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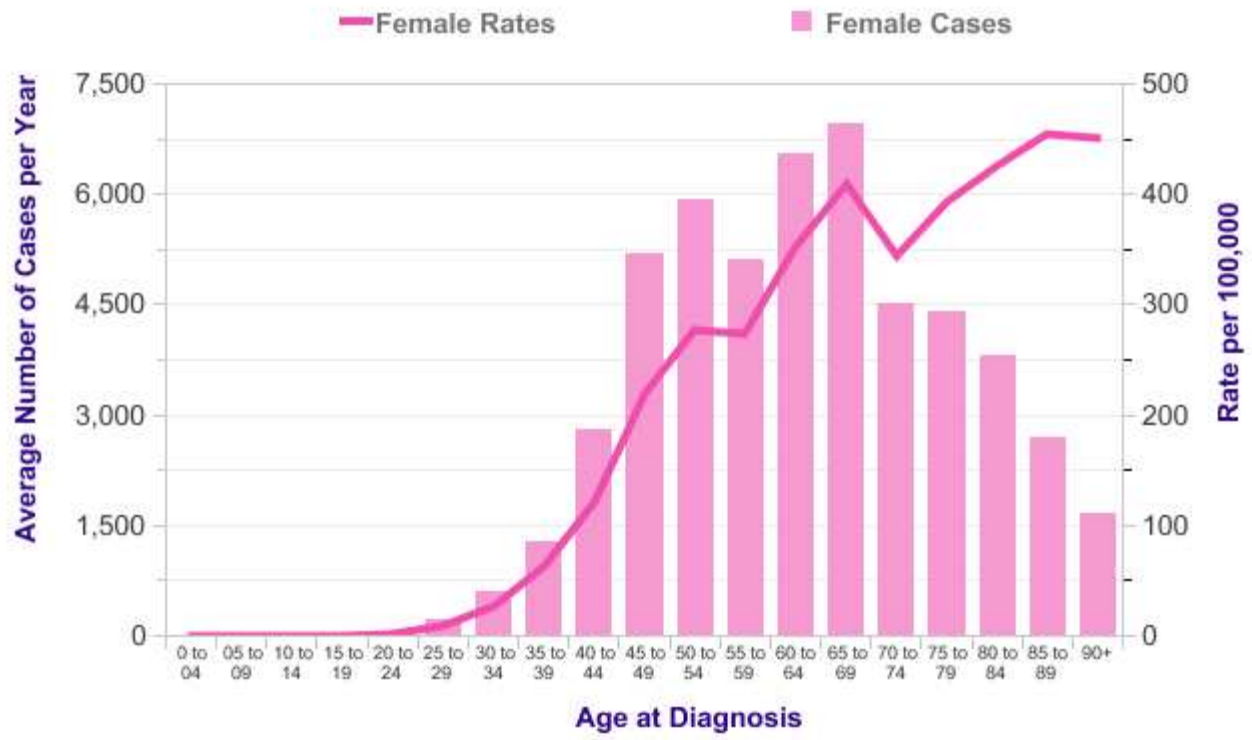
Early detection of breast cancer

Professor Denise Kendrick
Division of Primary Care

Average Number of New Cases Per Year and Age-Specific Incidence Rates per 100,000 Population Females, UK 2011-2013

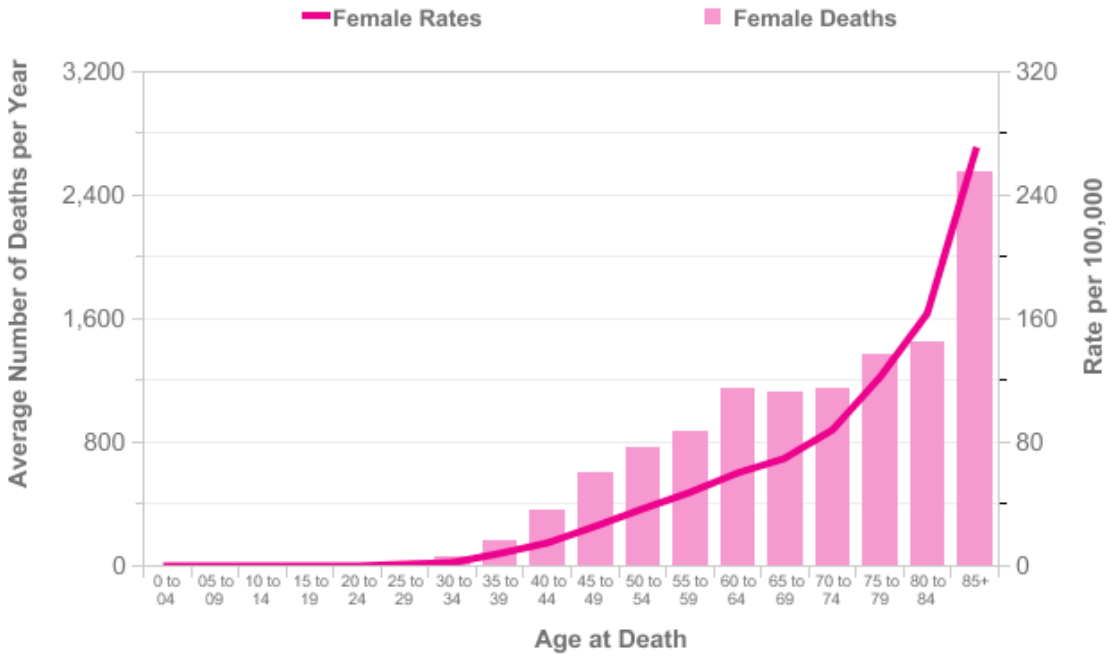


CANCER RESEARCH UK

Source: cruk.org/cancerstats

Cancer Research UK, http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/incidence-invasive#heading-One
Accessed 6/5/16

Average Number of Deaths per Year and Age-Specific Mortality Rates per 100,000 Population UK 2010-2012

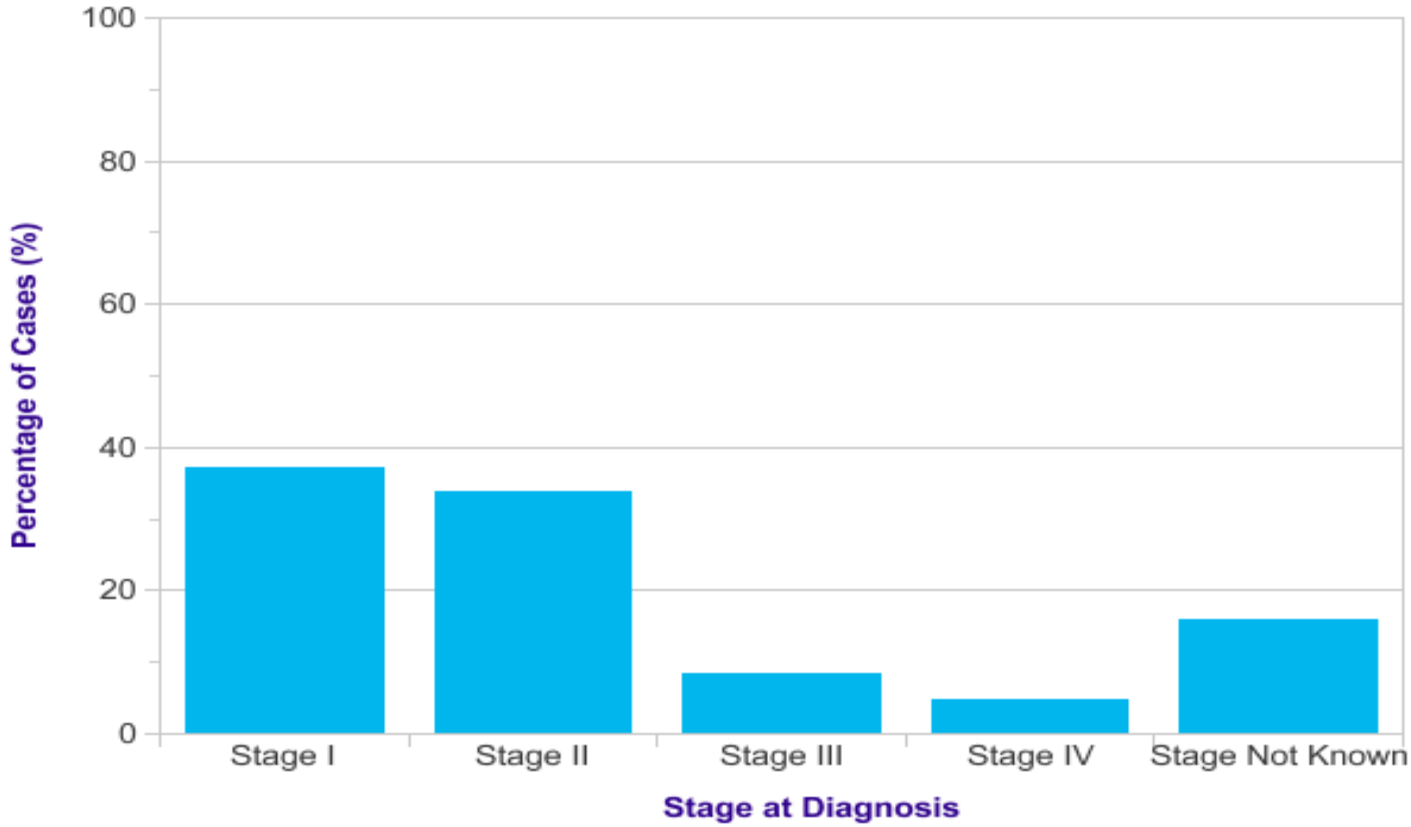


CANCER RESEARCH UK

Source: cruk.org/cancerstats

Cancer Research UK, http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/mortality#heading-One
Accessed 6/5/16

Proportion of Cancers Diagnosed at Each Stage, All Ages, England 2013

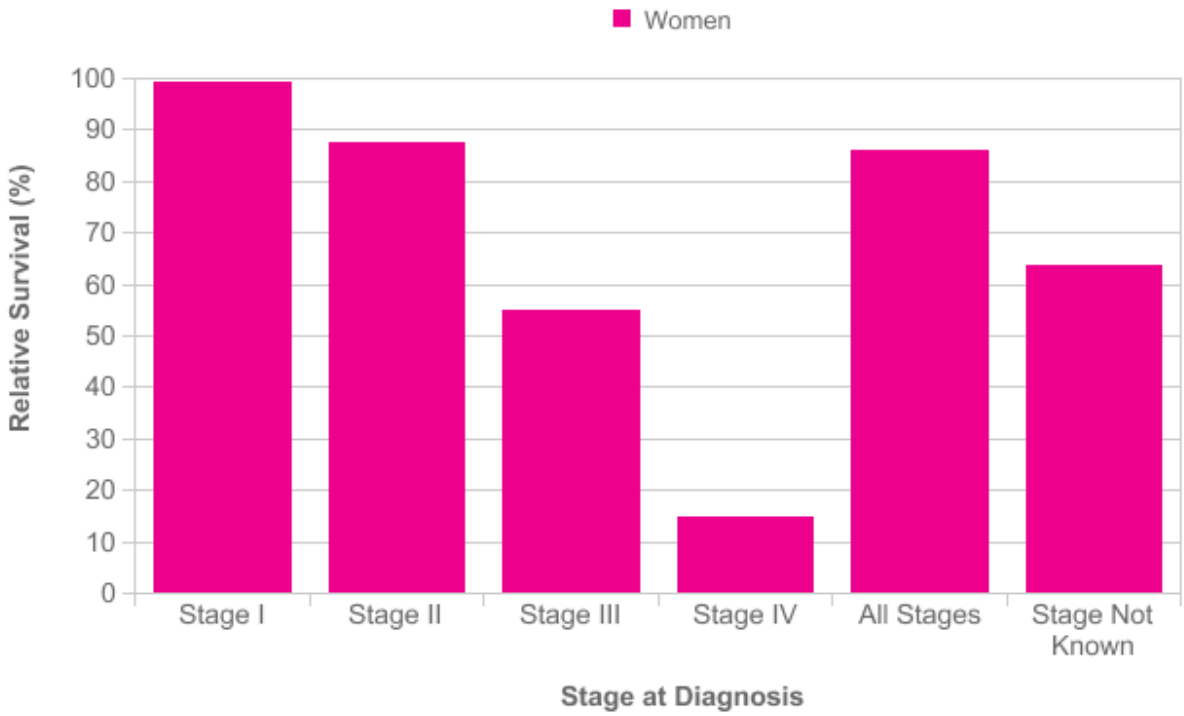


CANCER RESEARCH UK

Source: cruk.org/cancerstats

Cancer Research UK, http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/incidence-invasive#heading-Three
Accessed 6/5/16

Five-Year Relative Survival (%) by Stage, Adults Aged 15-99, Former Anglia Cancer Network, 2002-2006



CANCER RESEARCH UK

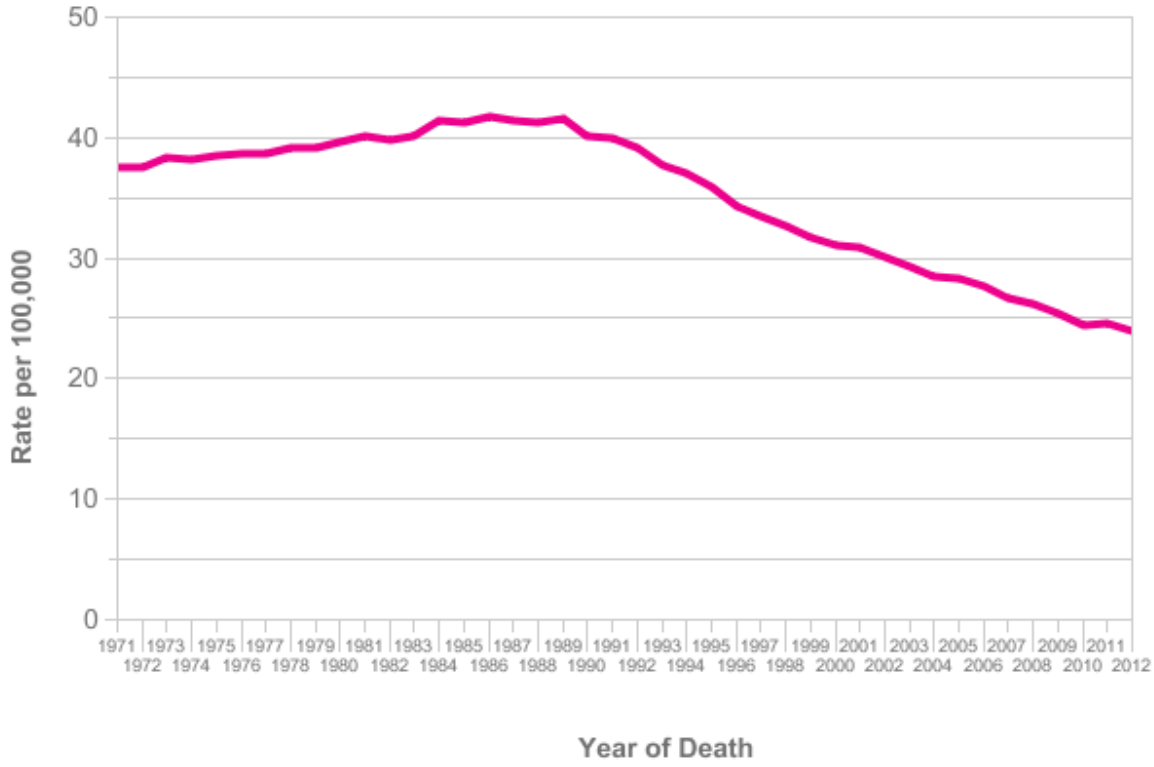
Source: cruk.org/cancerstats

Cancer Research UK, http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/survival#heading-Three
Accessed 6/5/16

Prepared by Cancer Research UK

Original data source: The National Cancer Registration Service, Eastern Office. Personal communication.
http://ecric.org.uk/

European Age-Standardised Mortality Rates per 100,000 Population, Females, UK 1971-2012



Mammography (50-74yrs): **23% reduction** breast cancer deaths

Only ~1/3rd of breast cancers occur between 50-74

CANCER RESEARCH UK

Source: cruk.org/cancerstats

Cancer Research UK, http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/breast-cancer/mortality#heading-Two
Accessed 6/5/16

Proven preventative treatments:
potential to prevent ~35% of all breast cancer cases

70% of all breast cancers are stimulated to grow by oestrogen

X

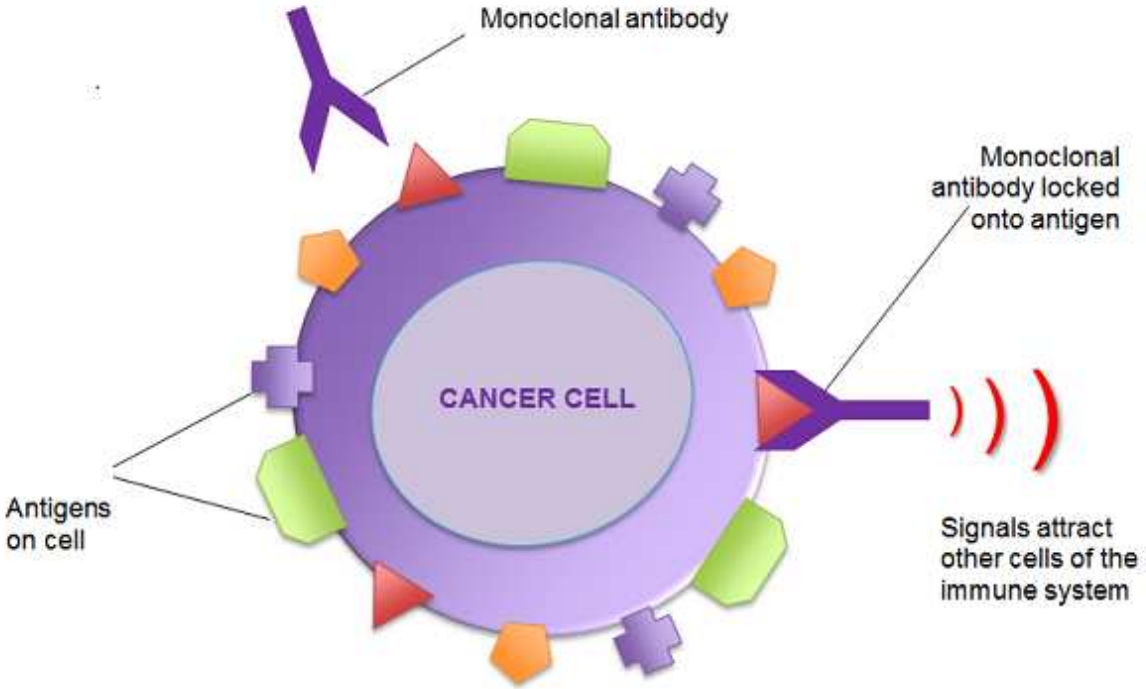
50% Prevented by drugs like tamoxifen

=

~35% of cases could be prevented

Blood test to identify at early stage

How a blood test for early detection of breast cancer works



Developing a blood test for early detection of breast cancer

- Identify antibodies that could be used
- Confirm antibodies present in early stage cancer
- **Confirm antibodies identify sufficient early stage cancers (sensitive)**
- Develop blood test combining multiple antibodies
- Test blood test on new samples (often stored)
- Evaluate blood test in the population it will be used in – clinical and cost-effectiveness

Early detection of breast cancer means

- More women have a greater chance of survival
- Improved life expectancy
- Less aggressive treatments and improved quality of life
- Less money spent on treatment – most spent in last 6 months of life
- Worldwide impact – applicable to low & medium income countries

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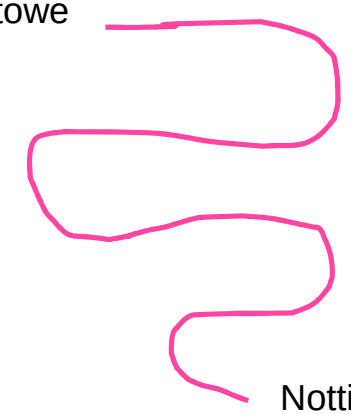
Robin Hood Walk for early detection of breast cancer, June 11th-17th



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RHWW50 £5 to 70070

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100% of all funds raised goes direct to our research

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STOPPING BREAST CANCER FROM SPREADING

Understanding, targeting and stopping metastasis

Stewart Martin, Ian Ellis, Emad Rakha, Andrew Green, Mohammed Aleskandarany and Sarah Storr (and associated research teams)

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1 in 8 UK women will be diagnosed with breast cancer

Breast cancer is the most common cancer in women worldwide

There were 1.7 million new cases in 2012 (2nd most common cancer) and 10,000 women worldwide die of breast cancer each week

In the UK over 50,000 women and around 350 men are diagnosed with breast cancer every year

10yr survival rate (women only) is ~78% **BUT**

120,000 UK women will still lose their lives over the next decade

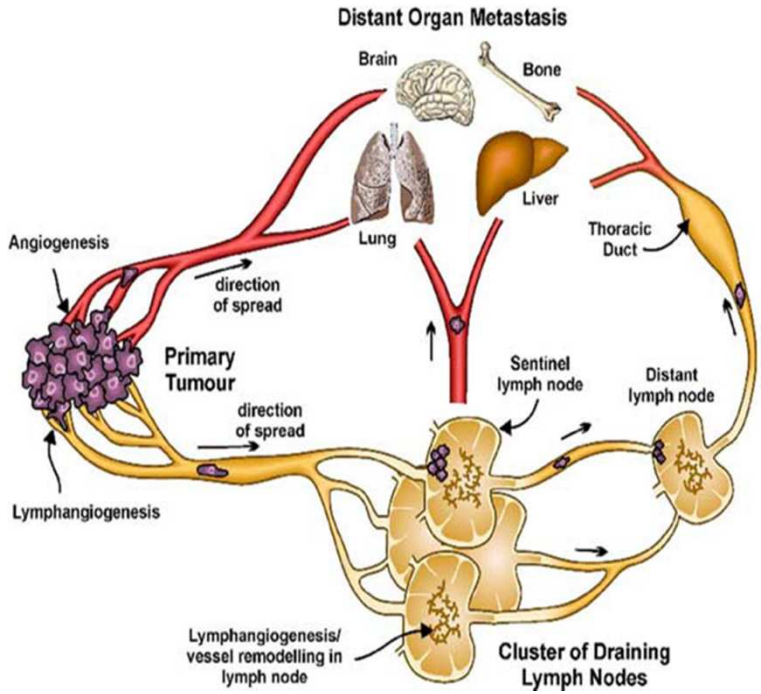
Once cancer spreads to other sites in the body, away from the site in which it originally started, it becomes much more difficult to cure.

This process of movement to other sites is called '***Metastasis***'

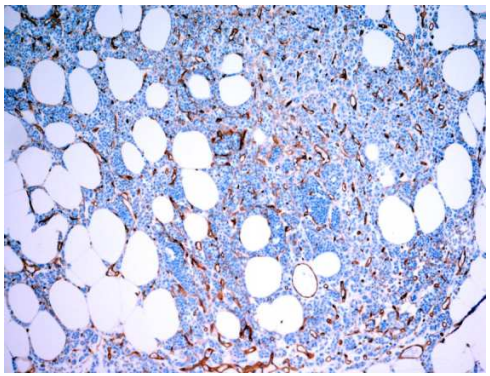
We are trying to understand why and how breast cancer spreads, with the aim of finding ways to prevent it, and to treat secondary tumours more effectively

One of the earliest stages of metastasis is lymphovascular invasion (LVI) i.e. when the tumour cells move into the blood vessels or lymphatic vessels that are present in and around the tumour.

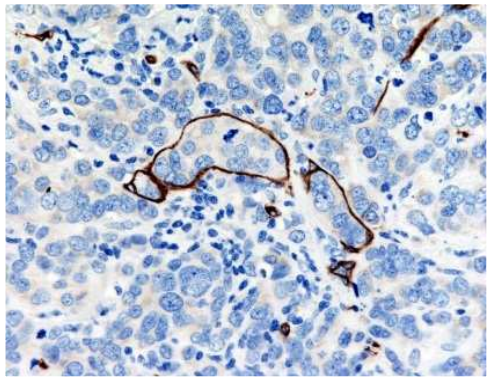
The molecular pathways/ mechanisms associated with development in breast cancer remain poorly defined (understand metastasis & LVI to **stop the spread**)



As research techniques improved we were able to examine blood and lymphatic vessels in tumours, via microscopy, to more fully understand LVI.



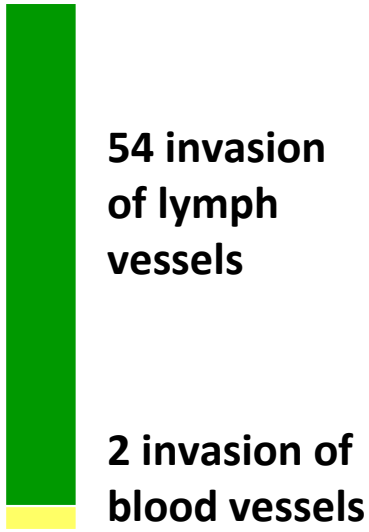
Blood vessels (CD34)



Lymphatic vessels (D2-40/Podoplanin)

In an initial study using tumours from 177 women, that although tumours had a very rich network of blood vessels **LVI was almost entirely invasion of lymphatic vessels.**

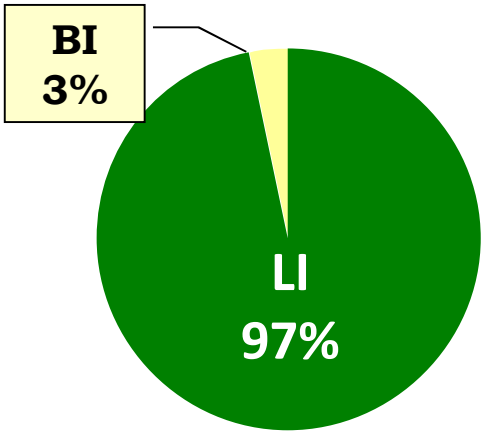
56 IHC LVI positive specimens from 177 patient cohort

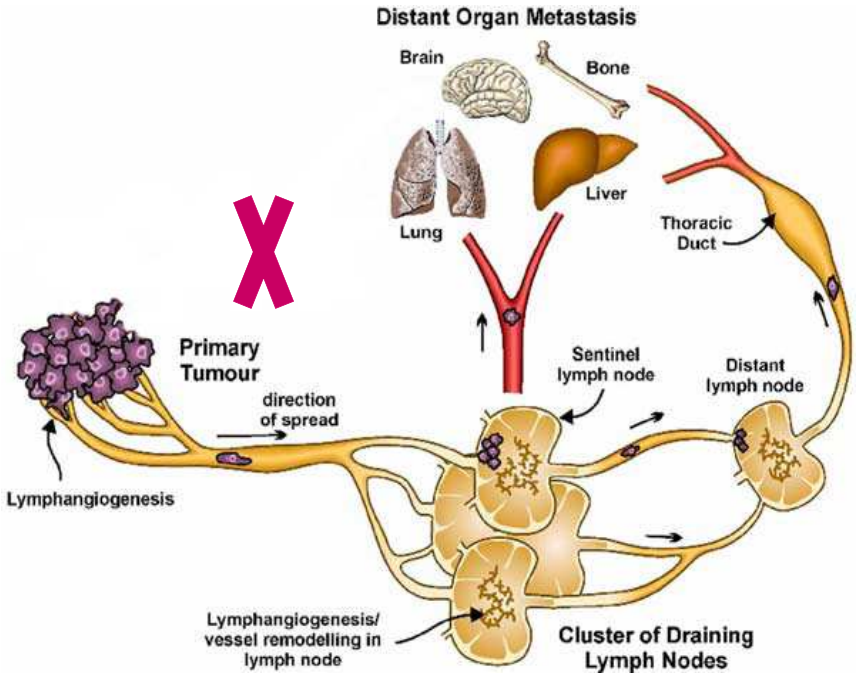


54 invasion of lymph vessels

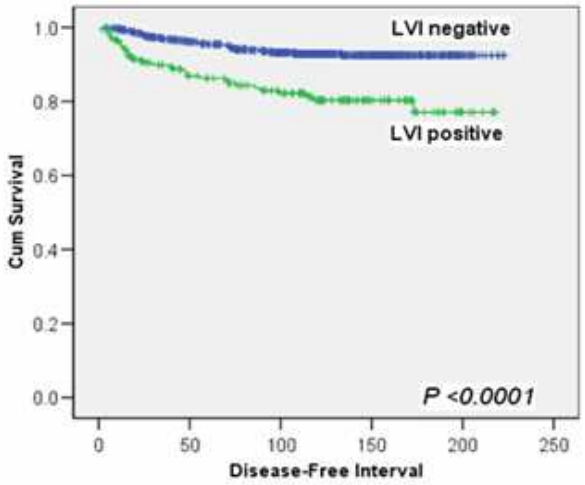
2 invasion of blood vessels

LVI in breast cancer





Verification?



1,000 patients

Such results led us to two research questions:

Why do tumour cells preferentially invade lymphatic vessels when there are so many blood vessels?

Can assessment of LVI be incorporated into routine clinical assessments and used to improve prognosis/survival?

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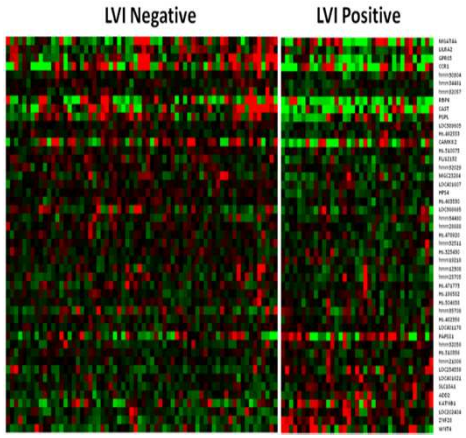
Gene Expression Profiling

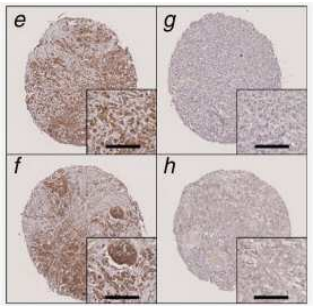
177 patients (LVI- / LVI+)

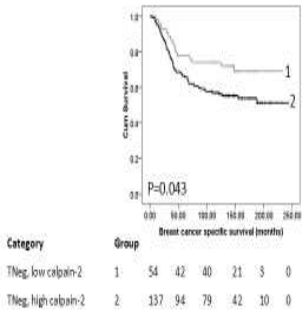


>48,000 genes → 47

Gene 2 – significantly down regulated (Calpastatin)

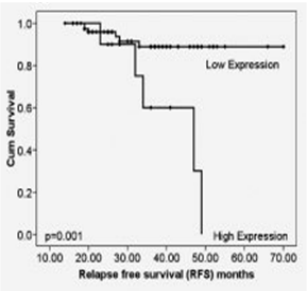
Calpastatin: Endogenous inhibitor of Calpain





IHC to examine Calpain/ Calpastatin expression in patient tumours:

- Association with LVI verified (2 independent patient cohorts, n=1371 and n=387)
- Expression particularly important in patients with Basal/TN breast cancer
- Expression is also linked to treatment response (Herceptin)



We will STOP THE SPREAD by **targeting the calpain system** – to **also improve response** to treatment and **increase patient survival**

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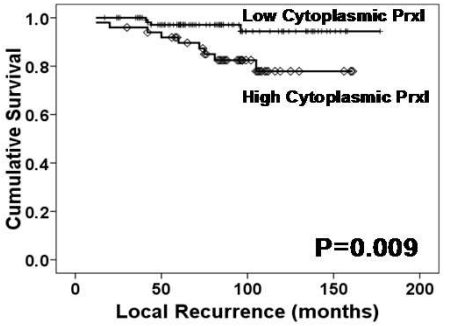
Redox protein expression:
Increased migration / metastasis & resistance to treatment

Upregulation of the Trx system also equates to a worse response to **Radiotherapy**



We will **target the Trx system** to:

- Stop the spread
- Improve response to radiotherapy

A: Novel Drugs
(Nottingham - School of Chemistry)
– Prof Chris Moody

B: Conventional drugs
– new actions (re-purposing / recycling)
e.g. Metformin

PANTHER Classification System

Other Regulators?

Global gene expression analysis
METABRIC transcriptomic data (>34,000 transcripts)
2000 patients
Genes identified belong to 21 Protein Classes

extracellular matrix protein (PC00102)
protease (PC00190) cytoskeletal protein (PC00085)
transporter (PC00227) transferase (PC00220)
cell adhesion molecule (PC00069) ligase (PC00142)
nucleic acid binding (PC00171) signaling (PC00207)
enzyme modulator (PC00095)
calcium-binding protein (PC00060)

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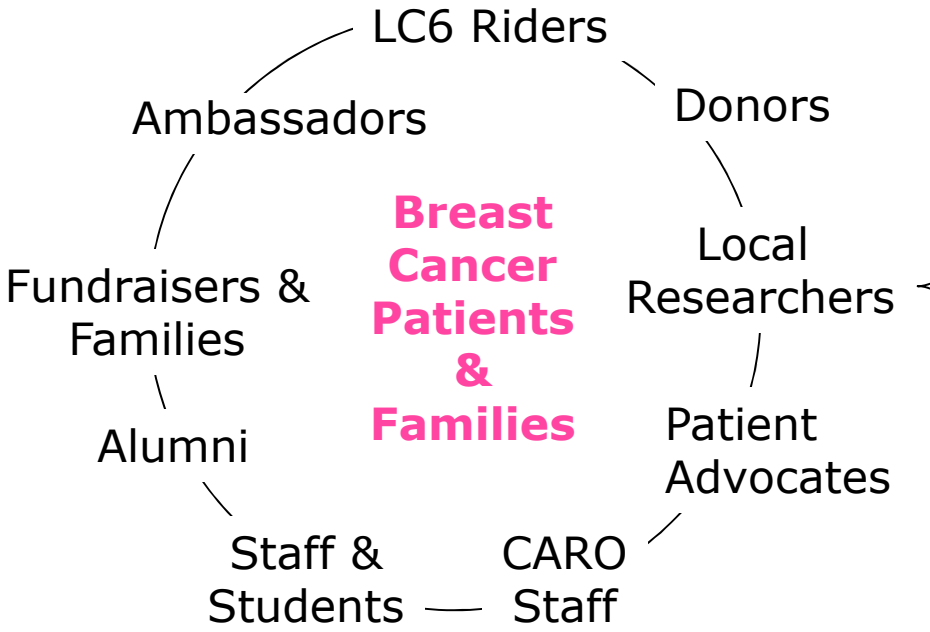
Thank You!



John Robertson (JR)

Ian Ellis
Emad Rakha
Stewart Martin

JR & KL Cheung

S Madhusudan
Anna Grabowska
Steve Chan

You can support this research

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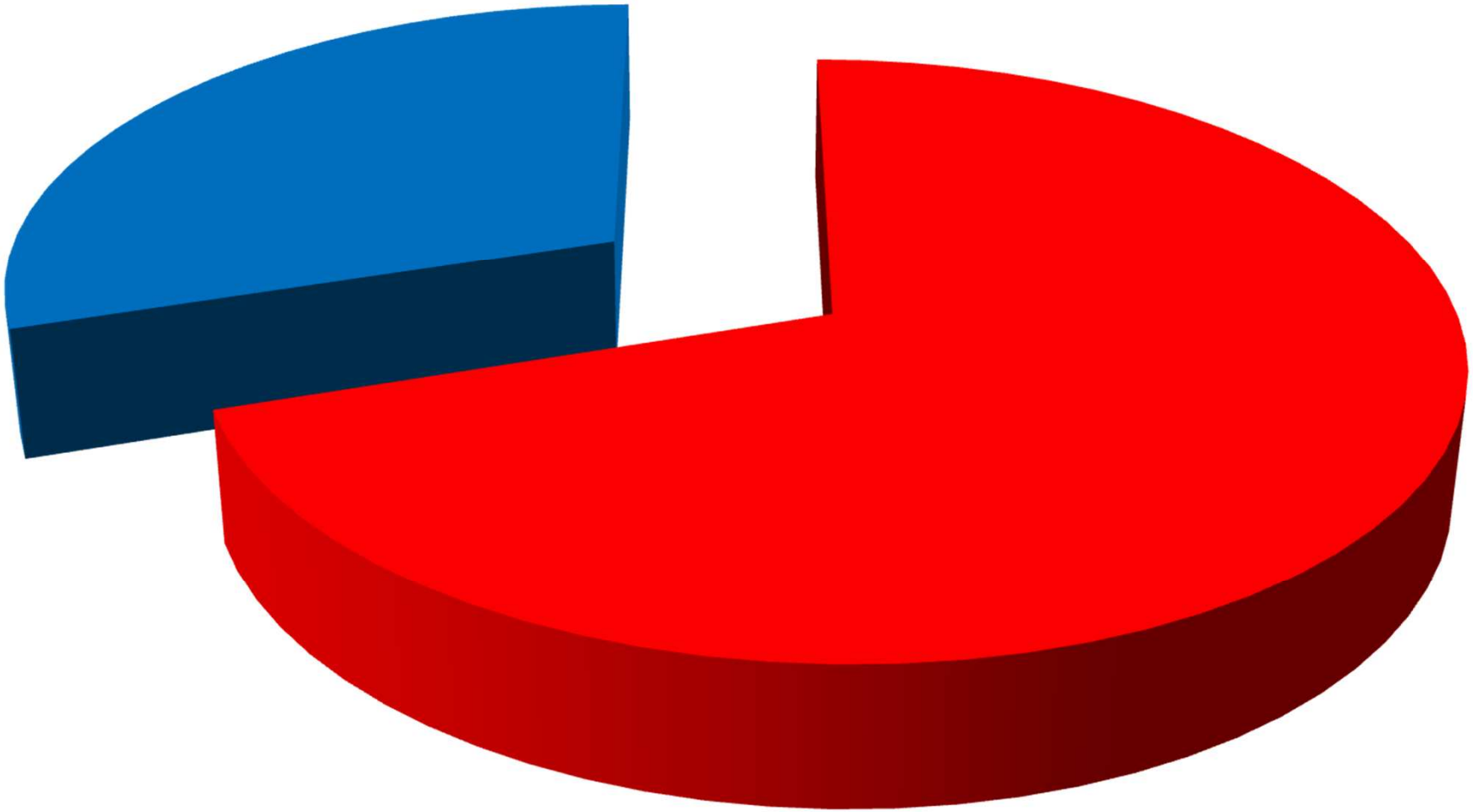
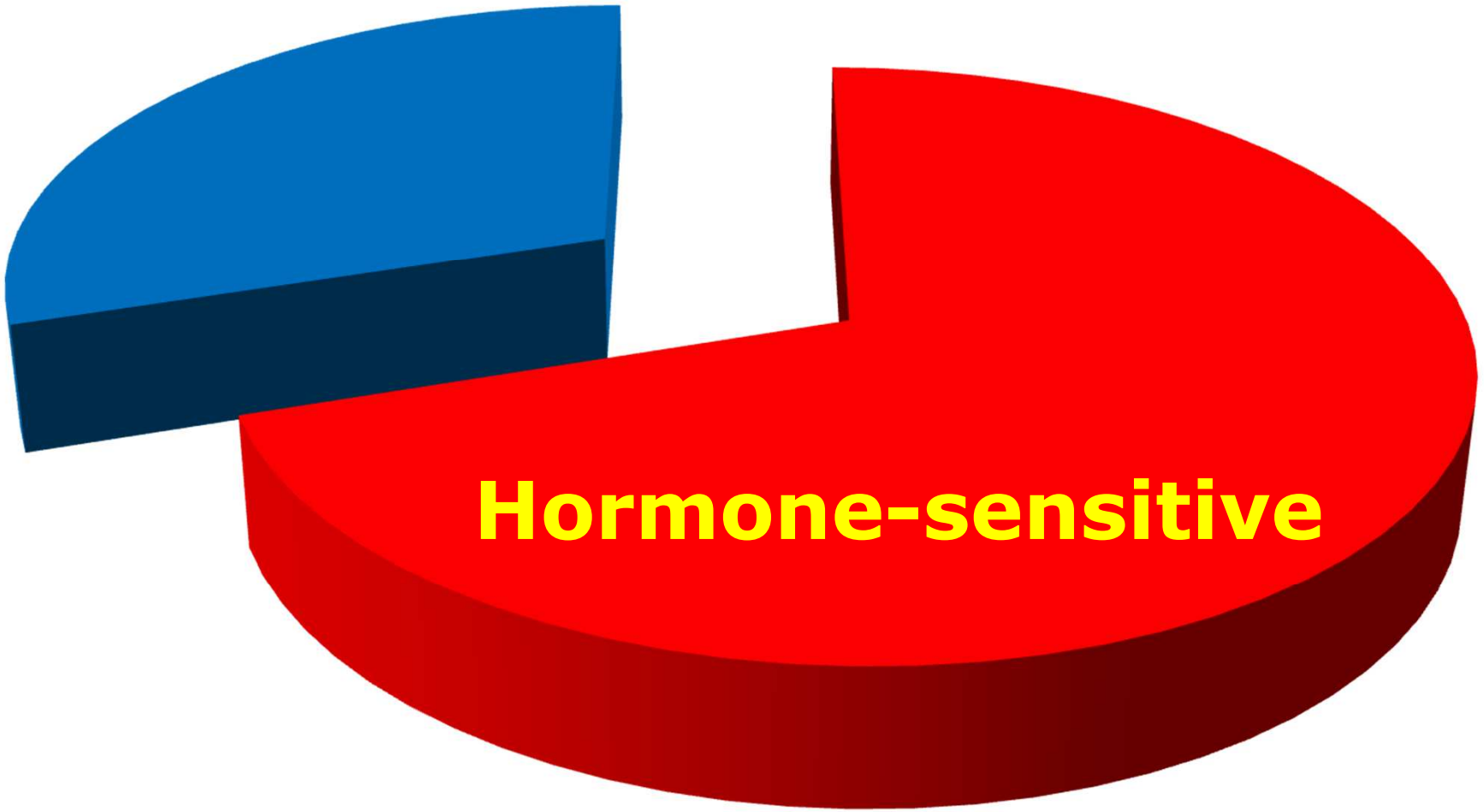
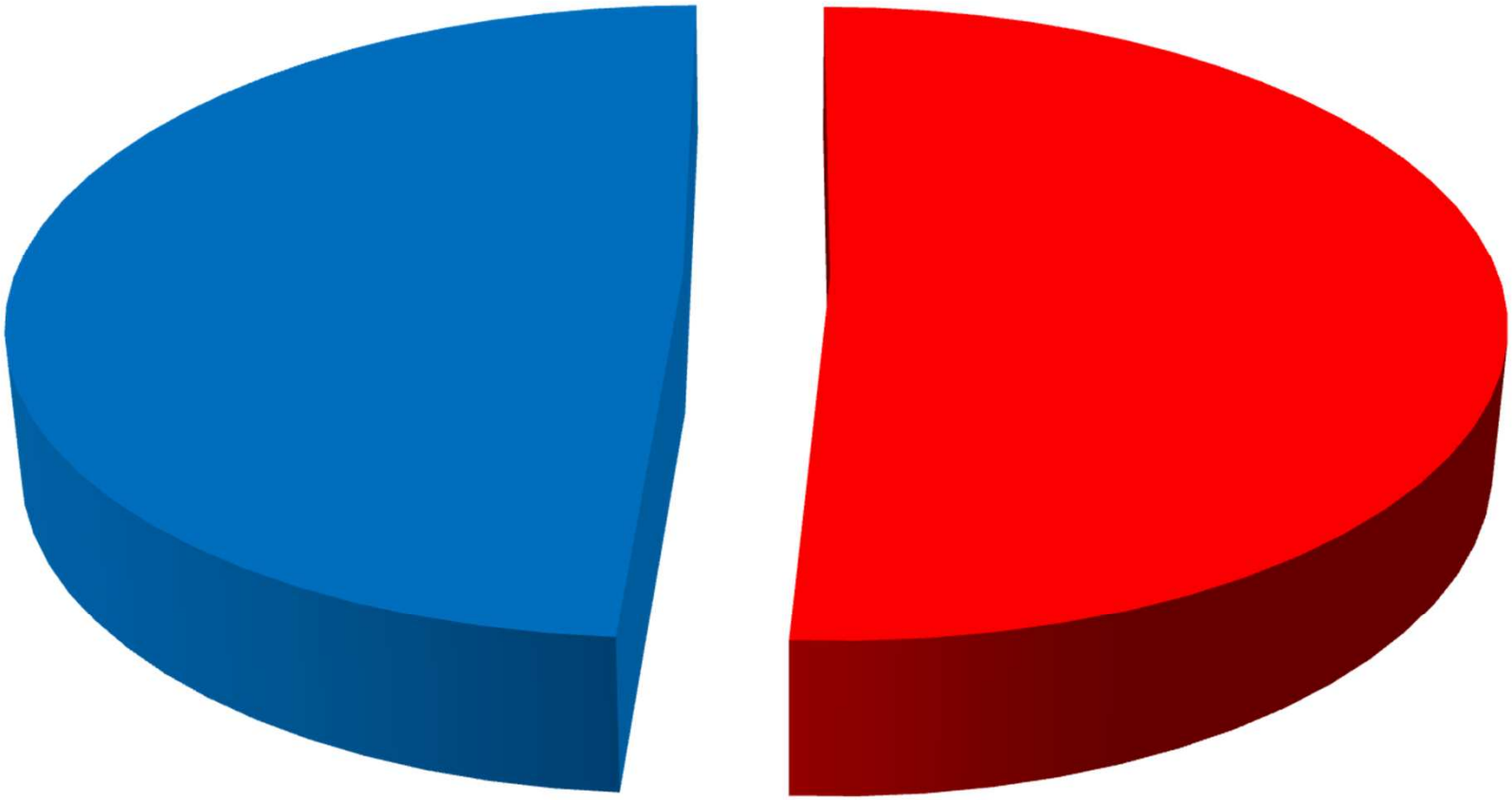
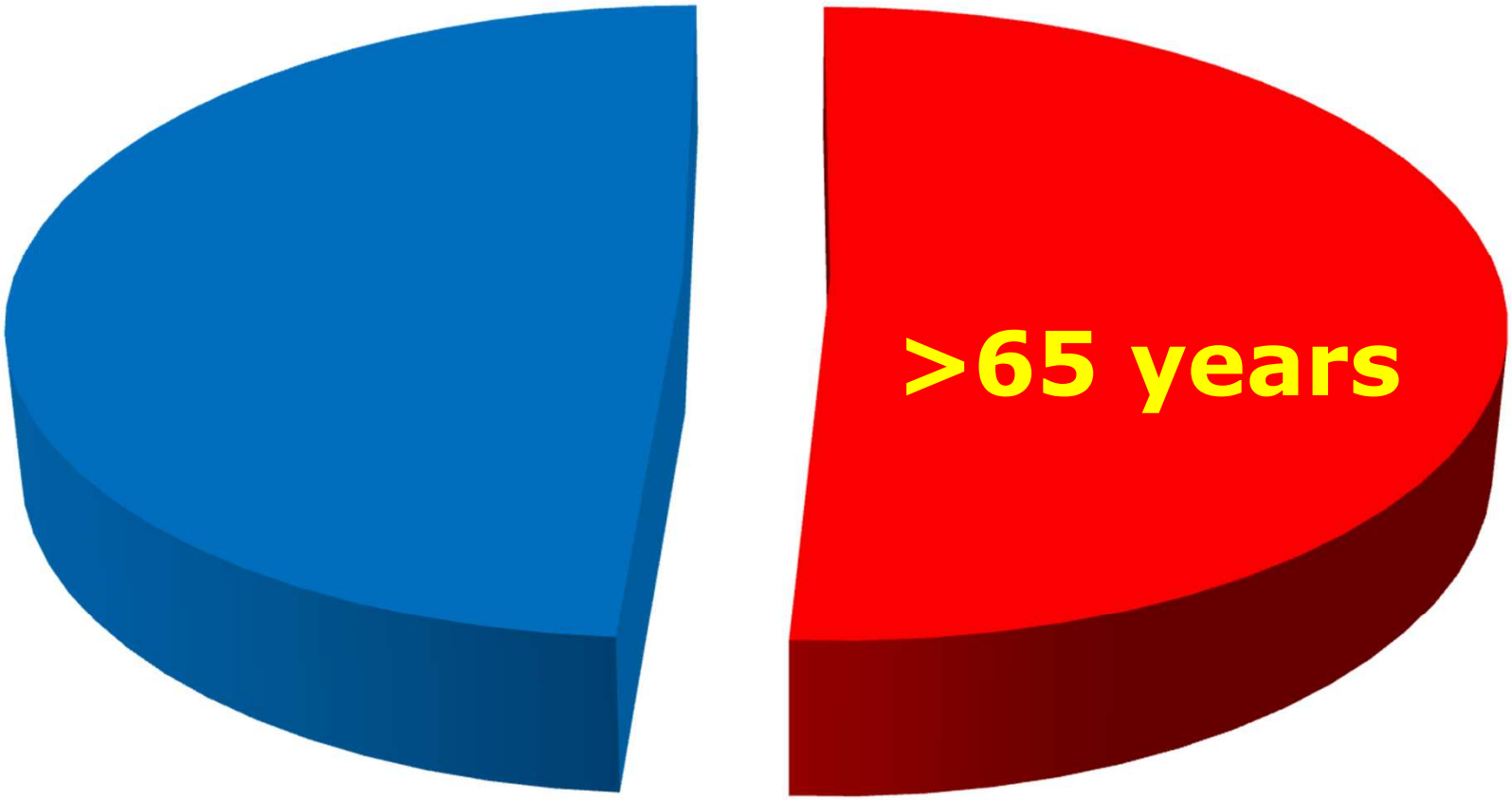



Hormone-sensitive




>65 years

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Treat it right

Personalised management of breast cancer

Breast Surgery Group, School of Medicine

Breast Cancer Research Open Day

21st May 2016

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Kwok-Leung Cheung
Clinical Associate Professor
Consultant Breast Surgeon

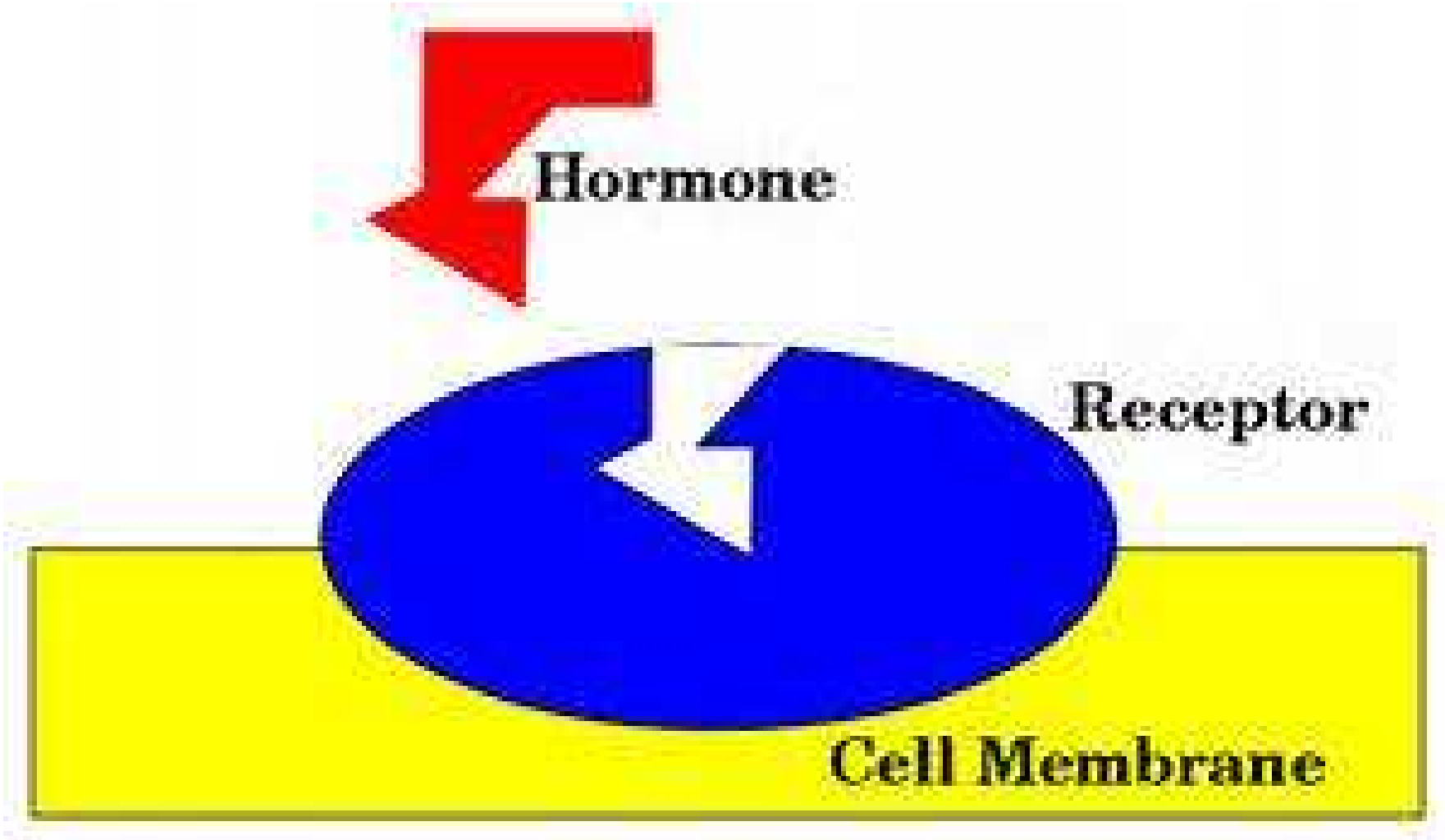
Treat it right

- **Hormone-sensitive breast cancer**
- **Breast cancer in older women**

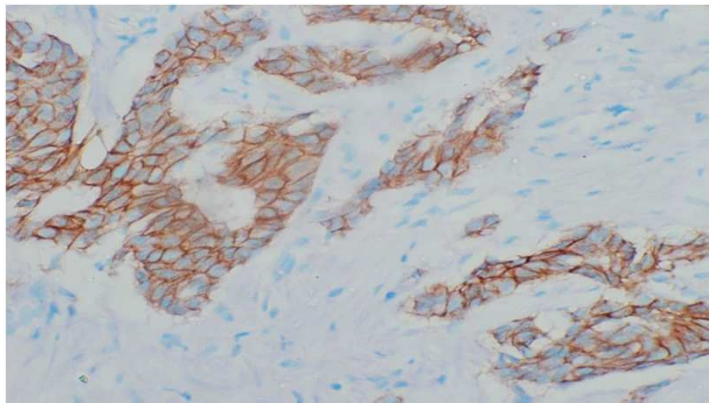
Treat it right

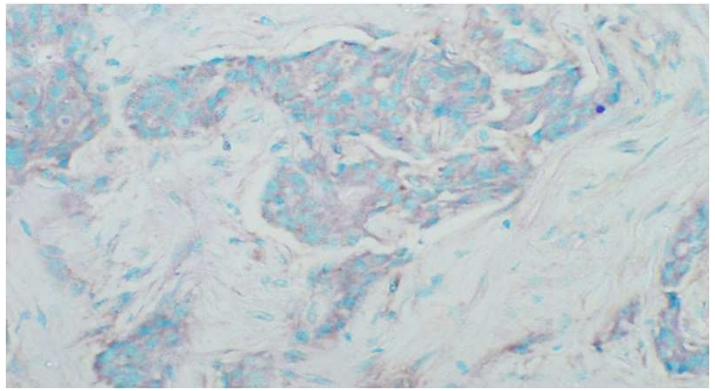
- **Hormone-sensitive breast cancer**
- **Breast cancer in older women**

Hormone-sensitive breast cancer



Hormone-sensitive breast cancer

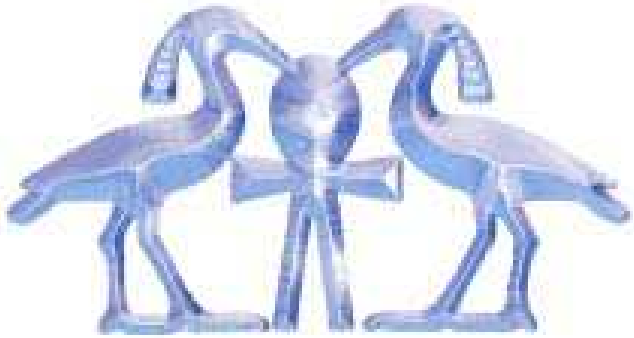




Hormone-sensitive breast cancer

Poetic

STAKT

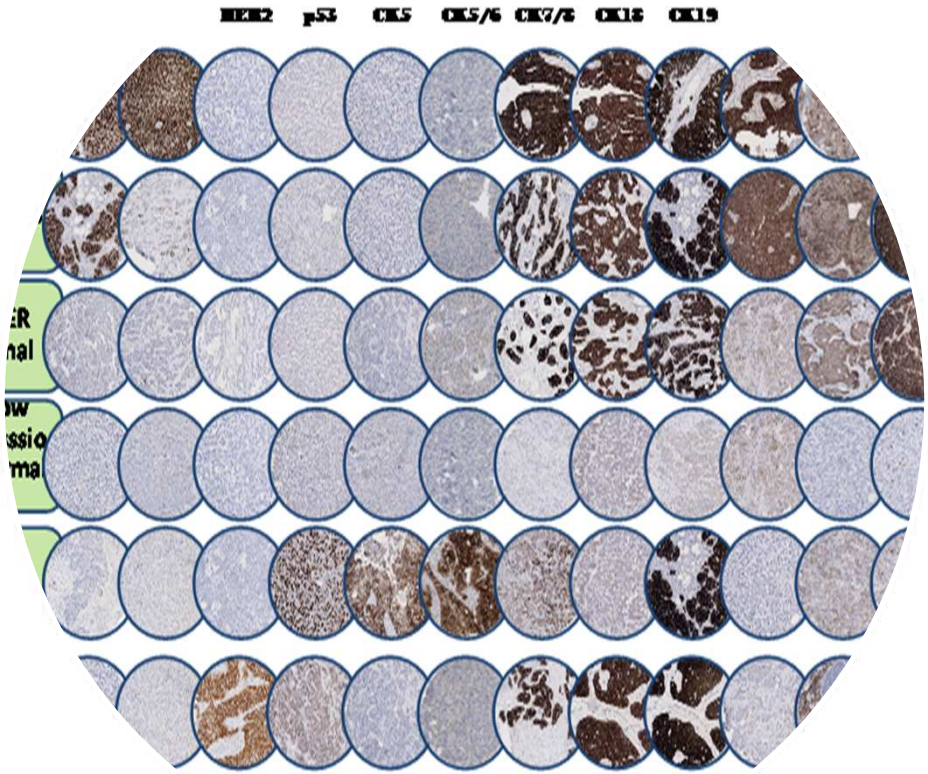


FASLODEX™
fulvestrant

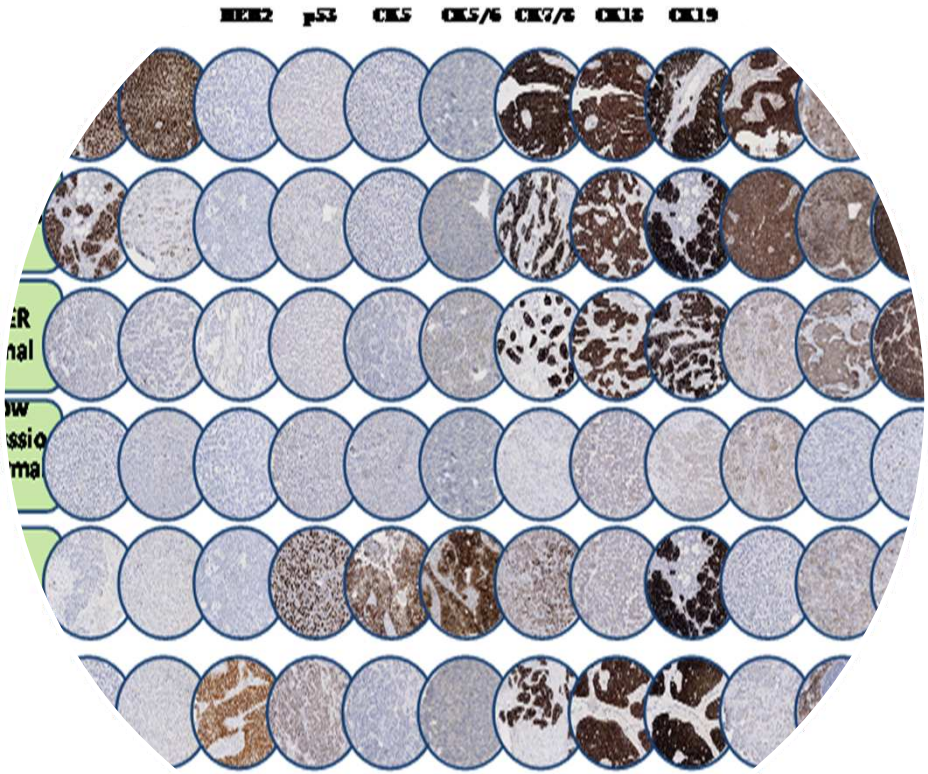
Treat it right

- Hormone-sensitive breast cancer
- **Breast cancer in older women**

Breast cancer in older women



Breast cancer in older women



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Treat it right

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breast cancer care

NHS National Institute for Health Research

The University Of Sheffield.

Derby Teaching Hospitals NHS Foundation Trust

SIOG INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY

City of Hope

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center Making Cancer History®

CARDIFF UNIVERSITY PRIFYSGOL CAERDYDD

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100% of all funds raised goes direct to our research

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Targeting Triple Negative Breast Cancers

S Madhusudan

Professor of Medical Oncology and

Head of Translational DNA repair group
Division of Cancer & Stem Cells

You can support this life-changing research

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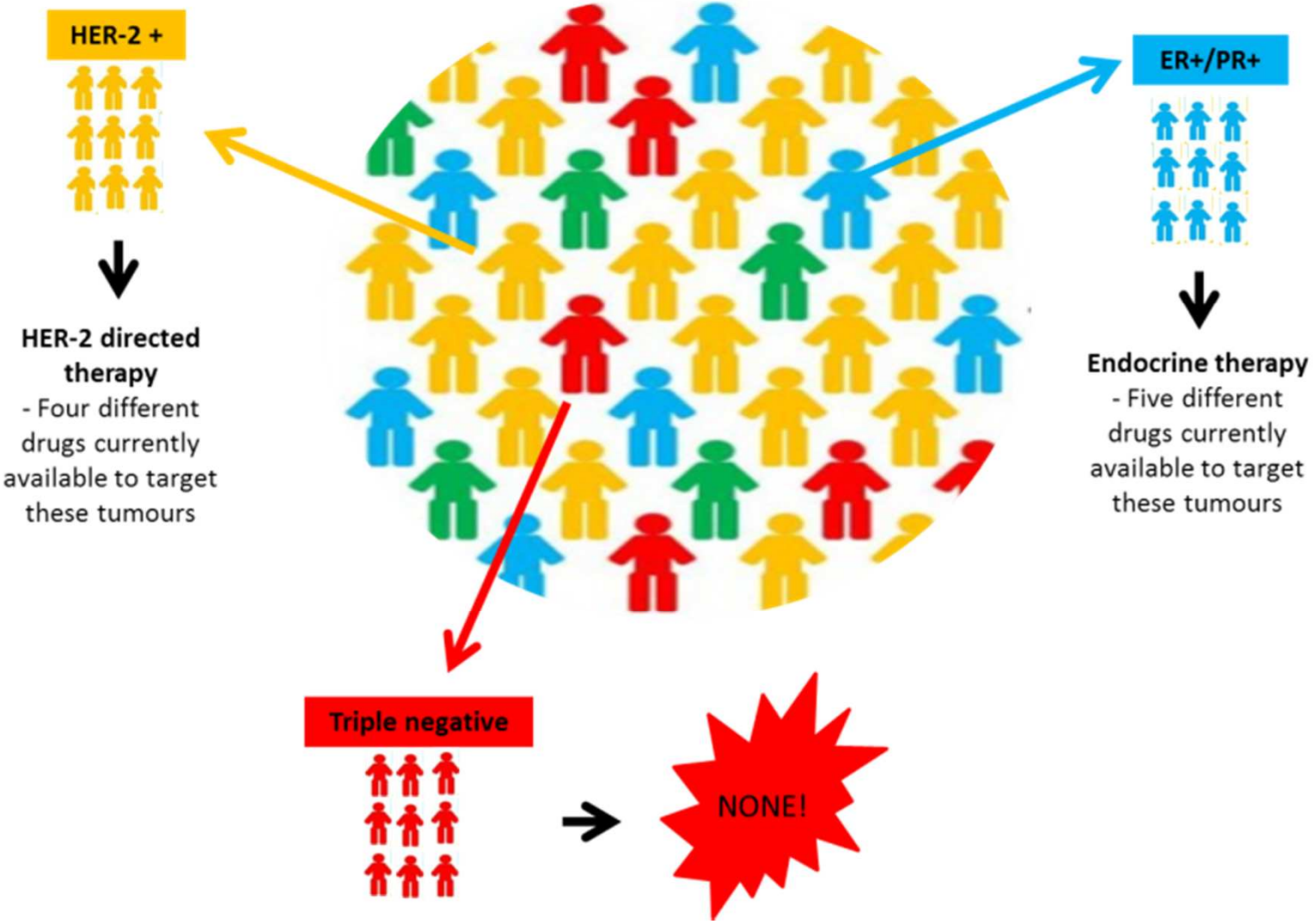
Types of breast cancers

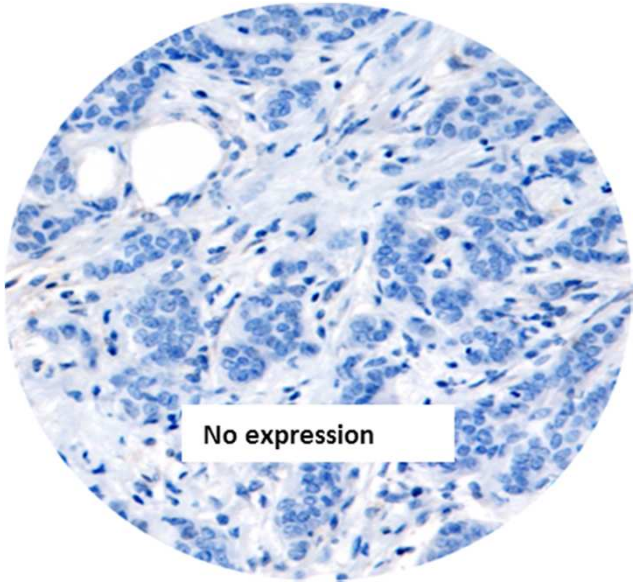


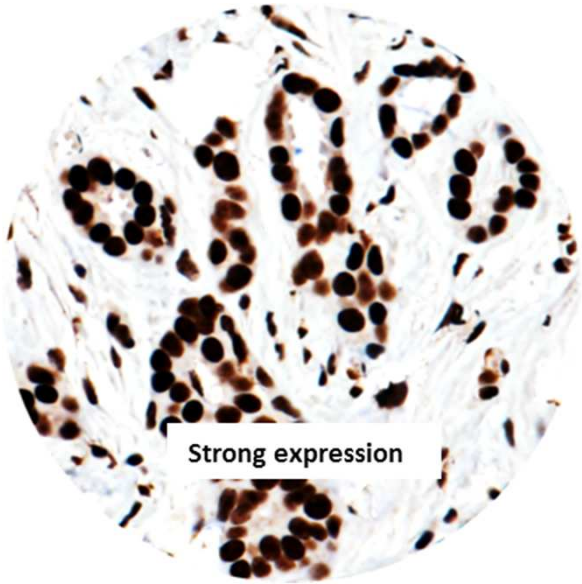
Triple negative breast cancers (TNBCs)

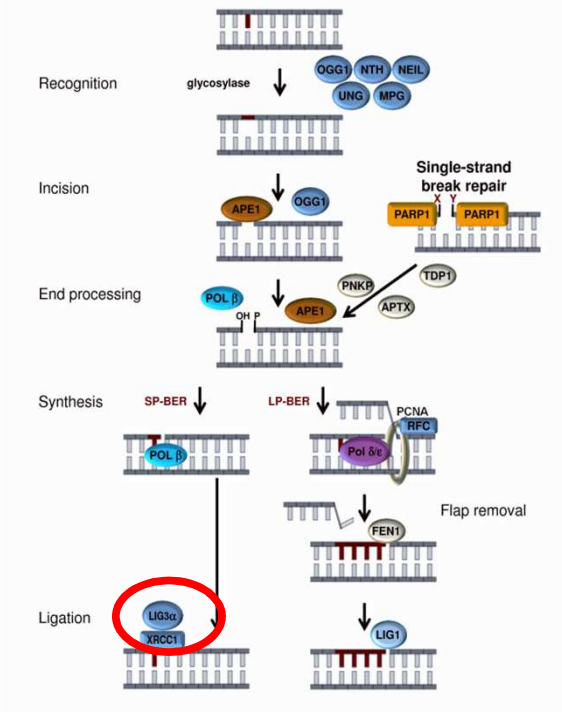
- 20% of breast cancers are triple negative, i.e. do not express hormone receptors (ER, PR) or HER-2 receptors
- More likely in younger people (<50 years)
- More aggressive
- More people die from TNBC compared to other types of breast cancers
- Currently there are no personalized treatments available for this disease
- In Nottingham, we are doing intense research to develop new treatments for TNBCs

A new treatment strategy in TNBCs

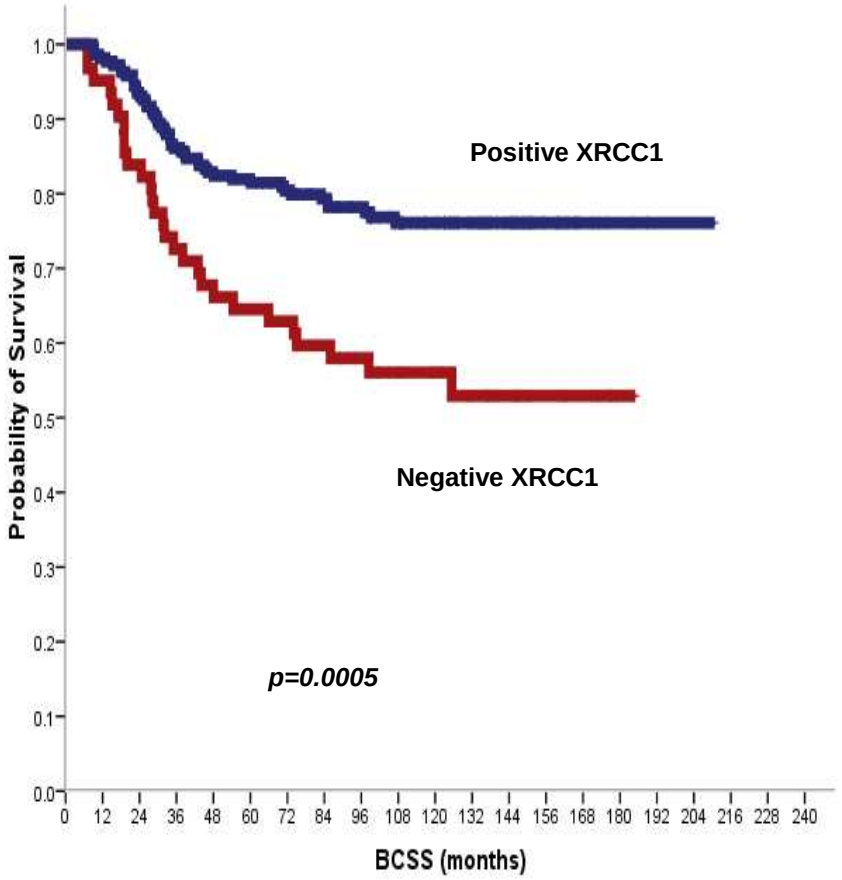
- We have discovered that TNBCs are deficient in a protein called XRCC1, which is a DNA repair protein.







Aggressive tumours have low XRCC1 and linked to poor survival



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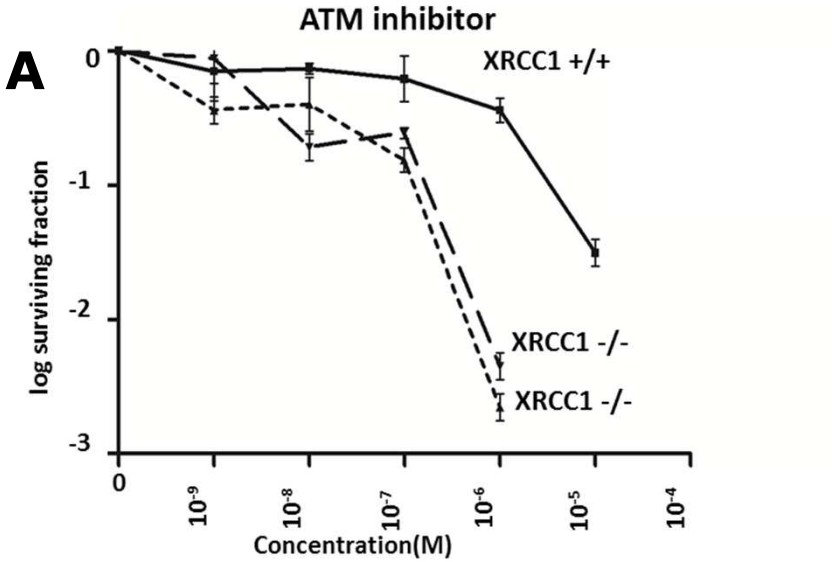
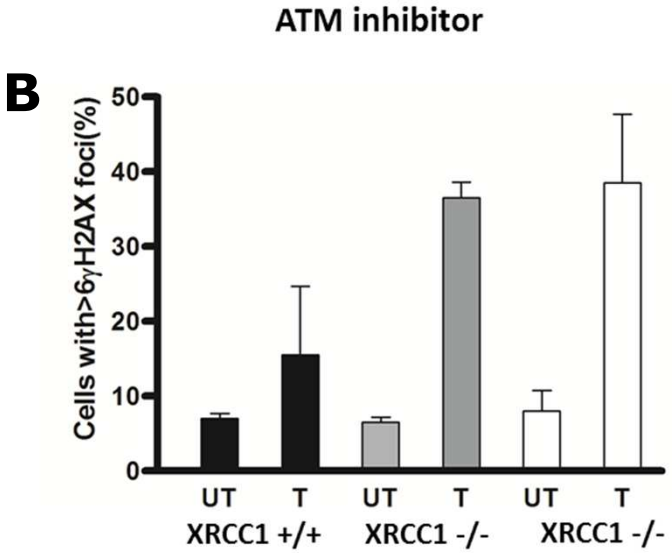
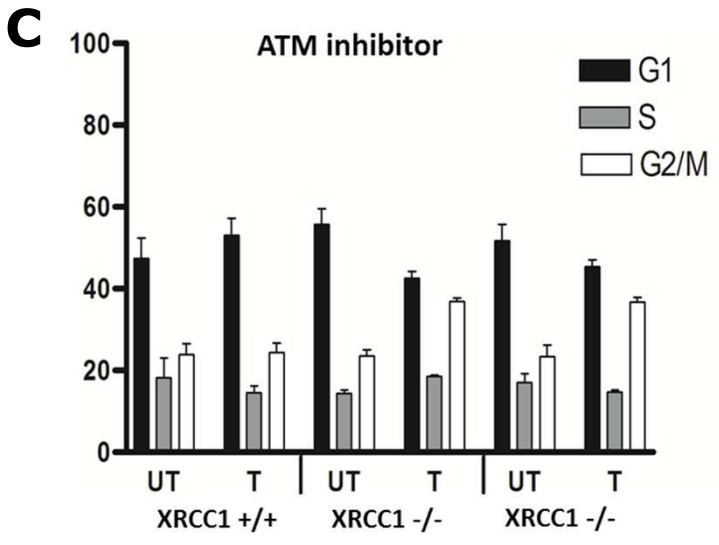
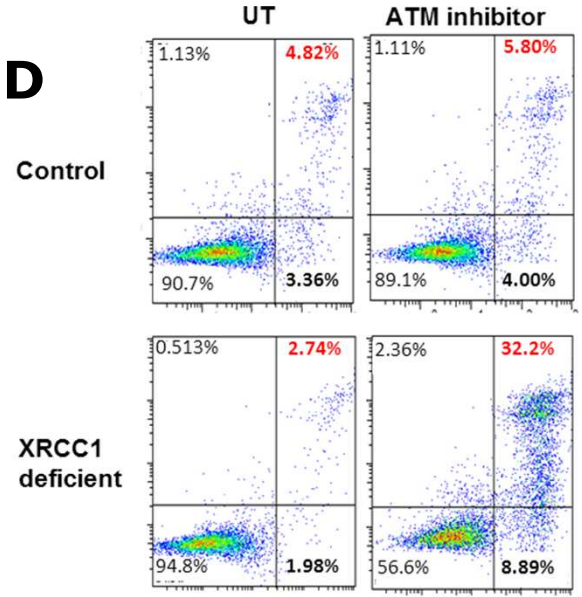
XRCC1 deficient cells are sensitive to inhibitors of DNA damage signalling









OUR AIMS

- Take ATM and ATR inhibitors to clinical trials in TNBCs.
- To initiate a clinical trial in 2018, we need to complete additional validation experiments (between 2016-2017).
- Our research will establish a new treatment strategy in TNBCs.

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