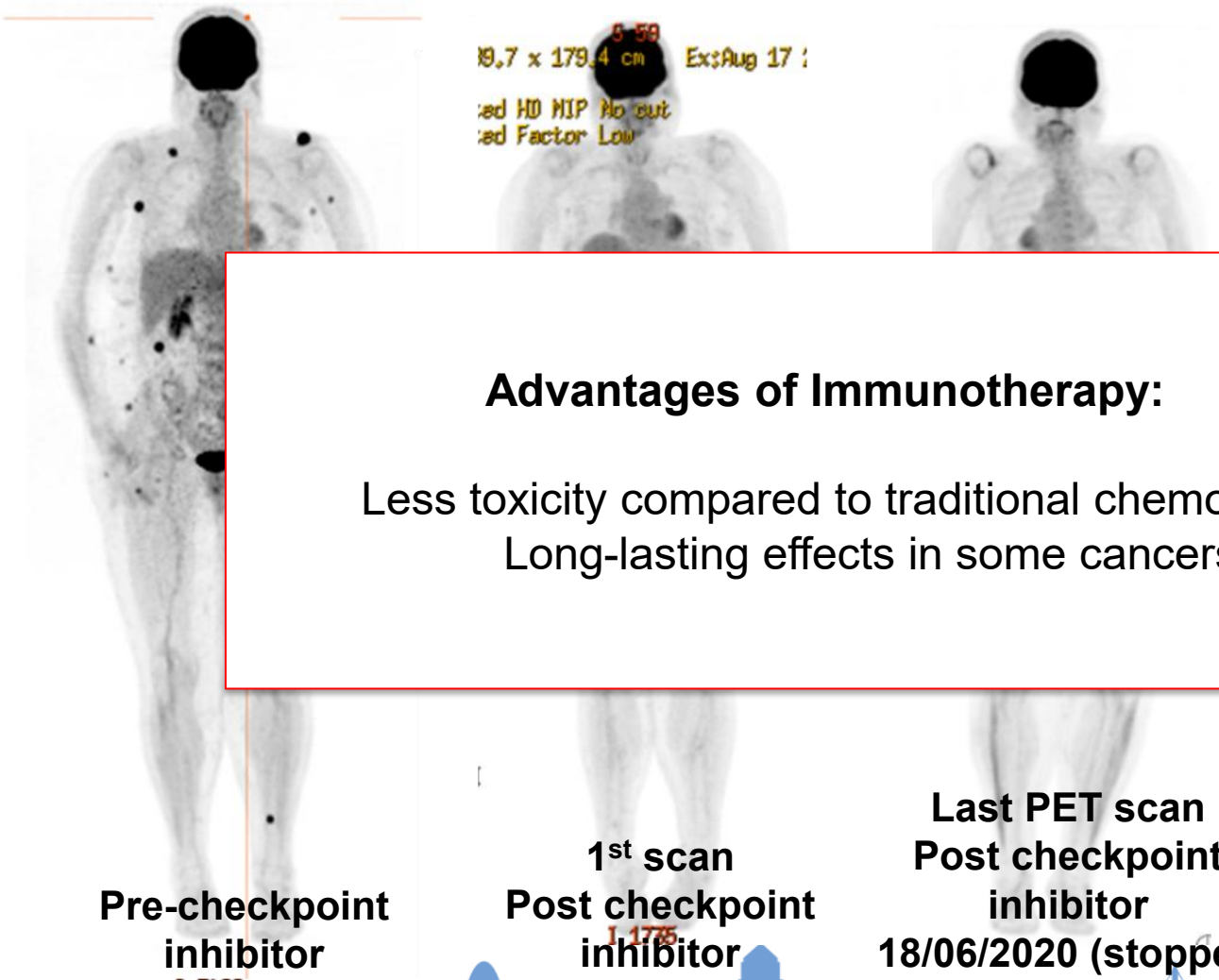


Advantages of Immunotherapy



Advantages of Immunotherapy:

Less toxicity compared to traditional chemotherapy
Long-lasting effects in some cancers

ng CMR

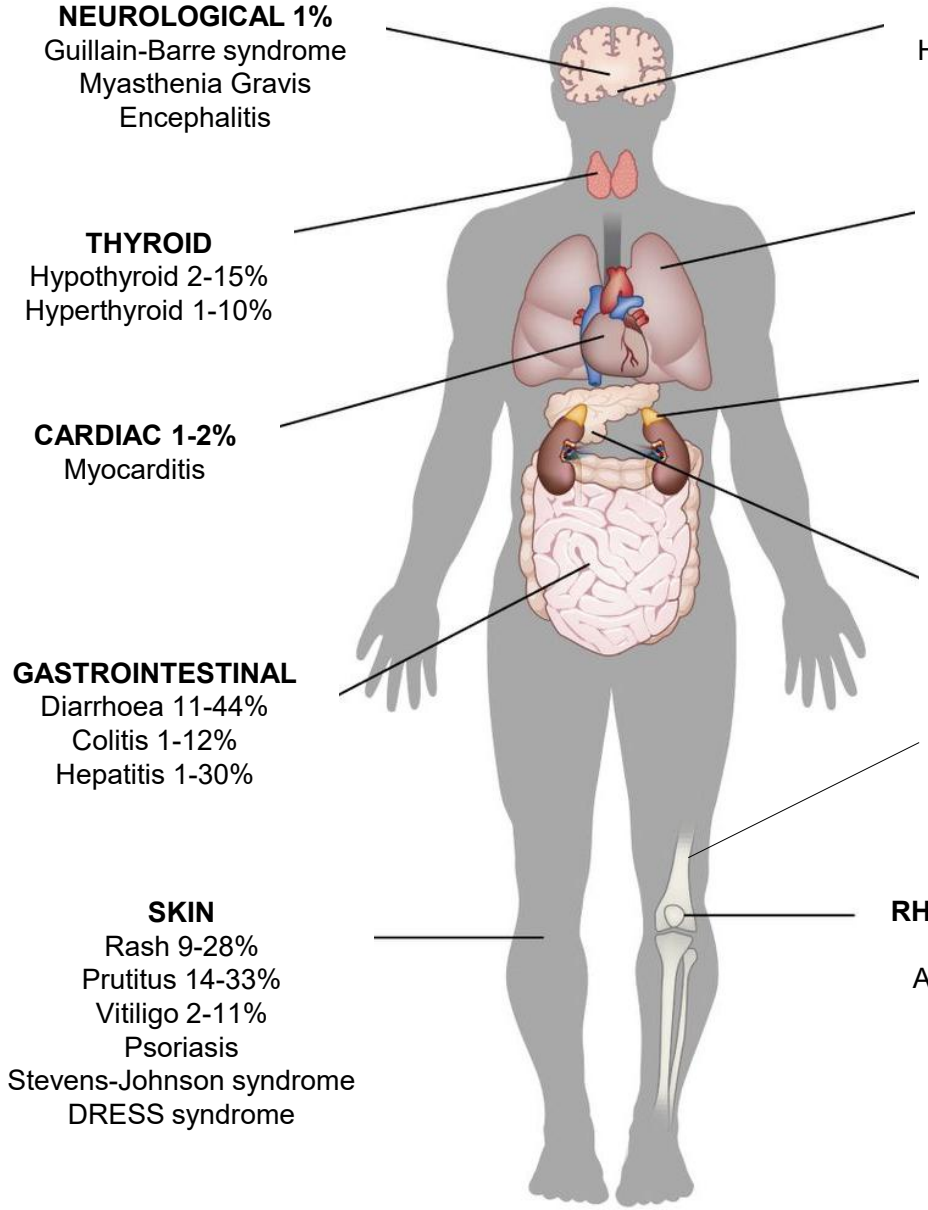
Pre-checkpoint inhibitor 21/03/2018

1st scan Post checkpoint inhibitor 17/08/2018

Last PET scan Post checkpoint inhibitor 18/06/2020 (stopped treatment)

Clinical Toxicity

Grade ≥3 toxicity
59% of patients
(ipililumab&nivolumab in MM)



June et al. *Nature Medicine* **23**, 540–547 (2017)
Spain et al. *Cancer Treat Rev* **44**, 51-60 (2016)

Innovative Approaches in Cancer Therapy- Monoclonal Antibodies

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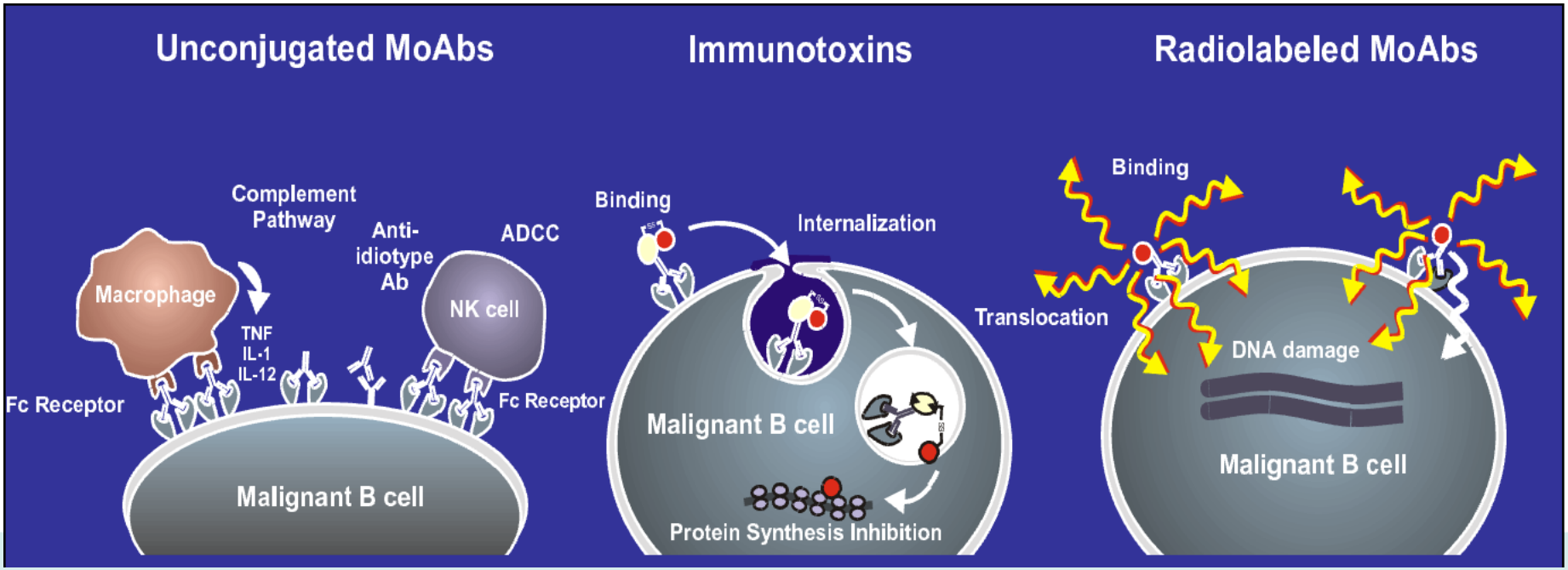
Type	Function	Example Drugs
Unconjuagted mAbs	Work without carrying drugs/radioisotopes	Rituximab (CD20), Trastuzumab (HER2)
Conjugated mAbs	Linked to chemo/toxins or radiation	Brentuximab vedotin, Ibritumomab tiuxetan
Bispecific mAbs	Bind two targets at once (e.g., T-cell + cancer cell)	Blinatumomab (CD19 & CD3)



Innovative Approaches in Cancer Therapy- Monoclonal Antibodies

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Herceptin/Trastuzumab

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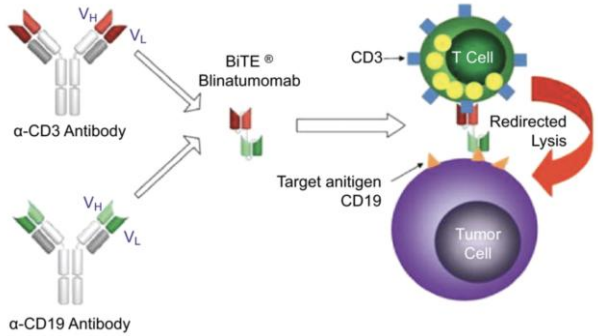
Blinatumomab

a bi-specific monoclonal antibody targeting CD19 on malignant B-cells but also CD3 on normal T-cells, bringing them together to enhance cytotoxicity



Innovative Approaches in Cancer Therapy- Antibody-Drug Conjugates

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1. Targeting Tumour-Specific Antigens

2. Inte

Drug l

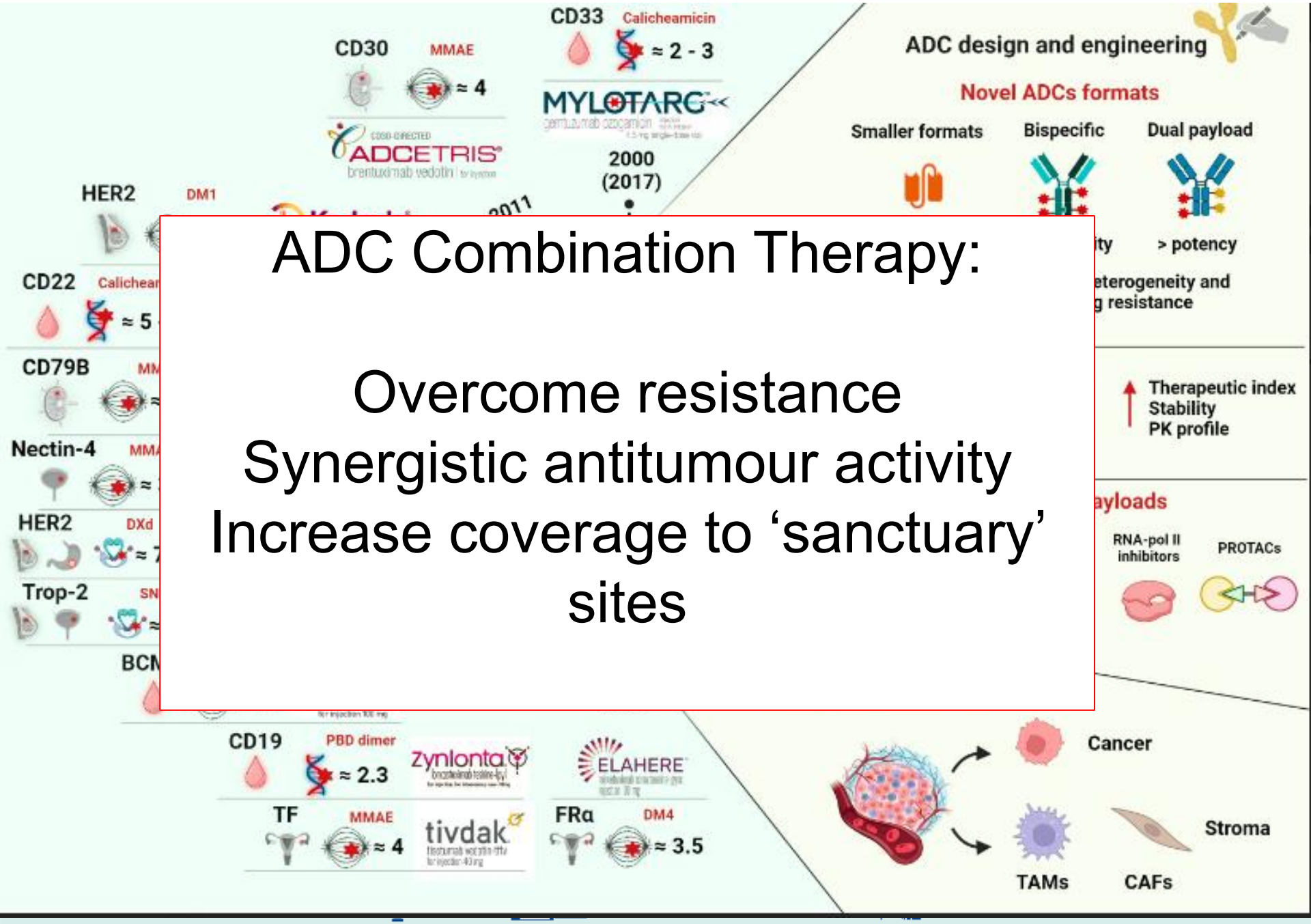
3. Linl

Drug l

4. Cell

5. Bys

Targeted Delivery
Potent Chemotherapy
Evolving technology



ADC Combination Therapy:

Overcome resistance

Synergistic antitumour activity

Increase coverage to ‘sanctuary’ sites

Innovative Approaches in Cancer Therapy- CAR-T Cell Therapy

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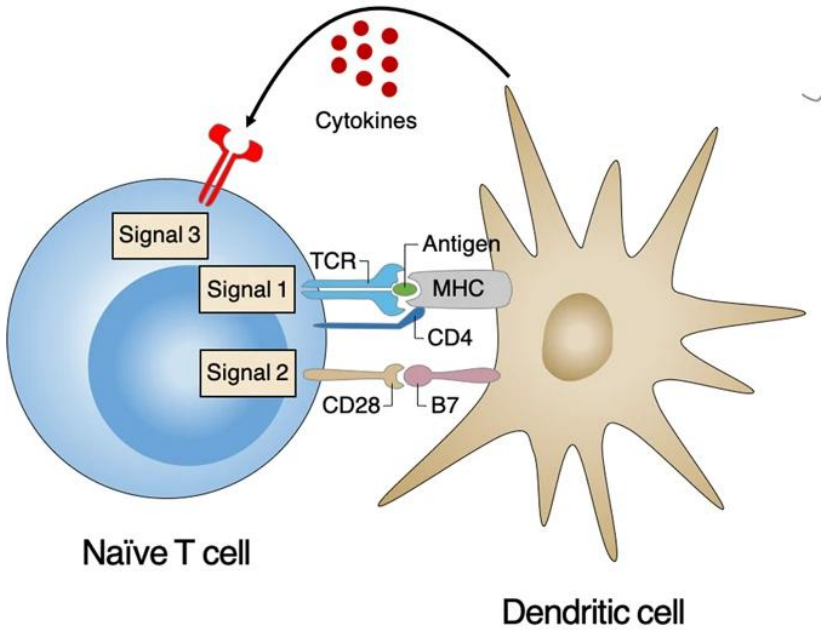
Chimeric Antigen Receptor T-cell therapy involves genetically modifying a patient's T-cells to target specific cancer cells.
CAR-T Cell targeting CD19

Axicabtagene ciloleucel for treating relapsed/refractory diffuse large B-cell lymphoma (DLBCL) or high ho relapse within 12 months of compl would otherwise be intended for p ractory to 1st line chemoimmunotherapy AND who would otherwise be intended for potential stem cell transplantation

NICE APPROVED

Why do our T cell's not attack cancer?

- Cancer cells arise from our own tissues
- *Our own T cells are trained not to attack our own tissues*
- Only a small proportion of our own T cells are specific for cancer antigens
- Cancer cells develop ways to suppress T cell attack



How can we help T cells attack cancer?

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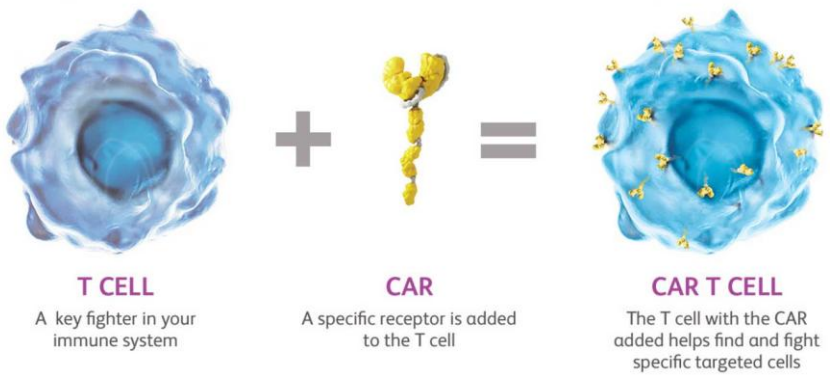
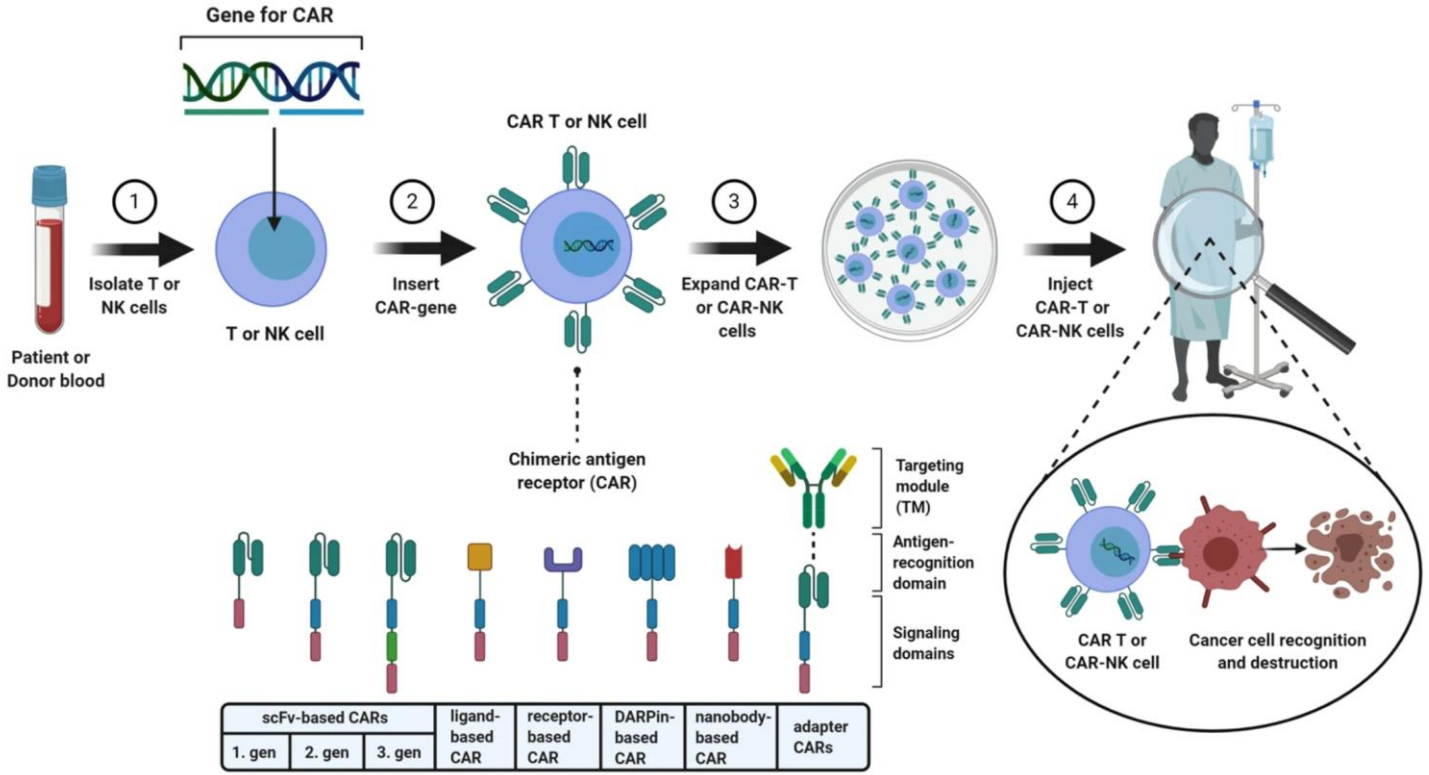
- We can modify some of our own T cells to attack cancer cells
- This is called ***redirecting specificity***
- *One way to do this is to put a Chimeric antigen receptor (CAR) into a T cell to turn it into a CAR T cell*
- The target can be cancer specific OR a target found on cancer cells and some normal cells

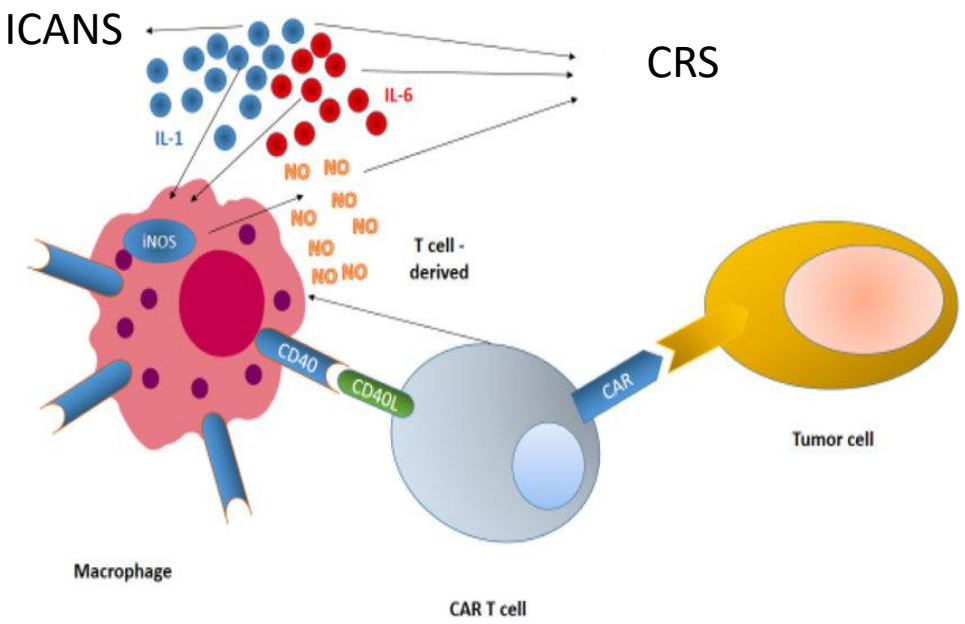




Albinger et al; PMID 33753909

Clinical Toxicity

- Cytokine release syndrome (CRS)
- Neurotoxicity (ICANS)
- Haematotoxicity
- 30-50% need ITU support
- Multidisciplinary infrastructure required



Innovative Approaches in Cancer Therapy- Tumour-Infiltrating Lymphocytes TILs

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- High TIL levels often correlate with **better prognosis** in cancers such as melanoma, breast, and colorectal cancer
- Serve as a **biomarker** for response to immunotherapies (e.g., checkpoint inhibitors)
- TILs harvested from a patient's tumour → expanded ex vivo → reinfused to enhance anti-tumour activity
- Shown clinical benefit in metastatic melanoma and being tested in multiple solid tumours

TUMOR-INFILTRATING LYMPHOCYTE (TIL) THERAPY

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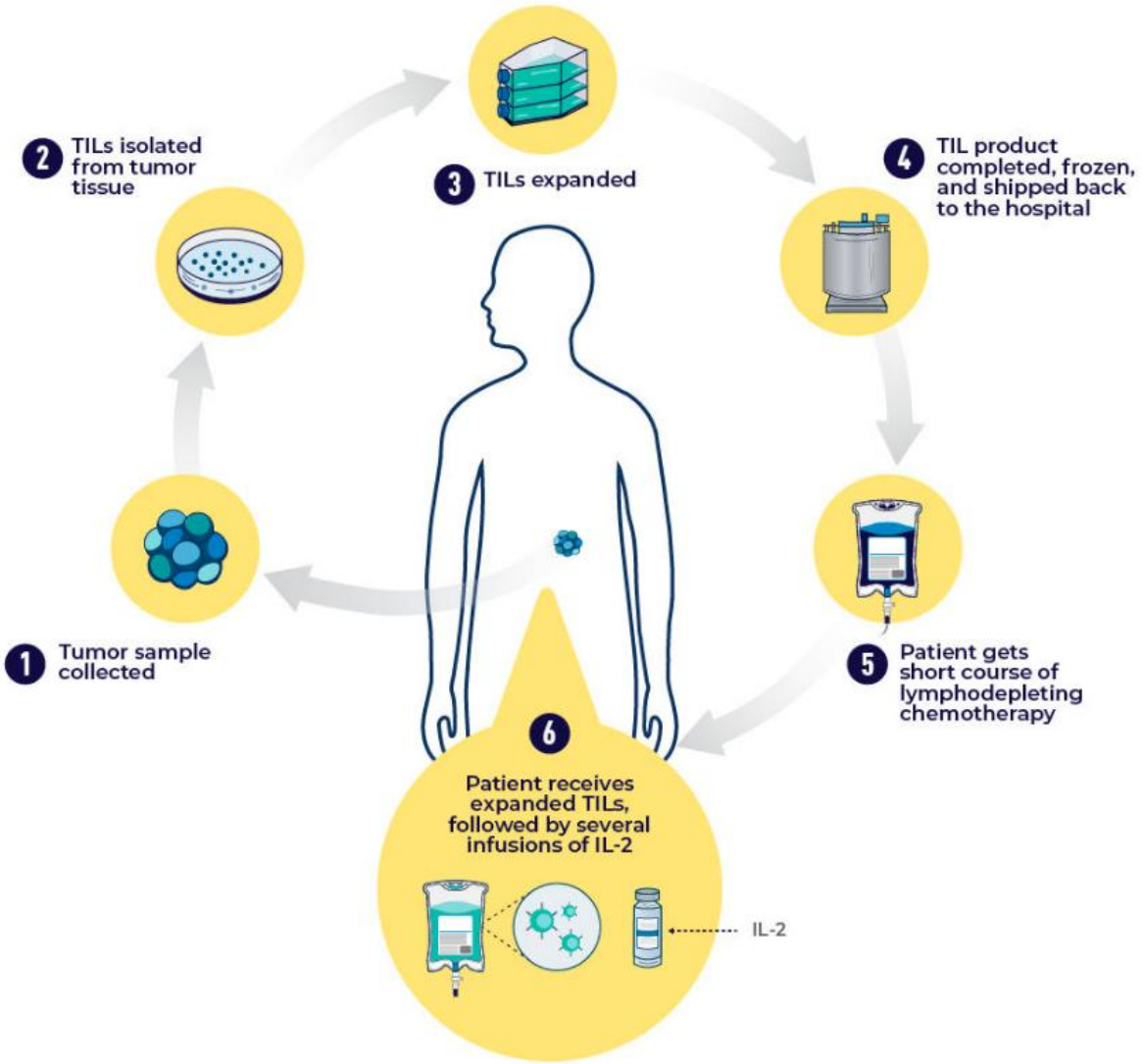

Innovative Approaches in Cancer Therapy- Cancer vaccines

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- **Preventive Cancer Vaccines:**
  - **HPV Vaccine**: Protects against the human papillomavirus, which causes cervical cancer.
  - **Hepatitis B Vaccine**: Prevents hepatitis B infection, reducing the risk of liver cancer.

- **Therapeutic Cancer Vaccines:**
  - Designed to stimulate the immune system to fight cancer cells after they have formed.
  - **Examples**: Sipuleucel-T (Provenge) for prostate cancer.

Innovative Approaches in Cancer Therapy- Gene Therapy and CRISPR

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- **Gene Therapy**: Involves modifying the genes within cancer cells or immune cells to treat the disease.
  - Goal: To correct or replace defective genes, or to introduce new genes to fight cancer.

- **CRISPR/Cas9 Technology**:
  - A powerful tool for editing genes with high precision.
  - Used to directly modify cancer cells or enhance immune cells for better cancer targeting.

- **Future Potential**:
  - Possible cure for genetic cancers by fixing the underlying genetic issues.

Innovative Approaches in Cancer Therapy- Artificial Intelligence and Machine Learning

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- **AI in Diagnosis and Prediction:**
  - AI can analyse vast amounts of medical data (such as imaging and genetic data) to diagnose cancer at earlier stages.
  - Machine learning models help predict cancer progression and response to treatment.
- **AI in Drug Discovery:**
  - AI systems can simulate and analyse chemical compounds, speeding up the discovery of new anticancer drugs.
- **Personalized Treatment Plans:**
  - AI algorithms can be used to create individualized treatment regimens based on genetic profiles and other patient-specific factors.

Innovative Approaches in Cancer Therapy- Proton and Heavy Ion Radiotherapy

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- **Proton Therapy**:
  - A type of radiation therapy that uses protons instead of X-rays to treat cancer.
  - Offers more precise targeting, reducing damage to surrounding healthy tissues.

- **Heavy Ion Therapy**:
  - Uses charged particles like carbon ions to target tumours.
  - More effective than traditional radiation in treating certain types of cancer, especially those that are resistant to standard radiation.

Innovative Approaches in Cancer Therapy- MRI guided Radiotherapy

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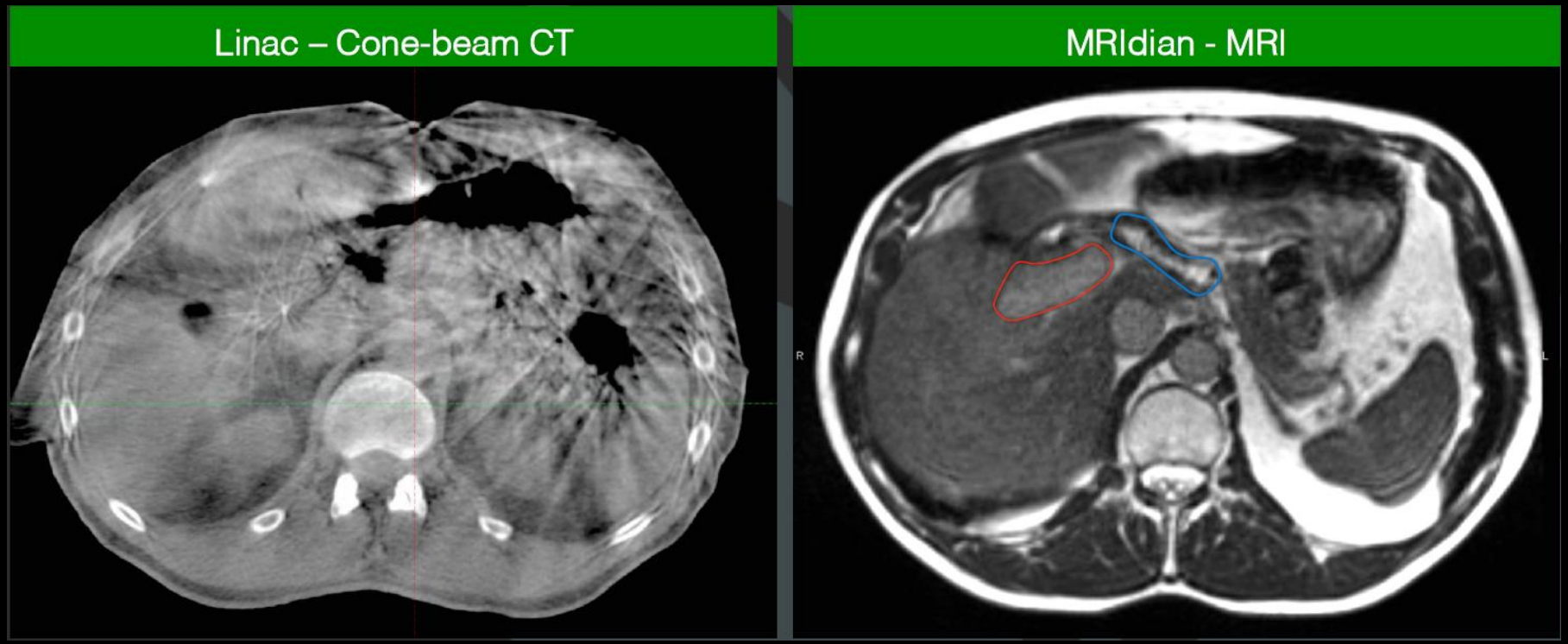
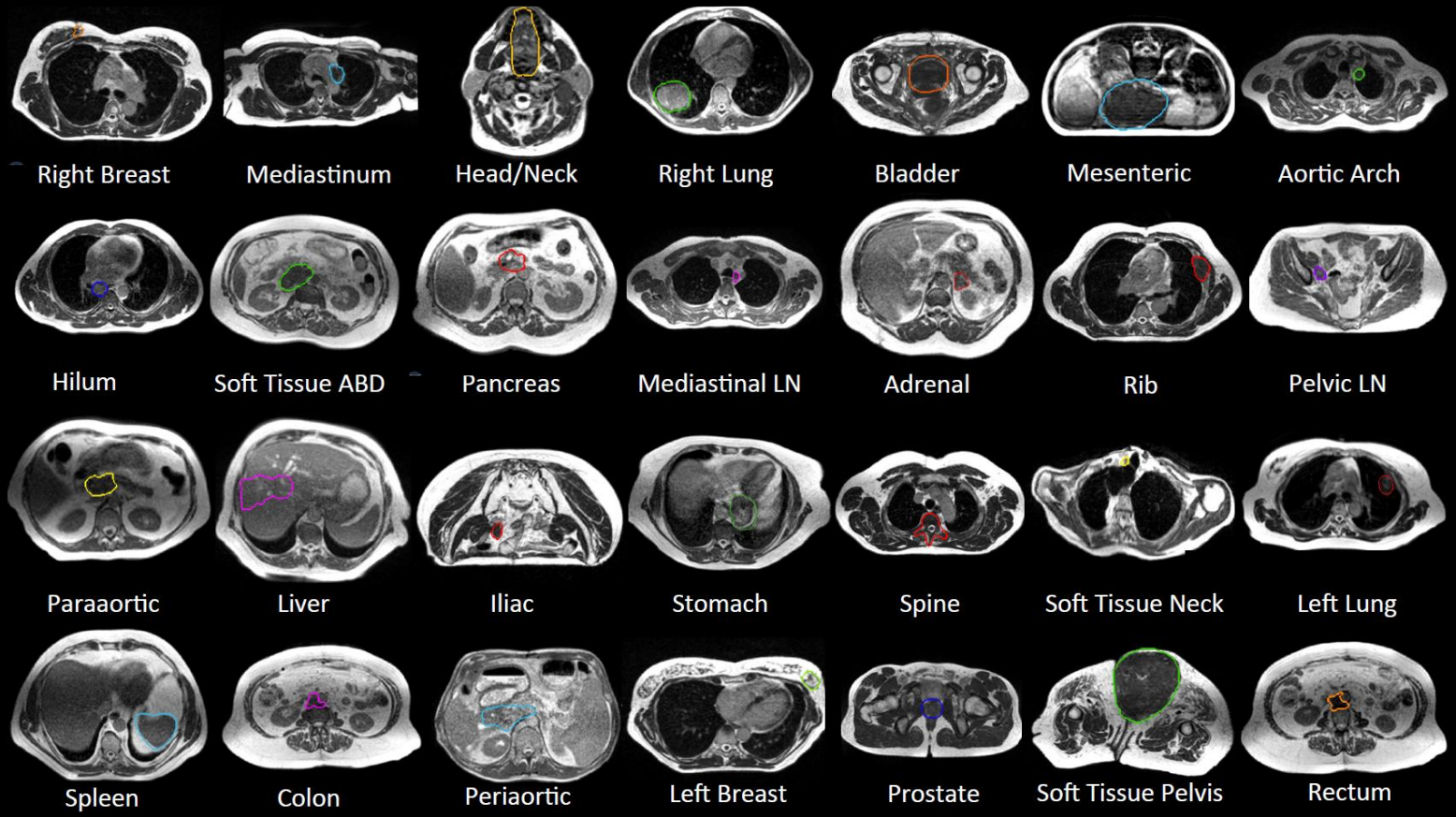
The Future of Radiotherapy

- ViewRay MRIdian MR-Linac, 2021

On line Imaging




Right Breast
Mediastinum
Head/Neck
Right Lung
Bladder
Mesenteric
Aortic Arch
Hilum
Soft Tissue ABD
Pancreas
Mediastinal LN
Adrenal
Rib
Pelvic LN
Paraaortic
Liver
Iliac
Stomach
Spine
Soft Tissue Neck
Left Lung
Spleen
Colon
Periaortic
Left Breast
Prostate
Soft Tissue Pelvis
Rectum

The Future of Cancer Treatment

- **Challenges**
  - **High Costs**: Many of these advanced therapies are expensive, limiting accessibility
  - **Complexity**: Technologies like gene therapy and CAR-T therapy require specialized expertise and equipment
  - **Side Effects**: While new therapies are more targeted, some still carry risks and side effects that need to be addressed

- **Collaboration Across Disciplines**: Integrating advancements in biotechnology, artificial intelligence, and nanotechnology will enhance cancer treatment

- **Personalized Medicine**: The future of cancer treatment lies in highly personalized regimens based on an individual's genetic profile

With thanks to all at Barts Cancer Centre who contributed to my learning and provided information for this talk.

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Prof Jeff Davies, Consultant Haemto-Oncology

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Thank you for listening
Any Questions?