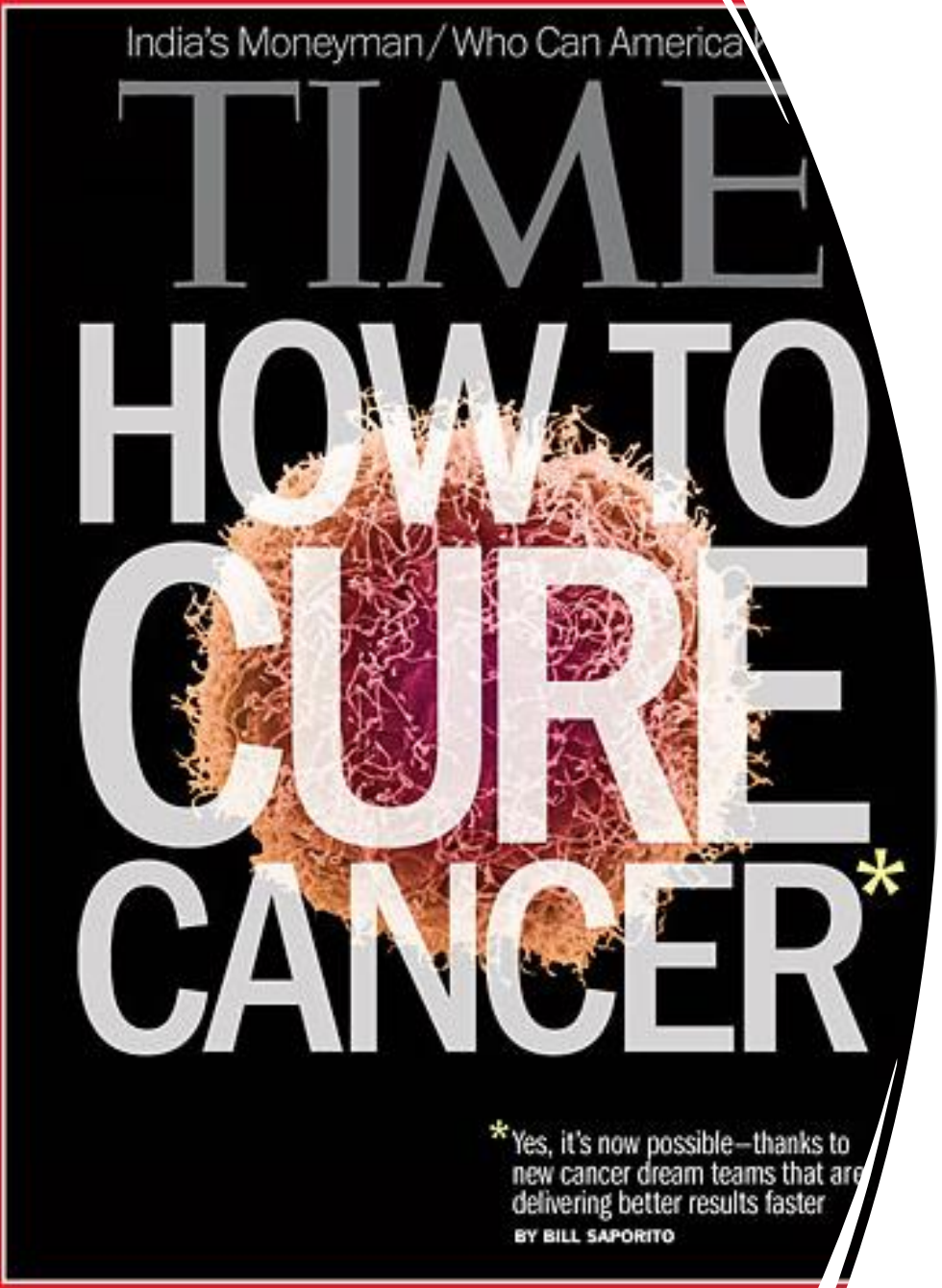
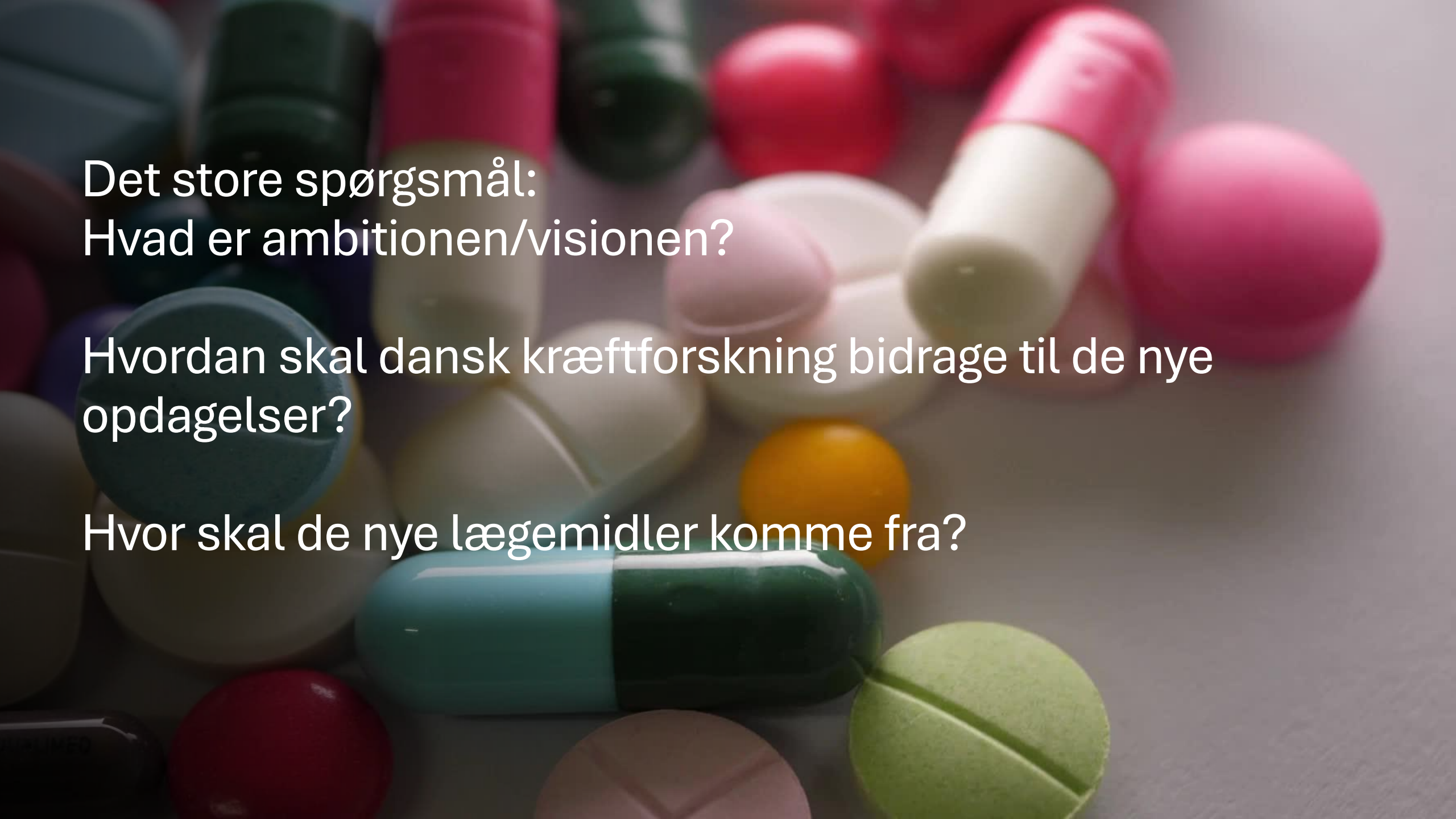



# Et blik udefra og ind - hvad kan vi lære af udlandet?



Det store spørgsmål:
Hvad er ambitionen/visionen?

Hvordan skal dansk kræftforskning bidrage til de nye opdagelser?

Hvor skal de nye lægemidler komme fra?

How to cure cancer?
From chemotherapy, targeted therapy to Refractory/Relapsed disease!
How to find the solutions and who will do the work?

How is cancer research organized abroad?

Vision, strategy, and impact!

# The Comprehensive Cancer Center

# Bridging the gaps
# - a continuum from research discoveries to clinical application

# Memorial Sloan Kettering Cancer Center

Numbers - 2023

- 133 research labs
- 21,077 total staff
- 25,591 patient admissions
- 1,002,260 outpatient visits
- 498 in-patient beds
- 738,363 diagnostic procedures
- 1,861 Clinical Investigation Protocols

# Sloan Kettering Institute

- Mission: To supply the scientific knowledge for new approaches to cancer treatment, diagnosis, and prevention through preclinical research.
- Opened in 1948.
- Mission-inspired, curiosity-driven cancer research.
- Basic Discoveries: genes, genomic events, molecular structures, cell organelles, signaling pathways, metabolic steps, cell fates, developmental routes, tumorigenic drivers, and metastatic processes.
- SKI research important for some of the first chemotherapy drugs (mercaptopurine), the first immunotherapies, and several targeted therapies. 10 new FDA approved drugs developed at MSKCC since 1980.

# The MSK Preclinical-Clinical Research Enterprise


## Programs (10)

Molecular Biology, Cell Biology, Structural Biology, Developmental Biology, Cancer Biology and Genetics, Computational Biology, Immunology, Chemical Biology, Molecular Pharmacology and Human Oncology and Pathogenesis

## Collaborative Research Centers (26)

Metastasis, Brain Tumor, Hematological Malignancies, Cell Engineering, Cancer Systems Immunology, Epigenetics Research, Experimental Therapeutics, Stem Cell Biology, Pancreatic Cancer Research, Experimental Immuno-Oncology .....

# Collaborative Cancer Center

ICR The Institute of Cancer Research

The ROYAL MARSDEN
NHS Foundation Trust

# The ICR

- A world-leading research institute
- A member institution of the University of London
- A charity
- Employs 1,100 scientific and professional staff plus 160 PhD students.
- 90 research groups.
- 8 research and clinical divisions: Genetics and Epidemiology, Structural Biology, Cancer Biology, Molecular Pathology, Cancer Therapeutics, Breast Cancer, Radiotherapy and Imaging, and Clinical Studies.
- 15 Collaborative and interdisciplinary research centers

# Driving discovery: from bench to bedside and back again

- The ICR has an outstanding track record of achievement dating back more than 100 years
- The research spans fundamental biology through to clinical trials – covering all tumour types, including common and rarer cancers
- The unique partnership with The Royal Marsden hospital and *'bench to bedside and back again'* approach means we can achieve a unique national and global impact
- The ICR has identified 21 new drug candidates since 2005, 13 progressing in clinical development.

# The ICR-Royal Marsden Partnership

- The ICR and The Royal Marsden have worked in partnership for more than a century.
- The ICR and The Royal Marsden together are ranked in the top four centres for cancer research and treatment worldwide.
- The Royal Marsden with the ICR has been a National Institute for Health and Care Research (NIHR) Biomedical Research Centre (BRC) for cancer since 2007.
- The ICR and Royal Marsden contributed to 23% of all cancer drugs licensed by the EMA between 2000 and 2016.



The ROYAL MARSDEN NHS Foundation Trust | ICR The Institute of Cancer Research

# Longstanding track record of impact

First proposed the link between smoking and lung cancer

*Cook et al., 1932, Proc. R. Soc. Lond. B.*

Discovered, and with RM, developed, chemotherapy drugs busulfan, chlorambucil, melphalan and carboplatin

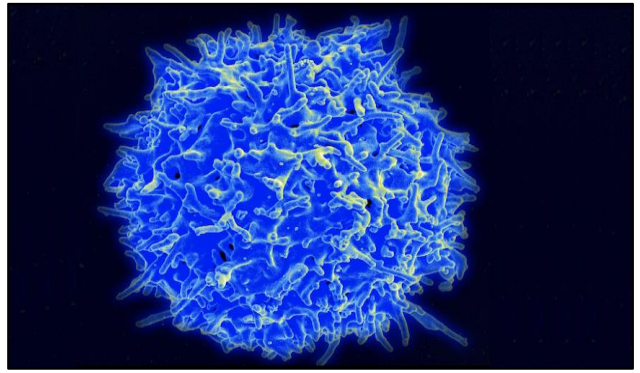
*Haddow et al., 1953, Lancet; Everett et al., 1953, J Chem Soc; Bergel and Stock, 1954, J Chem Soc.*

Provided the first conclusive evidence that damage to DNA is the cause of cancer

*Brookes and Lawley, 1960, Biochem J; Brookes and Lawley, Nature, 1964.*

Discovered the function of the thymus – paving the way for T cell checkpoint immunotherapy drugs

*Miller, 1961, Lancet.*



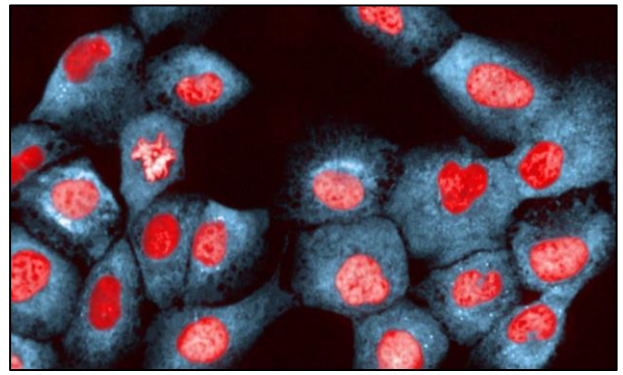
# Longstanding track record of impact

Revealed the biochemical steps of the RAS-RAF-MAP kinase pathway and discovered the oncogene NRAS.

*Hall, 1983, Nature; Leevers, 1992, EMBO J; de Vries-Smits, 1992, Nature: Howe, 1992, Cell; Cowley, 1994, Cell.*

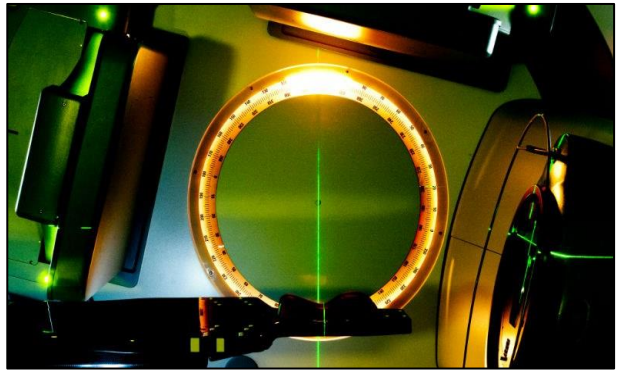
Identified the breast cancer gene *BRCA2*, which laid the groundwork for developing novel forms of therapy for BRCA-associated cancers.

*Wooster,1994, Science; Wooster, 1995, Nature.*



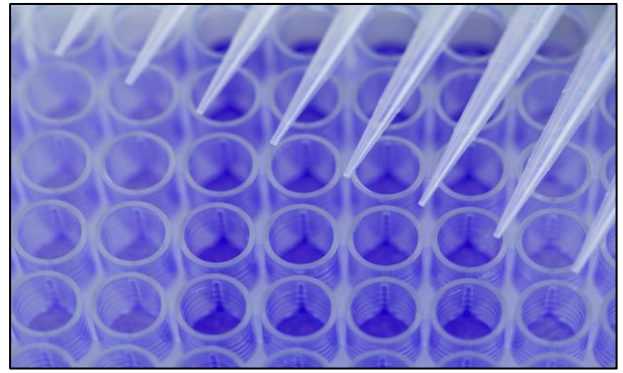
Made major contributions to modern high precision radiotherapy techniques – IMRT, IGRT

*Webb, 2005, Phys Med Bio; Nutting, 2011, Lancet Oncol.*



Played a major role in characterising the BRAF gene and its role in cancer, increasing our understanding of malignant melanoma.

*Davies, 2002, Nature; Wan, 2004, Cell.*



# Abiraterone – a life-extending prostate cancer drug

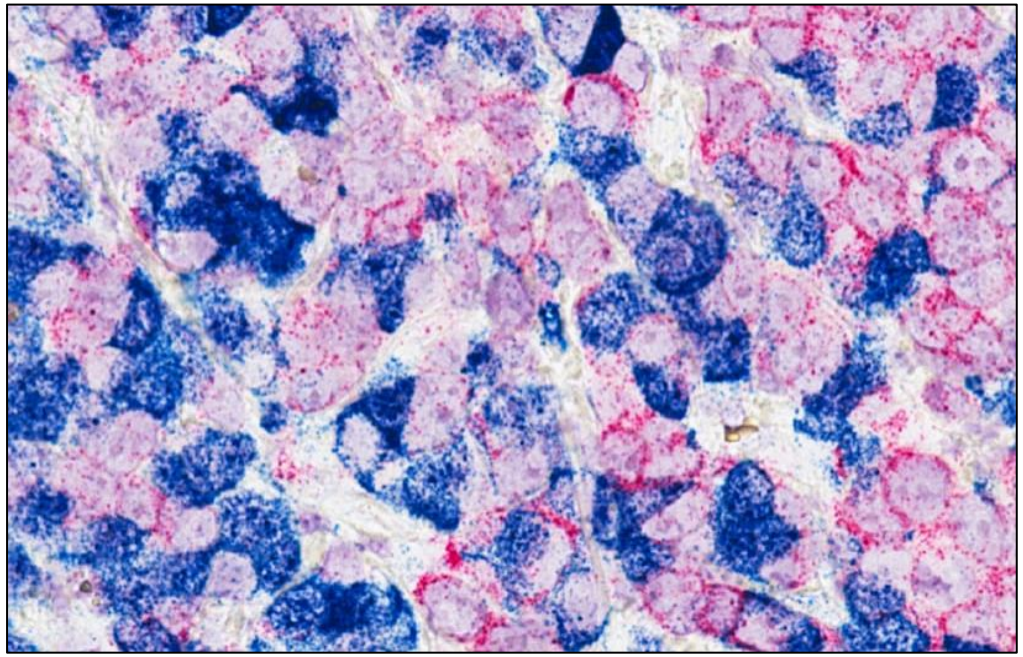
- ICR scientists showed that prostate cancers growth was driven by an alternative source of androgens, rather than being truly hormone refractory.
- Following this discovery abiraterone was designed, synthesised and developed at ICR.
- Subsequent ICR/RM-led phase I, II and III clinical trials demonstrated prolonged survival and improved quality of life for patients with prostate cancer.
- Abiraterone was first approved to cancers that stopped responding to standard treatment. Abiraterone is now approved in more than 100 countries and is used to treate new diagnosed advanced prostate cancer.
- Hundreds of thousands of men with prostate cancer across the world are now able to live longer and with a better quality of life, thanks to abiraterone.


*Zytiga (abiraterone) tablets*

O'Donnell A et al., *Br J Cancer,* 2004; Attard et al., *J Clin Oncol,* 2008; de Bono et al., *N Engl J Med*, 2011; Ryan et al., *N Engl J Med*, 2013; James et al., *N Engl J Med*, 2017.

# Targeting PARP inhibitors to patients with mutations in the BRCA genes

- After discovering the *BRCA2* gene, ICR scientists went on to show that BRCA2 is involved in DNA repair.
- In 2005, an ICR team showed that that compounds that block the activity of a DNA repair protein called PARP could selectively kill cancer cells with a faulty *BRCA1* or *BRCA2* gene, leaving normal cells relatively unharmed.
- In parallel, teams in Sheffield and Newcastle showed the same concept.
- The world's first phase I trial of olaparib, the first PARP inhibitor, was carried out in the ICR and RM Drug Development Unit (DDU). ICR/RM went on to lead a phase II multi-centre trail in ovarian cancer. Many phase III trials of olaparib and other PARP inhibitors have subsequently shown efficacy in ovarian, breast, prostate and pancreatic cancer.
- Olaparib was first approved for BRCA-mutated ovarian cancer in 2014. PARP inhibitors are now used to treat ovarian, breast, prostate and pancreatic cancers across the world.

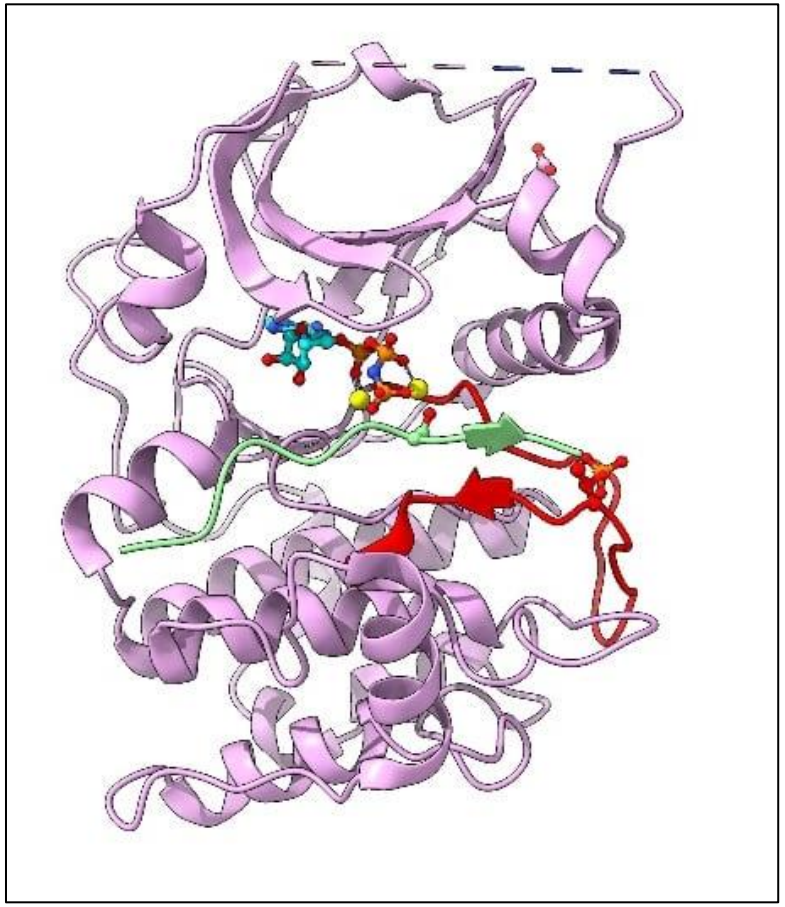


*Breast cancer cells. Credit: Min Yu, National Cancer Institute \ USC Norris Comprehensive Cancer Center*

Farmer et al., *Nature*, 2005; Fong et al., *N Engl J Med*, 2009; Kaye et al., *J Clin Oncol*, 2012. Hussain et al., *N Engl J Med*, 2020; Tutt et al., *N Engl J Med*, 2021

# Enabling the discovery and development of AKT inhibitors

- An ICR team solved the 3D protein structure of AKT and then ICR began a drug discovery research programme aiming to find AKT inhibitors.
- In 2005, one lead series discovered by the ICR and Astex was licensed to AstraZeneca.
- Capivasertib was discovered by AstraZeneca after a collaboration with Astex Therapeutics (and its collaboration with the ICR and Cancer Research Technology Limited).
- The first-in-human trial of capivasertib was carried out in the ICR/RM Drug Development Unit.
- The phase III CAPtello-291 trial, led by Prof. Nick Turner, showed the benefit of capivasertib alongside hormone therapy to treat patients with ER+, HER2- breast cancer. This trial underpinned the FDA and EMA approval of capivasertib along side fulvestrant.

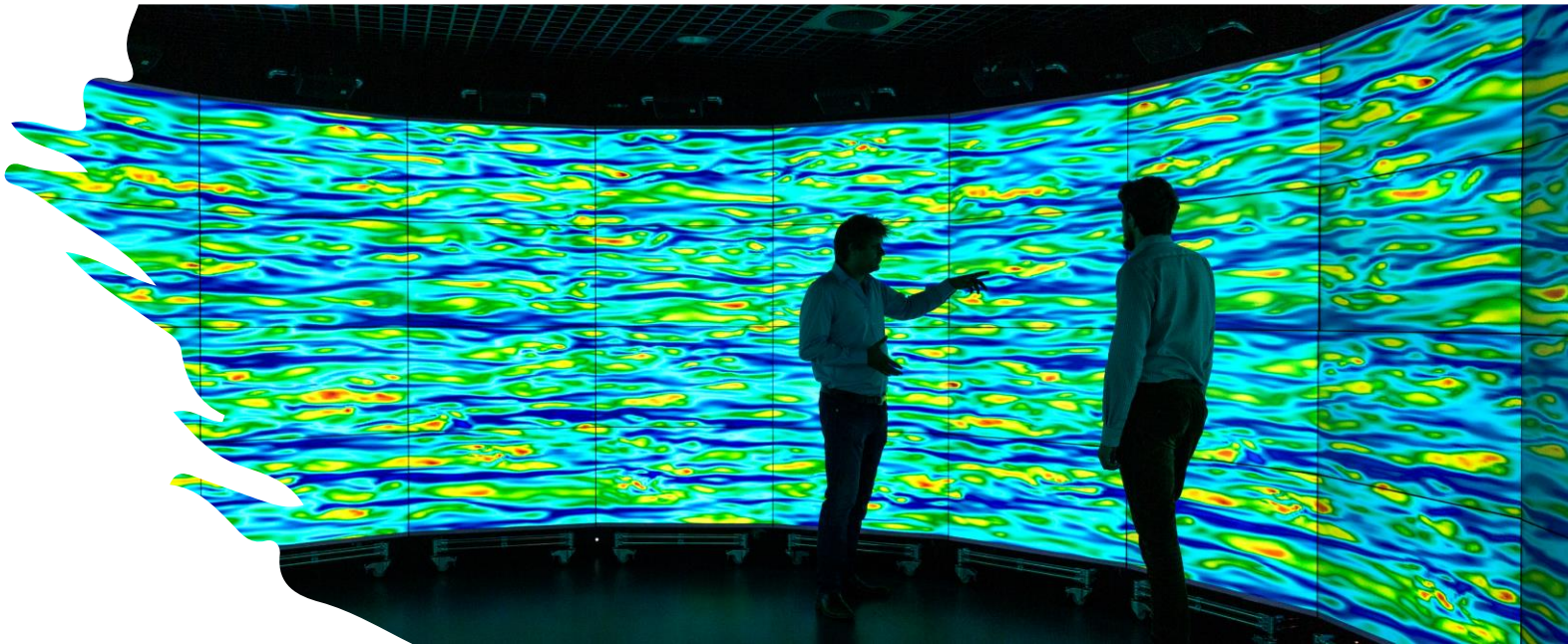


*Cartoon representation of AKT2 (PKB beta) kinase domain. Kinase domain in pink, activation segment in red, GSK3 substrate peptide in light green. The phosphorylated Thr309 residue (activation segment) and Asp474 (phosphoSer474 mimic), and ATP-Mn are shown. Credit: David Barford*

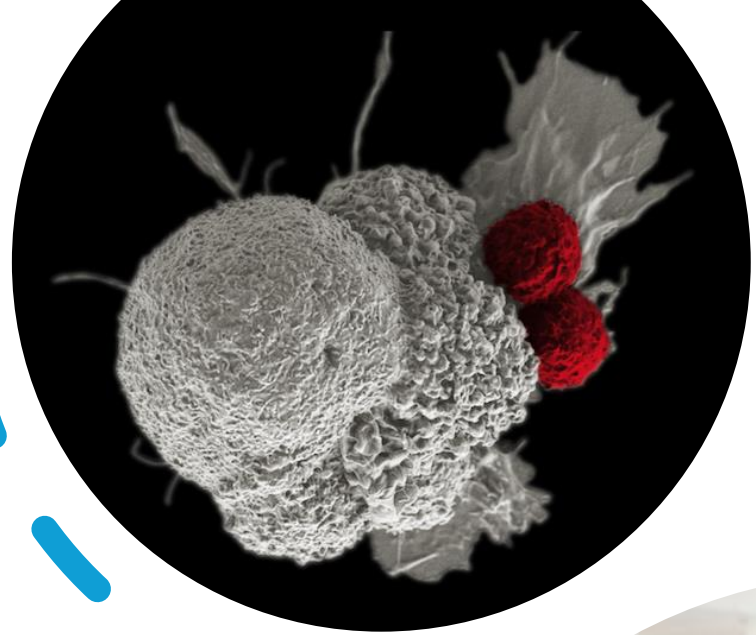
Yang et al., *Nat Struct Biol*, 2002, Yang et al., *Mol Cell*, 2002, Saxty, J *Med Chem*, 2007, Davies et al., *Mol Biol*, 2007.

# Hvad kan vi lære af udlandet?

- Vision – hvad vil vi opnå? Ambition?
- Strategi – hvordan opnår vi det ?
  - Samarbejde på tværs – organisering
  - Udvikle interdisciplinære og integrerede tilgange til identificering, udvikling og implementering af nye behandlinger for kræftpatienter
  - Karriereveje – har vi de rigtige personer?
  - Funding



# Hvad bør vi tænke over?

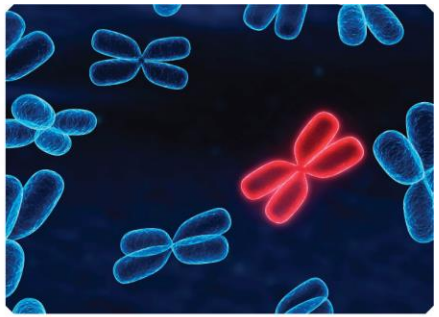


Vision og strategi for dansk kræftforskning

- Hvem er ansvarlige?
- Koordinering, samarbejde og integration af kræftforskningen
  - Regioner, hospitaler, universiteter, fonde, patienter
  - Lokalt og/eller nationalt?
  - Ressourcer – ministeriel koordinering
  - Uddannelses- og karriereforløb
  - Er dansk kræftforskning nationalt eller internationalt orienteret?

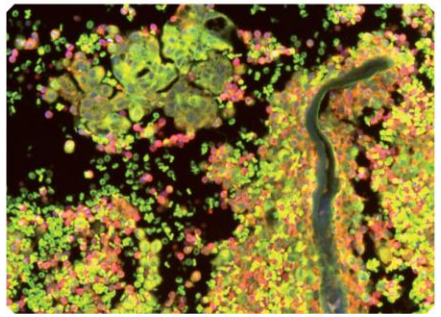
Unrivalled track record

ICR The Institute of Cancer Research



# Making the discoveries that defeat cancer

ICR



One of the world's most influential cancer research institutes