Trinity College Dublin
The University of Dublin

Cancer Diagnosis: Then and Now

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Academic Director, Trinity St James Cancer Institute

APCC Lecture, March 2022

Cancer described since earliest records…

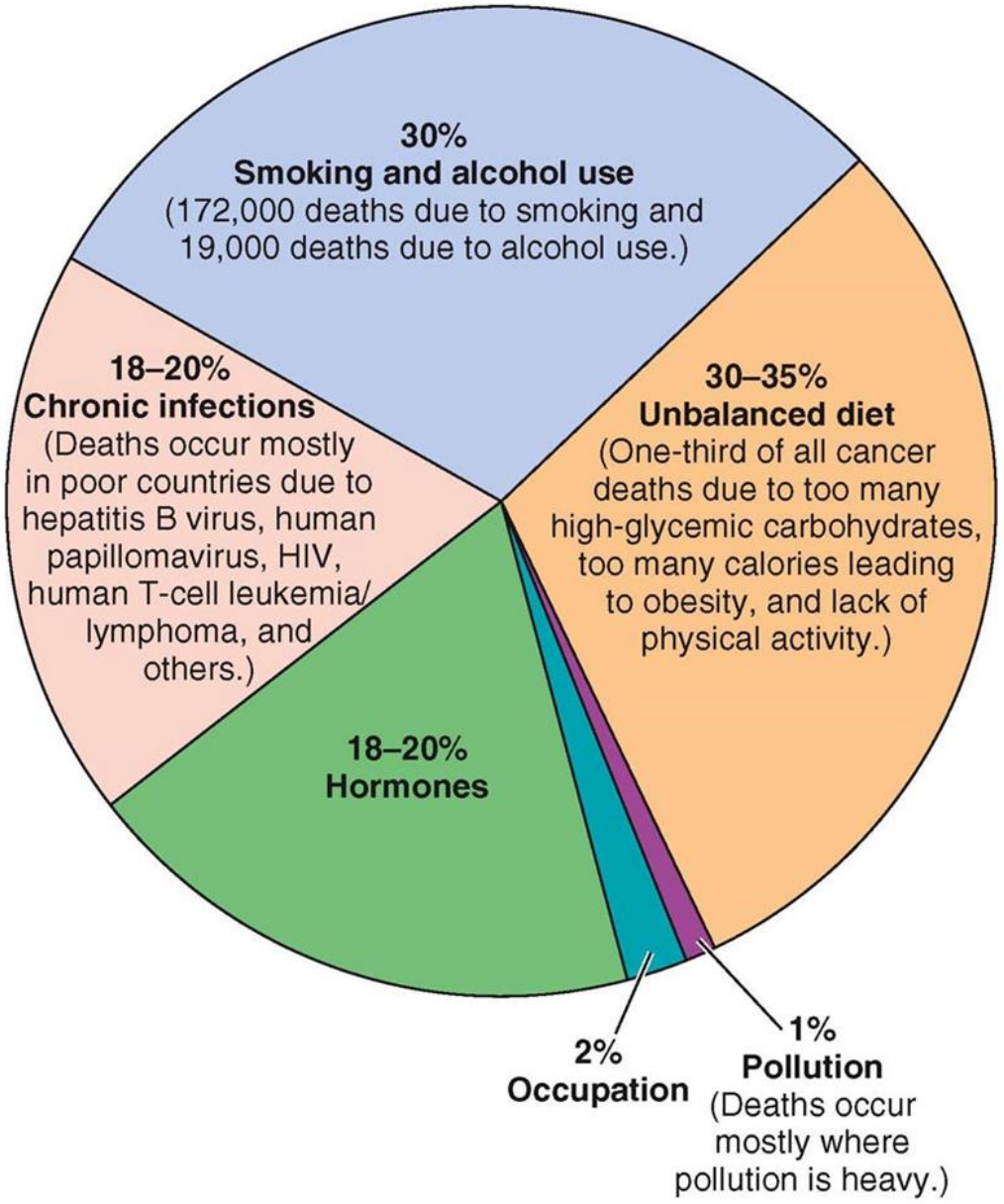
- Earliest description of cancer approx. 3000 BC
- Breast cancer removed with fire drill
- “There is no treatment”

Term ‘Cancer’ dates from 300 BC…

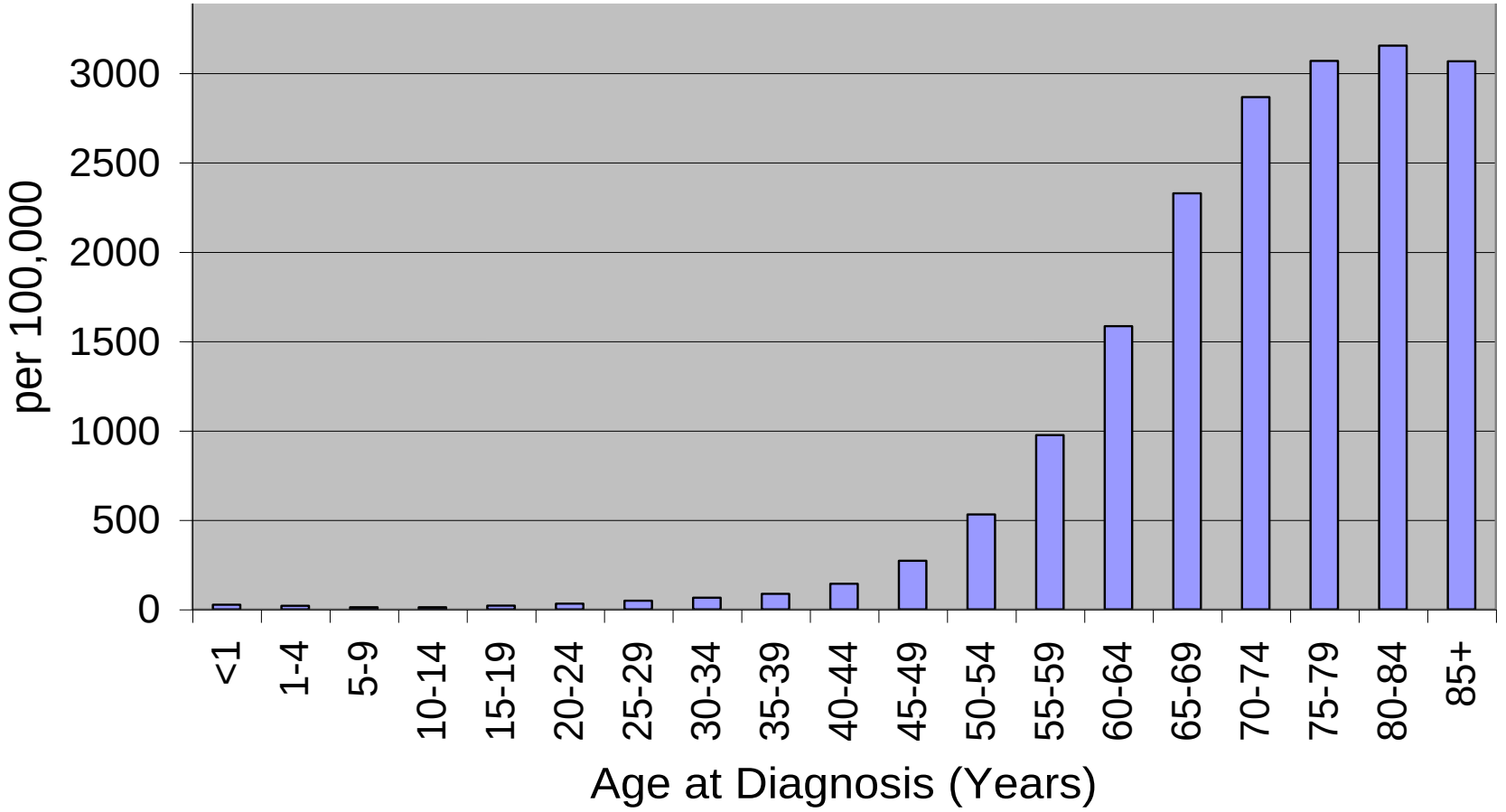
- Origin of word cancer from Hippocrates
- 1st proponent of ‘personalised therapy’
- Advocated for principles of communication with relatives, supportive care…

Global Causes of Cancer

- <u>Chemical Exposure</u>
  - Tobacco smoke
  - Environmental (PCBs)
  - Occupational (coal tar, asbestos, aniline dye)
  - Diet
  - Radiation (UV, ionizing)
- <u>Infection</u>
  - Viruses (EBV, hepatitis B, papilloma)
  - Bacteria (Helicobacter)
- Inherited familial cancer syndromes

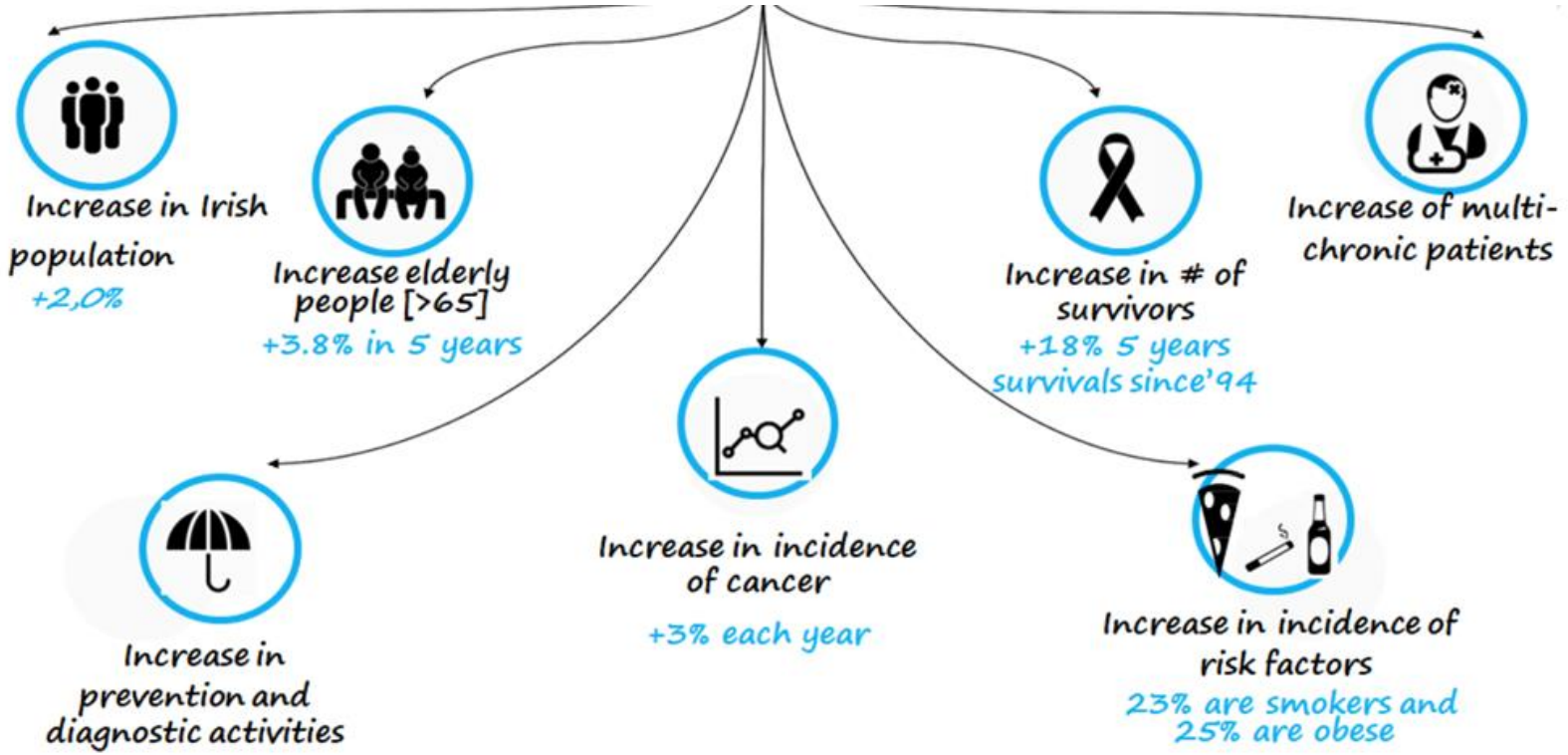


Cancer Incidence Increases with Age…



data from National Cancer Institute; http://www.cdc.gov/cancer

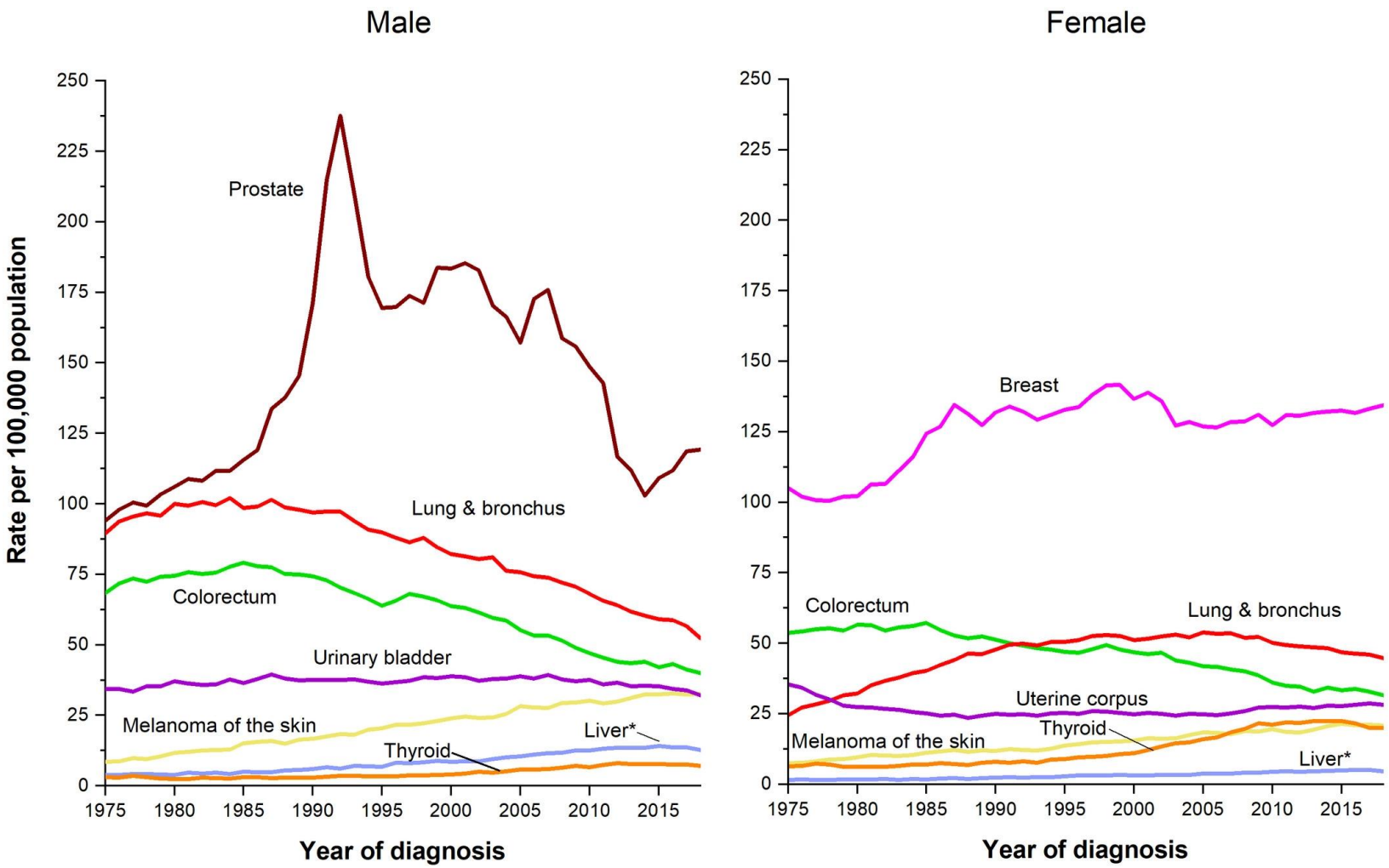
Cancer in Ireland – a growing problem



The incidence of cancer in Ireland will double by 2040*

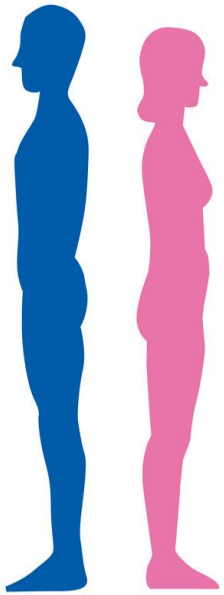
*Source: National Cancer Registry of Ireland

Cancer Incidence – 1975 - 2015



Cancer Statistics : 2022

Estimated New Cases

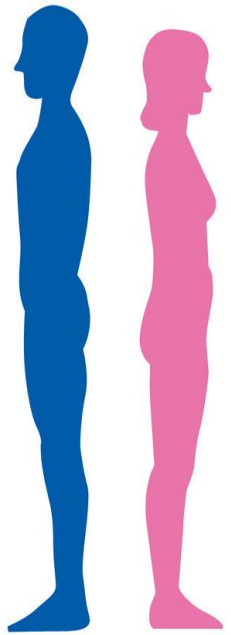
Males				Females		
Prostate	268,490	27%		Breast	287,850	31%
Lung & bronchus	117,910	12%		Lung & bronchus	118,830	13%
Colon & rectum	80,690	8%		Colon & rectum	70,340	8%
Urinary bladder	61,700	6%		Uterine corpus	65,950	7%
Melanoma of the skin	57,180	6%		Melanoma of the skin	42,600	5%
Kidney & renal pelvis	50,290	5%		Non-Hodgkin lymphoma	36,350	4%
Non-Hodgkin lymphoma	44,120	4%		Thyroid	31,940	3%
Oral cavity & pharynx	38,700	4%		Pancreas	29,240	3%
Leukemia	35,810	4%		Kidney & renal pelvis	28,710	3%
Pancreas	32,970	3%		Leukemia	24,840	3%
All Sites	**983,160**	**100%**		**All Sites**	**934,870**	**100%**

CA A Cancer J Clinicians, Volume: 72, Issue: 1, Pages: 7-33, First published: 12 January 2022, DOI: (10.3322/caac.21708)

Cancer Statistics : 2022

Estimated Deaths

Males			Females		
Lung & bronchus	68,820	21%	Lung & bronchus	61,360	21%
Prostate	34,500	11%	Breast	43,250	15%
Colon & rectum	28,400	9%	Colon & rectum	24,180	8%
Pancreas	25,970	8%	Pancreas	23,860	8%
Liver & intrahepatic bile duct	20,420	6%	Ovary	12,810	4%
Leukemia	14,020	4%	Uterine corpus	12,550	4%
Esophagus	13,250	4%	Liver & intrahepatic bile duct	10,100	4%
Urinary bladder	12,120	4%	Leukemia	9,980	3%
Non-Hodgkin lymphoma	11,700	4%	Non-Hodgkin lymphoma	8,550	3%
Brain & other nervous system	10,710	3%	Brain & other nervous system	7,570	3%
All Sites	**322,090**	**100%**	**All Sites**	**287,270**	**100%**



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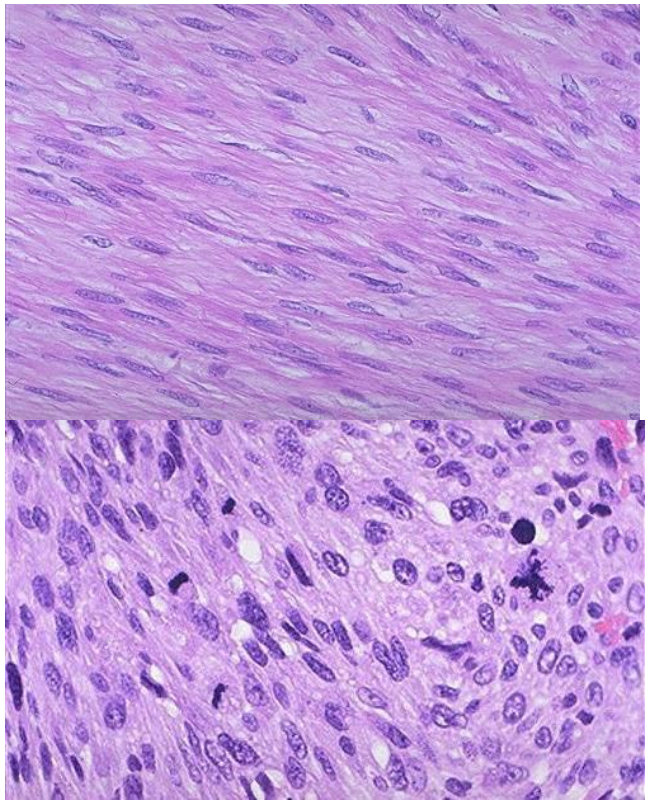
Cancer prevention – updated guidelines

What is cancer?

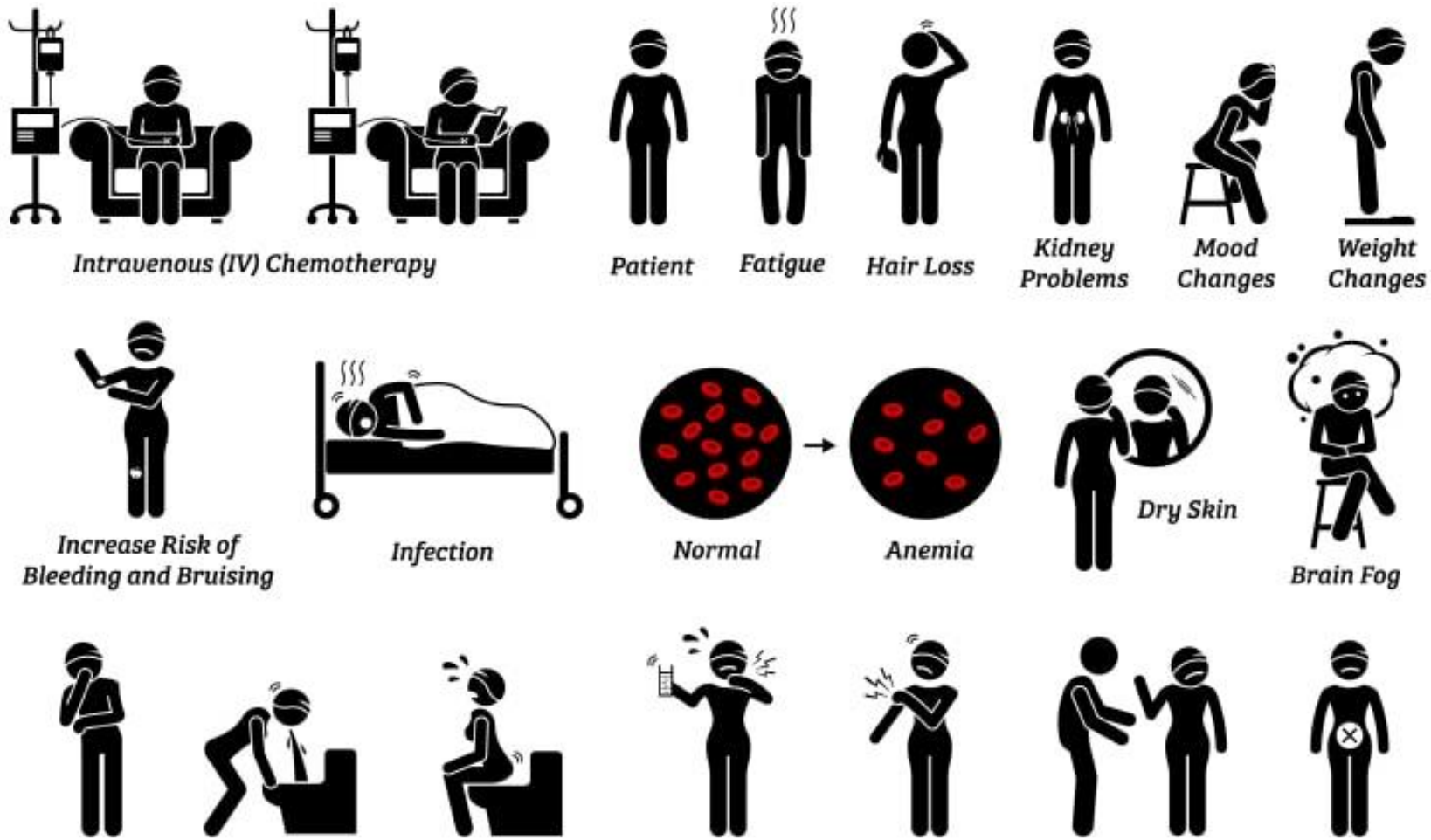
- Cancer = a malignant growth
- Growth of cells is uncontrolled
- Cells can spread to nearby & distant sites
- *Grade* – How bad do the cells look?
- *Stage* – Where has the cancer spread?



Cancer Treatment: Chemotherapy

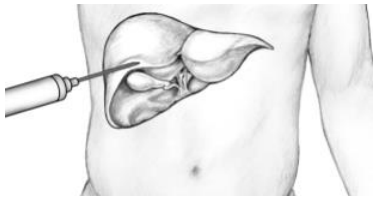
- Chemotherapy stops cancer cells from growing, dividing & making more cells.
- Cancer cells grow & divide faster than normal cells, so chemotherapy has more of an effect on them
- But it still has side effects…

Chemotherapy side effects….

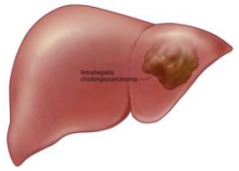


How can we do better?

Core biopsies



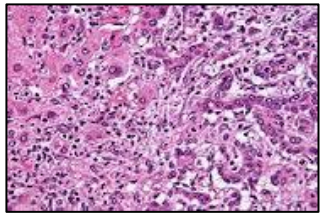
Surgical samples

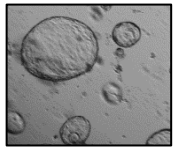


Paracentesis

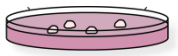
Collagenase digestion, DMEM/FBS wash

Sample bank

Blood sample for normal gDNA referen	Frozen tumor sample for gDNA isolation	FFPE for histology
		



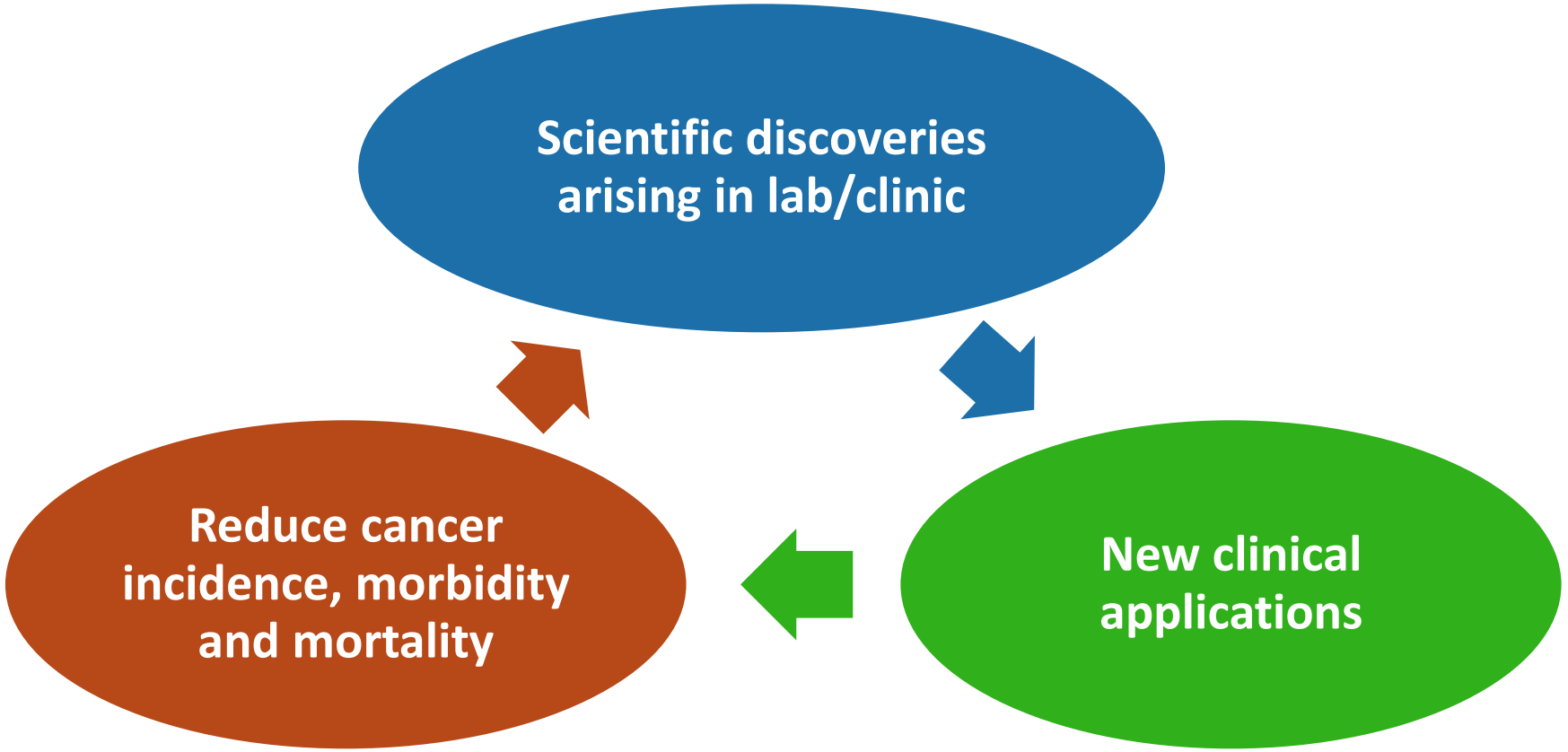
Organoids



Cell lines

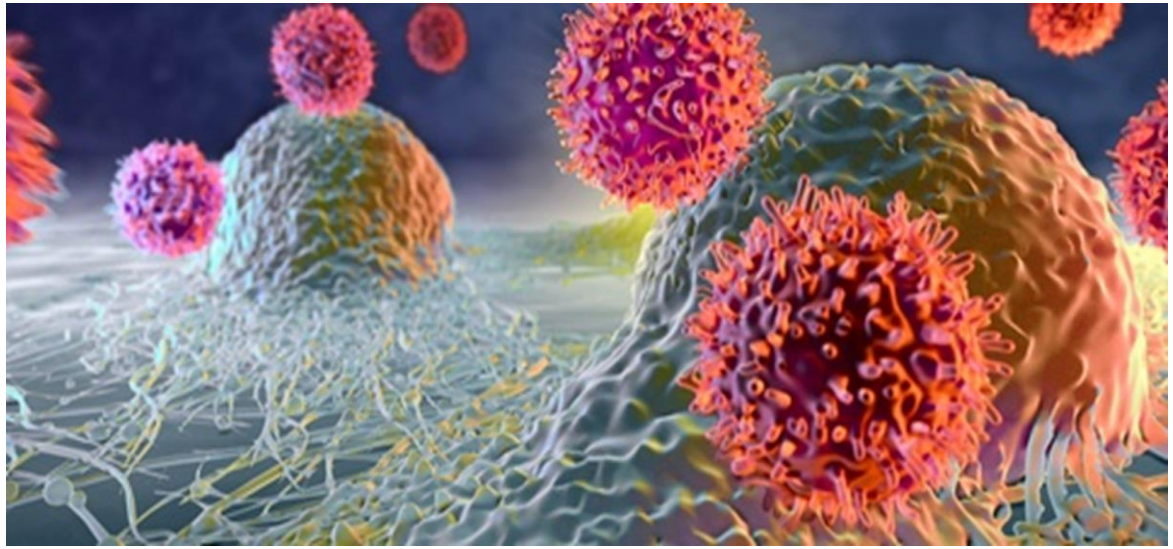
PDX

Translational Cancer Research

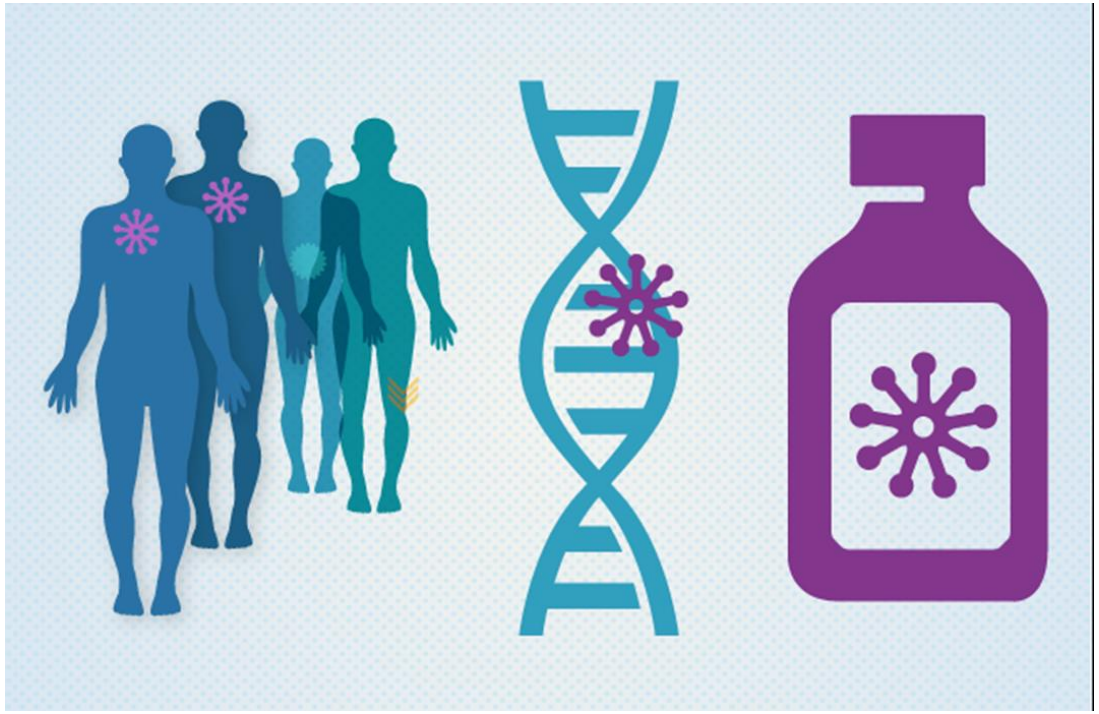


Transfer new understanding of cancer from the laboratory into strategies for diagnosis & treatment

How can we do better?

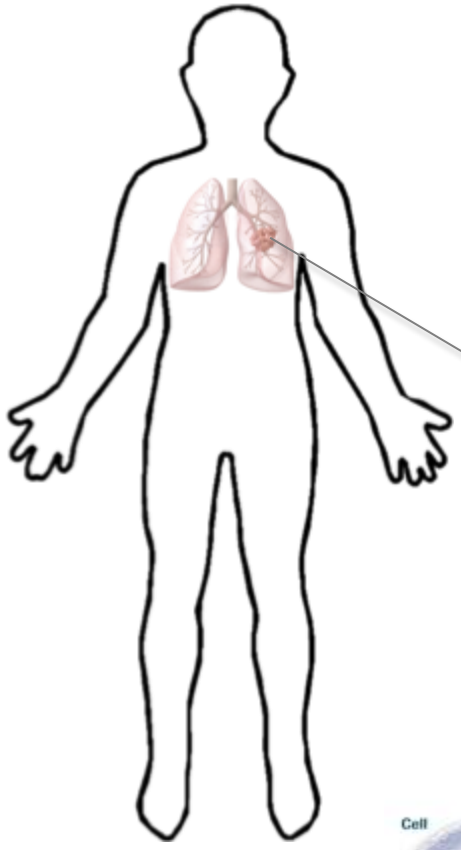


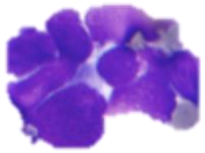
Immunotherapy



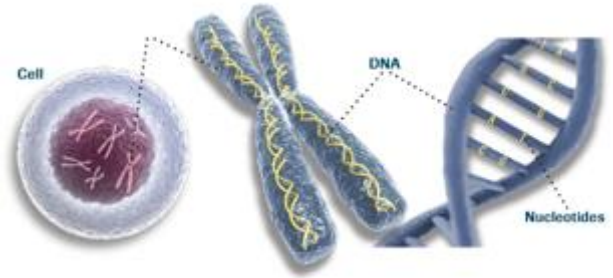
Targeted Therapy

Cancer Genetics: “Targeted Therapy”



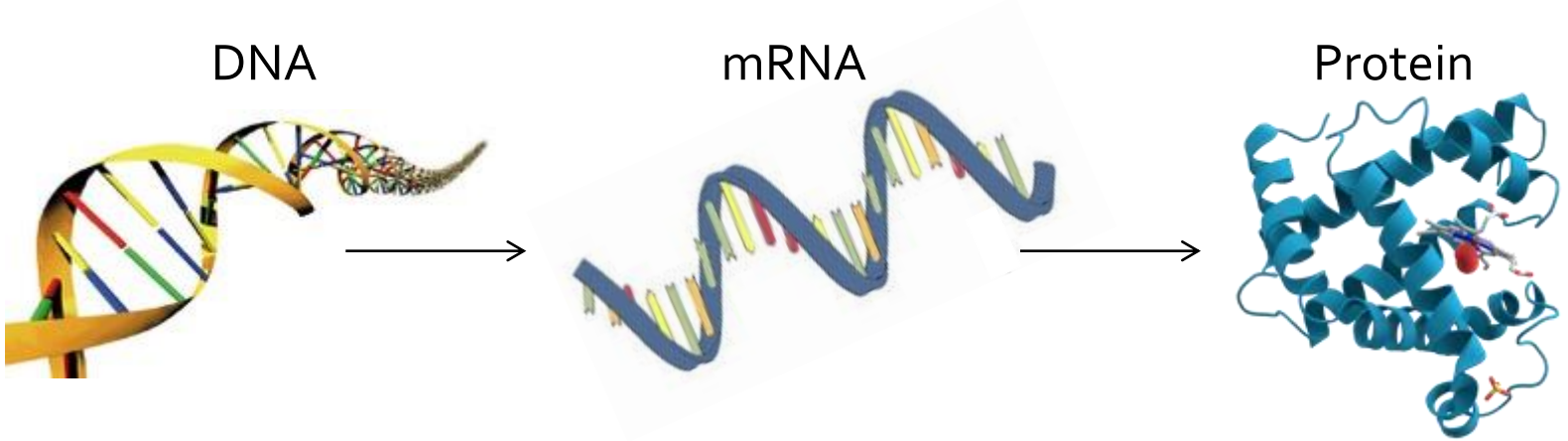


Lung Cancer Cells



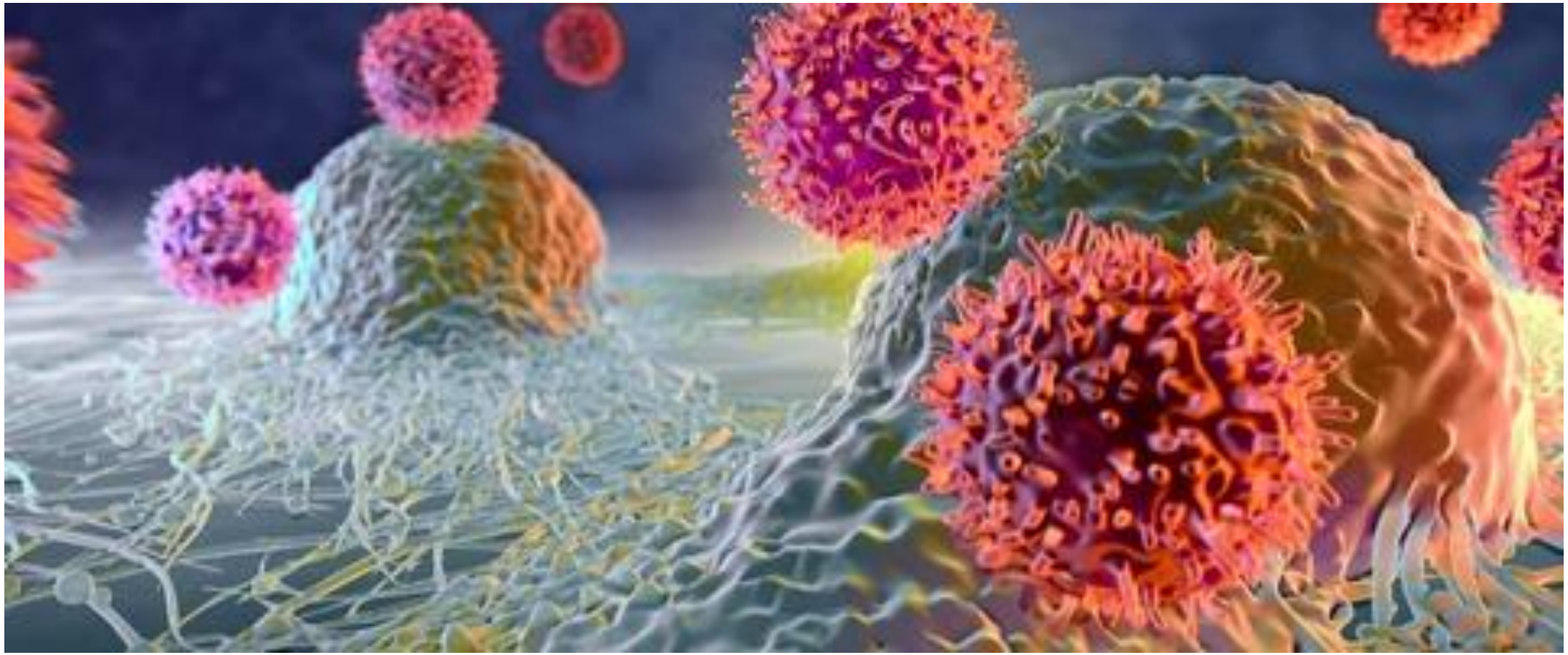
1 human genome
23 chromosomes
~3,000,000,000 nucleotides
~20,000 genes

Cancer Genetics: “Targeted Therapy”

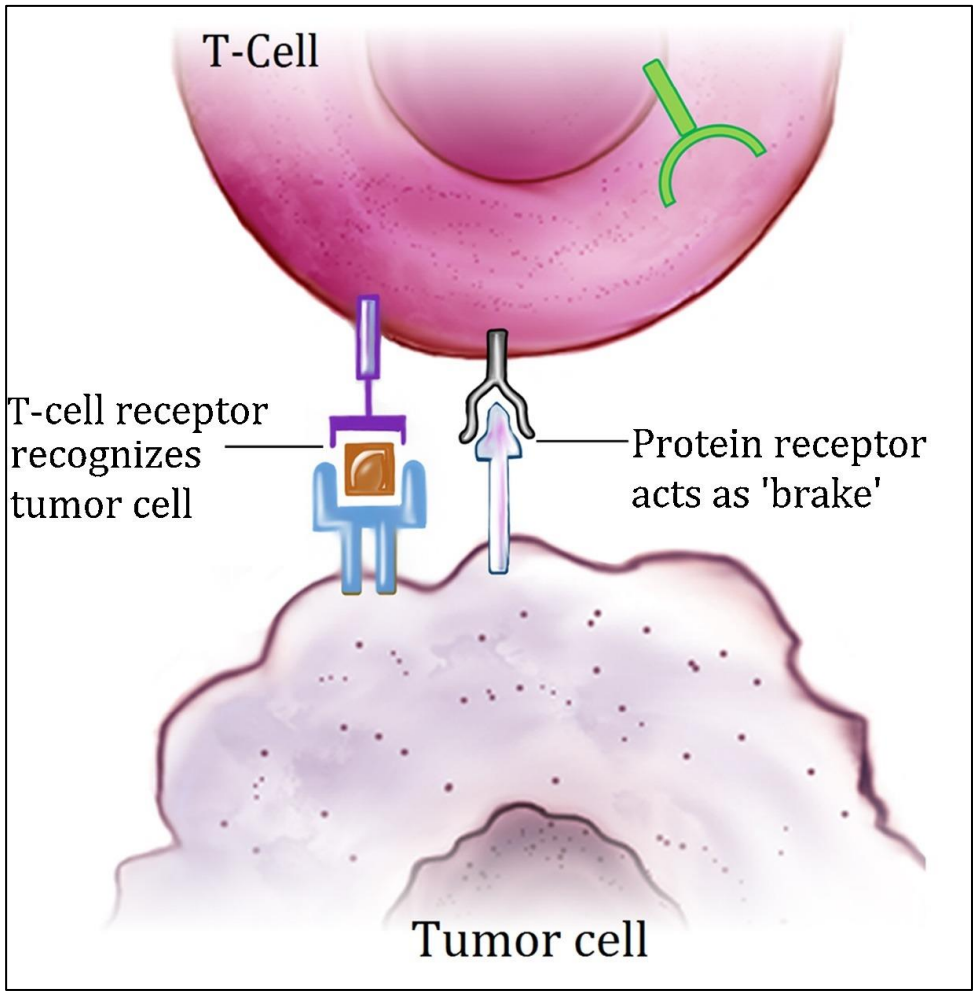


- Genes can be turned on and off in cancer cells
- Studying this allow us to develop drugs that block the growth and spread of cancer by interfering with specific molecules (“targets") involved in cancer growth

Immuno-oncology

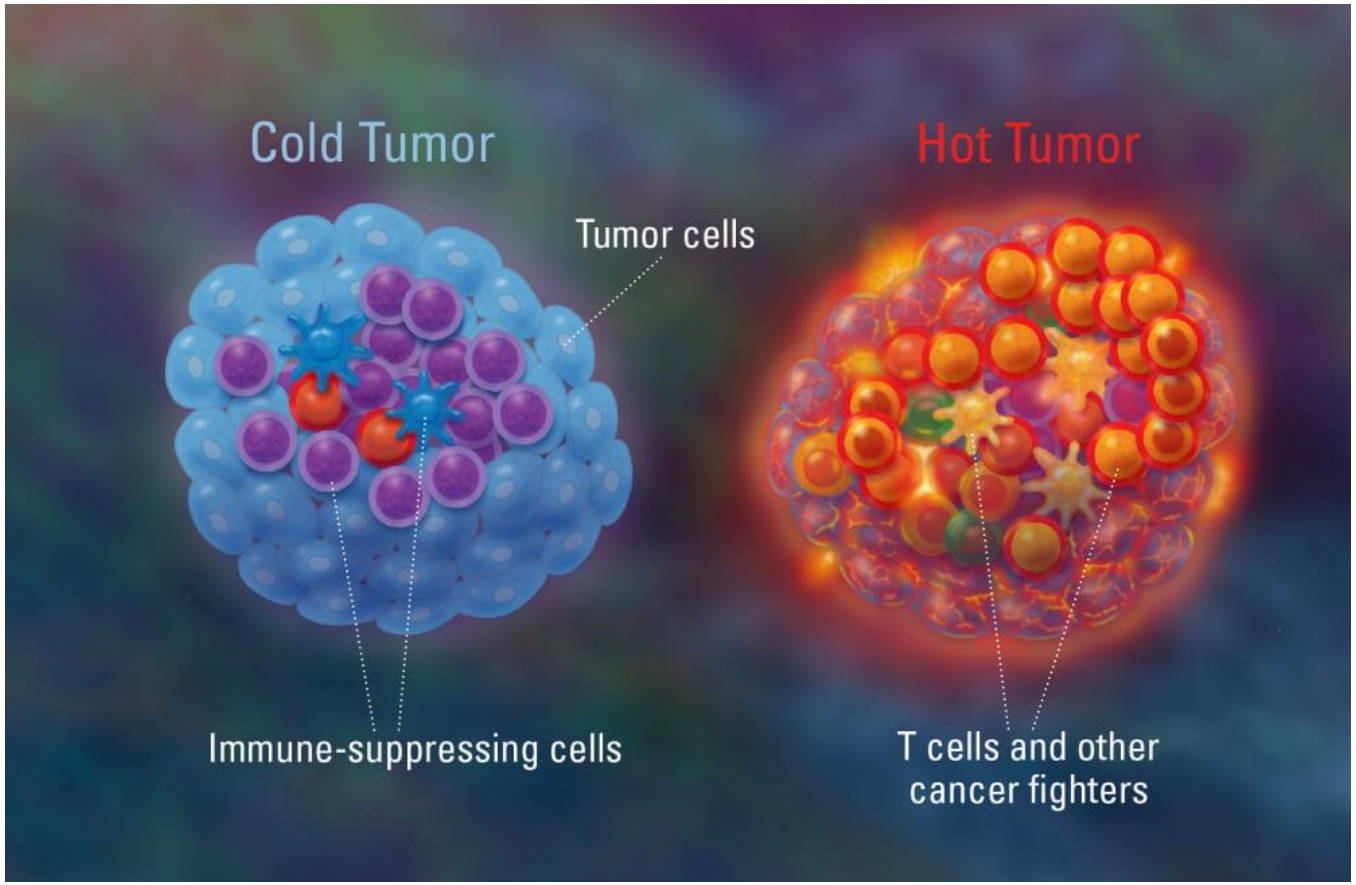


Cancer Therapy: Immuno-oncology



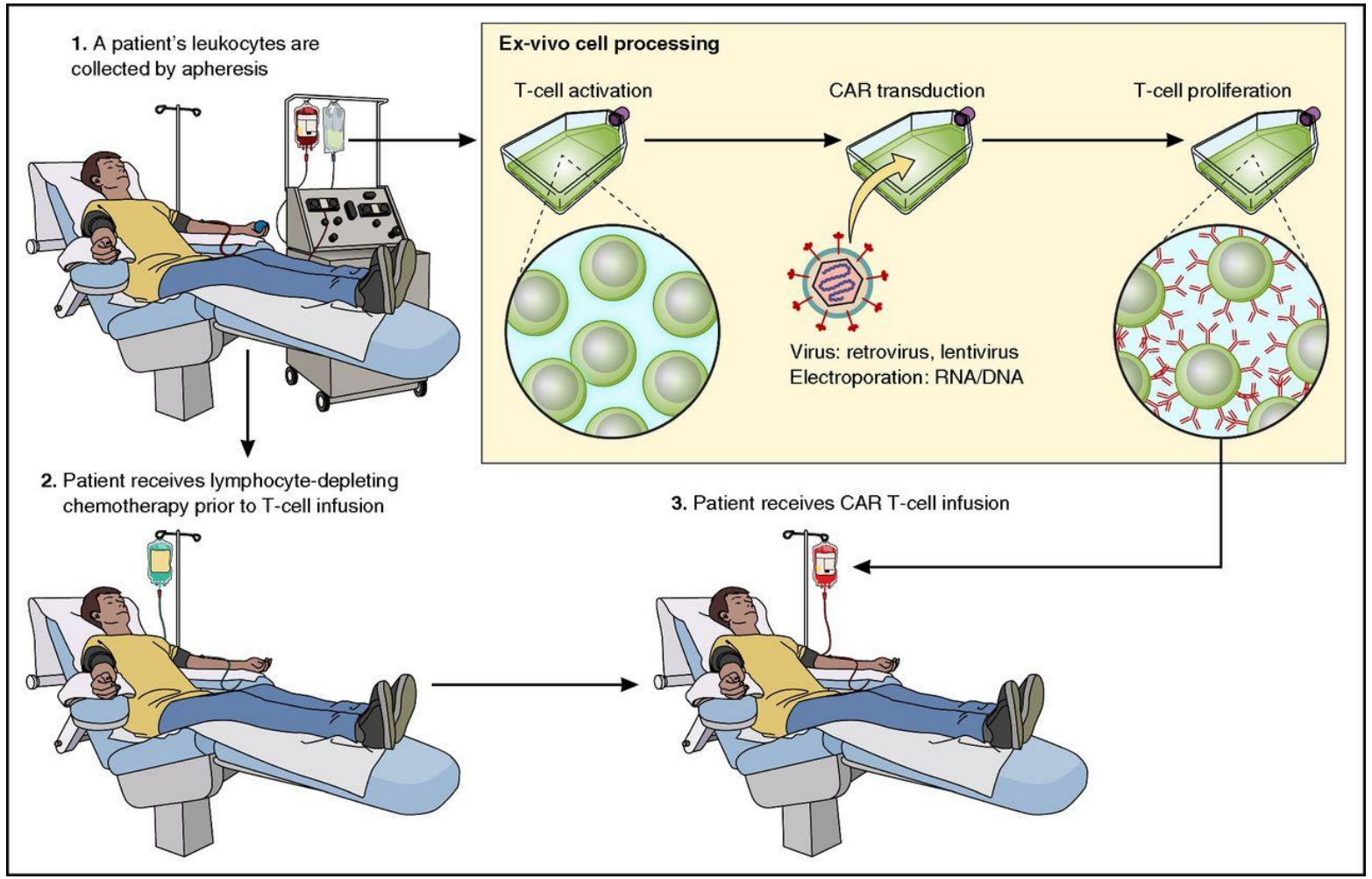
- New Immunotherapy drugs help the patients immune cells to recognise cancer cells as foreign and begin to attack…

Not all cancers respond to immunotherapy…



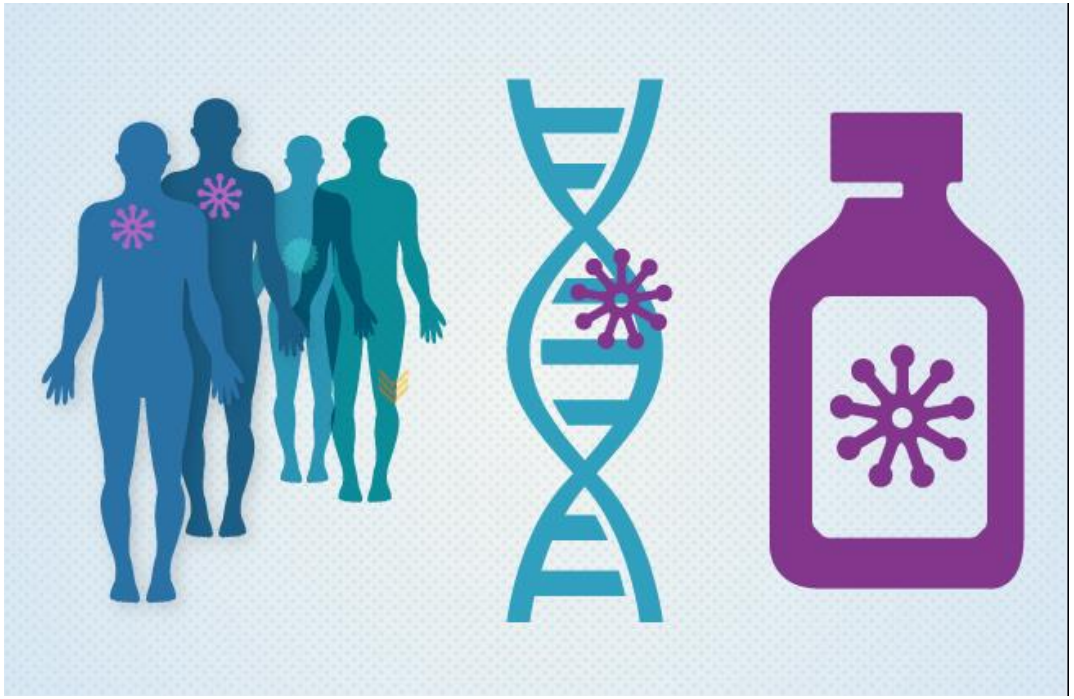
- Some cancers block the immune cells from reaching the tumour **“cold”**
- Some cancers are full of immune cells which activate quickly in response to immunotherapy drugs **“hot”**

CAR T Cell Therapy



Lekha Mikkilineni, and James N. Kochenderfer Blood 2017;130:2594-2602

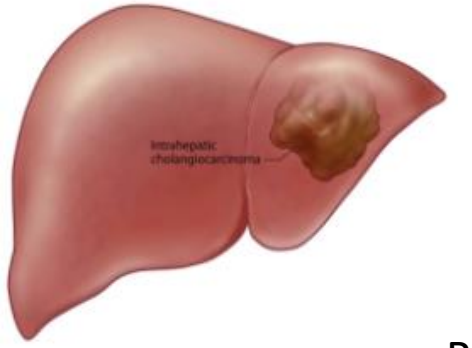
Precision Oncology Pilot Program

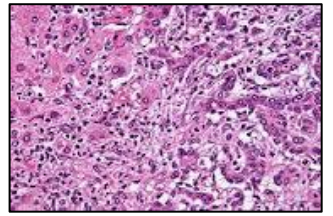


Personalised Cancer Treatment…

Step 1: Patients provide samples of blood and tumour tissue

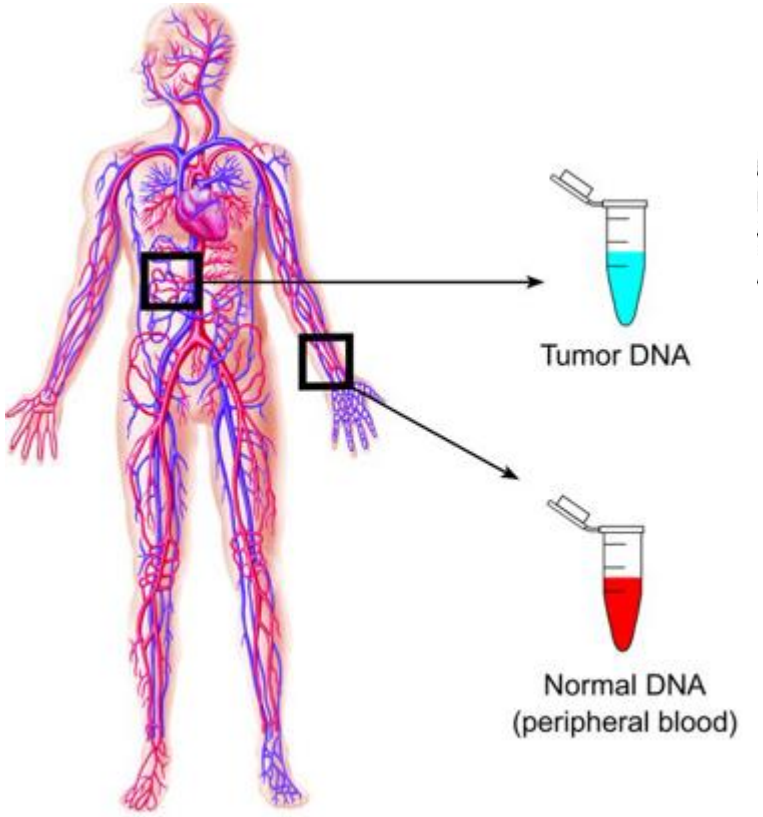
Informed consent





Research biopsies & blood samples

Step 2: Every letter of DNA & RNA is read…

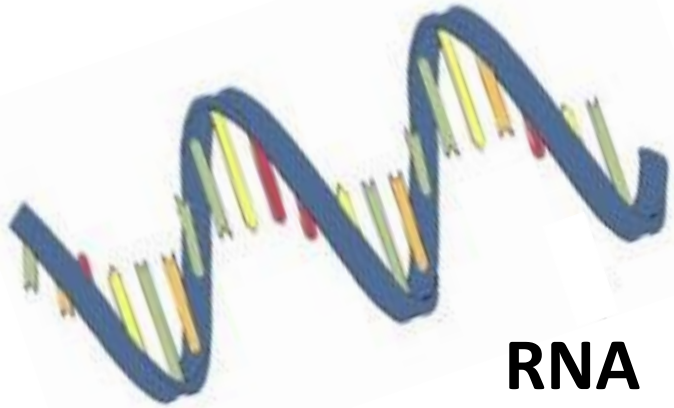


ACATATTCGATCGTAGCTAGTGCTATATCTGGAAGAAACTTTTAGCTAGC

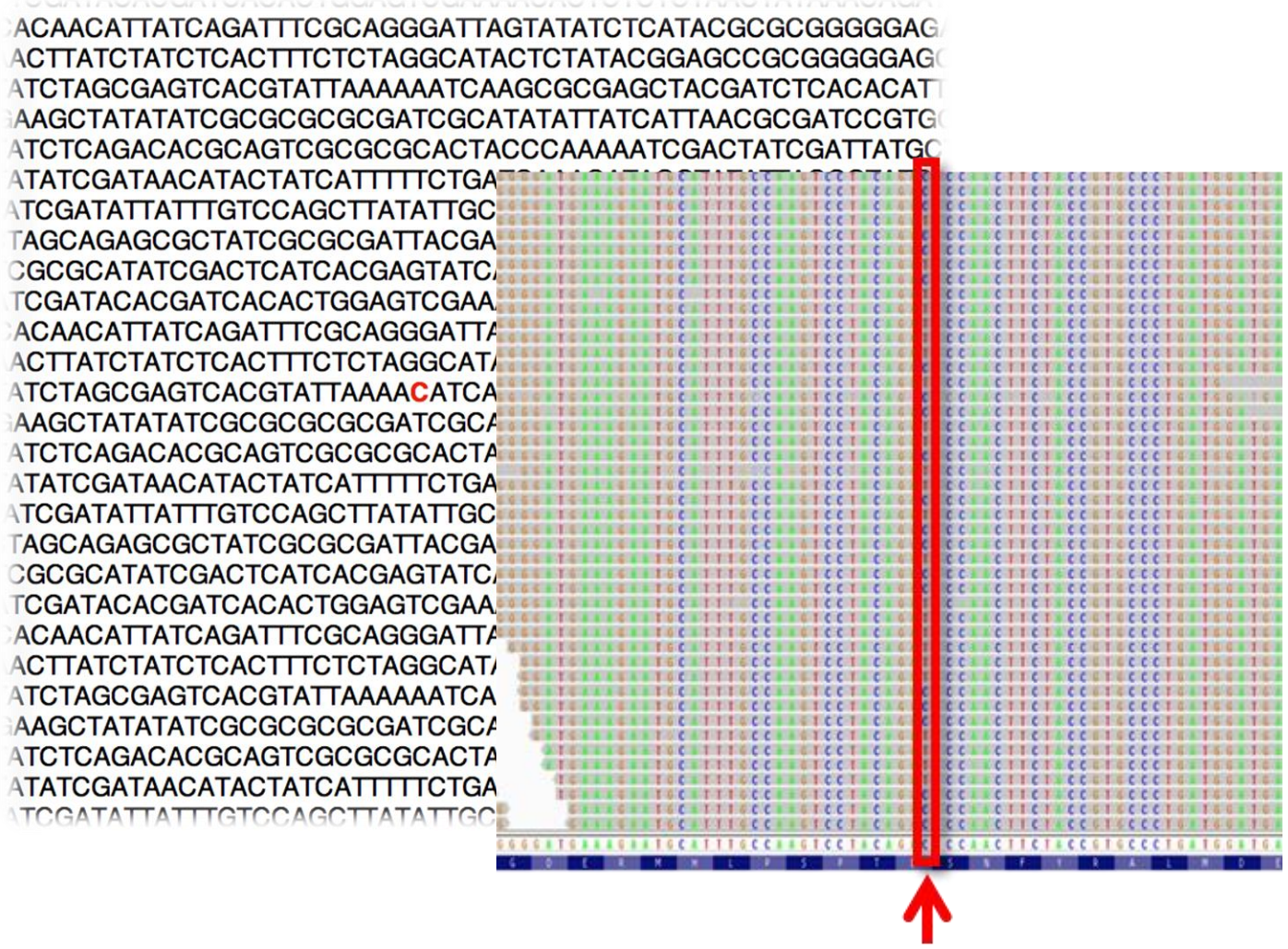
GGCTATCTGGGGGATATTTATCGATCGACACCCACTGCTACACTGATCGA

Step 3: The genetic code of each cancer is analysed to identify a “driver” gene

DNA

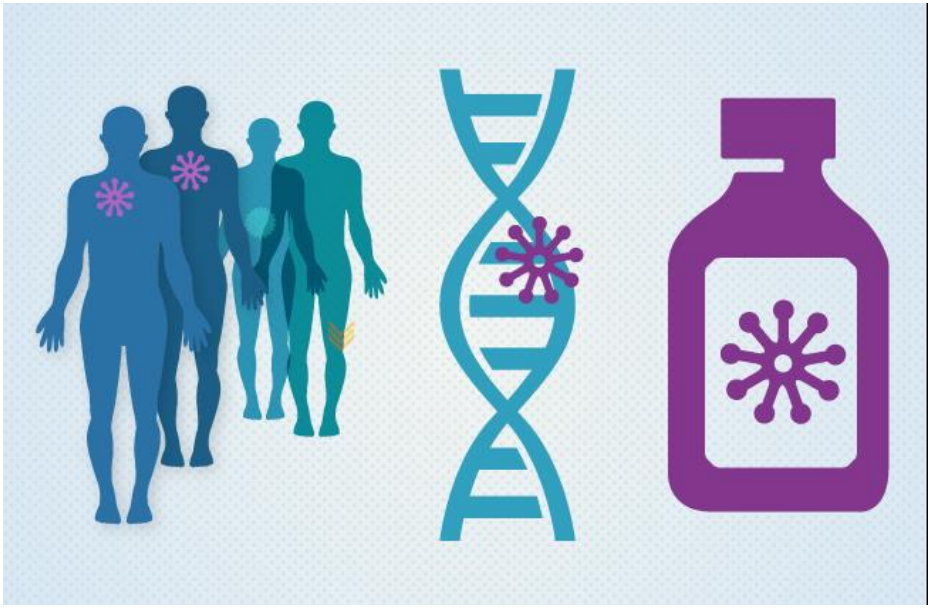


RNA



Step 4: Experts meet to discuss individual patient findings & consider best treatment

Genomics Tumour Board



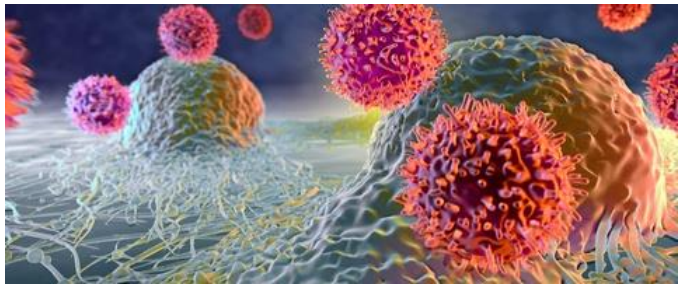
Personalised treatment plan

Step 5: Medical oncologist discusses results with patient in clinic

Treatment plan

Clinical Trials

Chemotherapy



Immunotherapy

Targeted therapy

PERSONALISED CANCER THERAPY

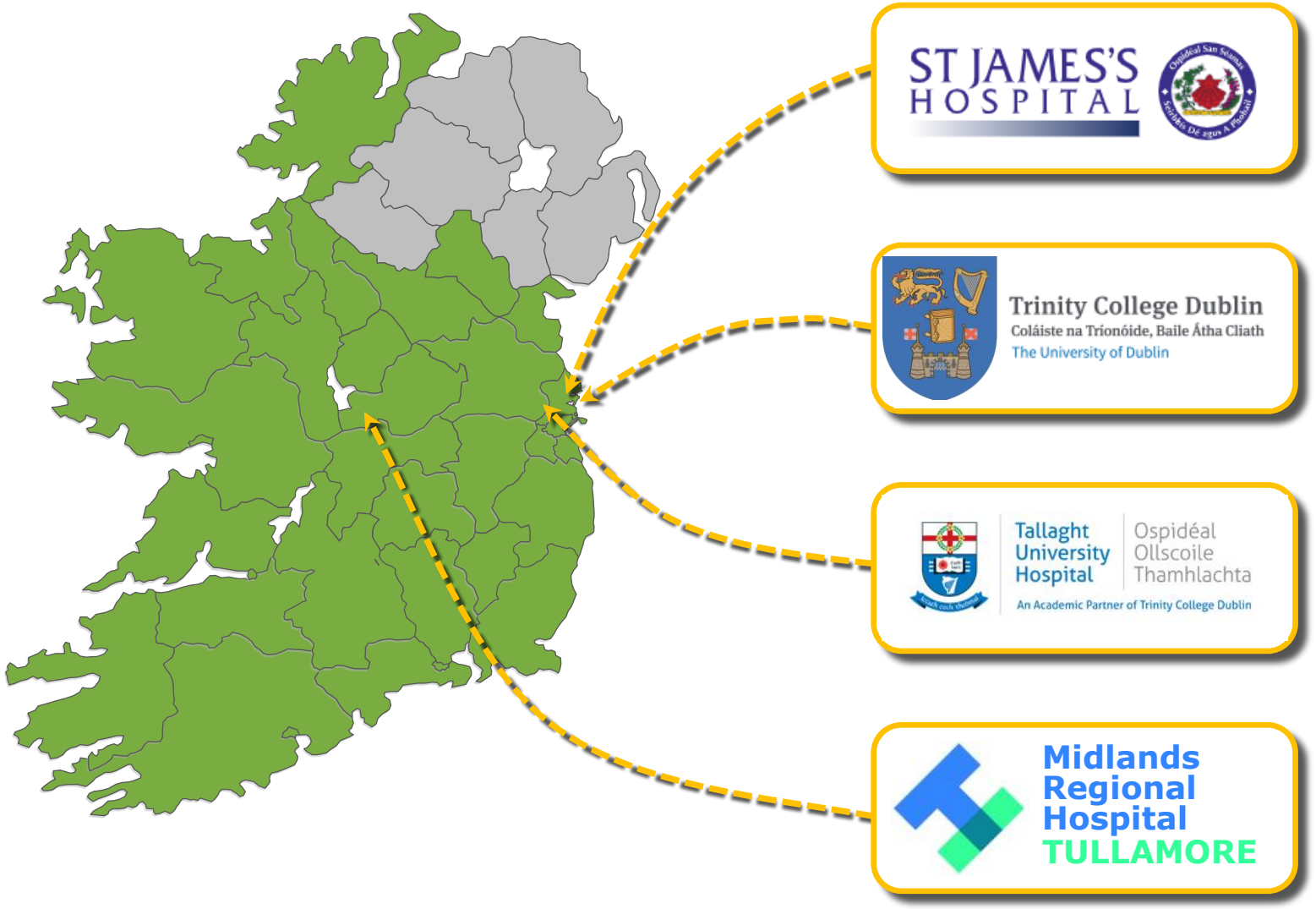
Cancer treatment – the future

- New treatments in development are mostly immuno-oncology or targeted therapies.

- We need more research to identify blood / tissue markers which can predict whether a patient will respond to chemotherapy and/or to novel agents.

- More and better clinical trials are essential

The Trinity Academic Cancer Trials Group



Trinity Academic Cancer Trials Group

PILLAR 1

Education & Training

Medical, Nursing and Admin staff across cancer clinical research

PILLAR 2

Driving Innovation

Improve development of cancer trials by securing competitive funding

PILLAR 3

Highest Standards

Professionalise the approach and minimise friction / duplication of effort

PILLAR 4

Breadth & Depth

Informed by PPI Programme, to transform patients' lives

Trinity St James Cancer Institute : A National Project

In November 2020, Trinity St. James's Cancer Institute (TSJCI) was formally accredited by the Organisation of European Cancer Institutes.

- TSJCI is the only OECI-accredited Cancer Centre in Ireland – hopefully more to follow soon

- Vision to combine cutting-edge scientific expertise with highly specialised clinical care and innovative education programmes to improve patient outcomes.

Vision of Trinity St James's Cancer Institute

To integrate innovative and ground-breaking cancer science with patient focussed clinical care through translation of key research finding into incremental advances in the prevention, diagnosis and treatment of cancer; providing national leadership to decrease cancer mortality and improve survival of patients with cancer in Ireland and internationally.

ST JAMES'S HOSPITAL

Ospidéal San Séamas
Seirbhís Dé agus A Phobail

OECI CANCER CENTRE

Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
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