Genomics Up Close And Personal: What Are The Implications For Cancer Nursing?

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Aims of this session

- Understand how genomic information will change your clinical practice
- Remind you about the difference between genetic alteration and inherited disease
- Explore how you will translate the science to explain the implications for your patient and their treatment decisions
Genomic healthcare uses many pieces of genetic information to inform the diagnosis and treatment of medical conditions.

Genetics is now often used when changes to just one or a pair of genes or chromosomes results in a condition, some of which are strongly inherited.
2 Years ago in Prague

Practical Application

- Translational medicine
- Prognostication
- Pharmacogenetics
- Validation
Practical Application

Clinical Practice

- Personalisation
- Translational medicine
- Prognostication
- Pharmacogenetics
What is a genome?

Most of the government-sponsored sequencing was performed in twenty universities and research centres in the United States, the United Kingdom, Japan, France, Germany, and China.

The Human Genome Project originally aimed to map the nucleotides contained in a human haploid reference genome (more than three billion). The "genome" of any given individual is unique; mapping "the human genome" involves sequencing multiple variations of each gene.
In “genomic healthcare” many pieces of genetic information from the human Genome are used to:

- Refine diagnoses and understand diseases
- Individualise clinical care
- Predict drug effects
- Diagnose infections and track epidemics
- Develop new therapies

The DNA of every person is 99.9% identical, but that 0.1% difference can affect our health, susceptibility to disease, and responses to medication
Gene expression

- Many diseases are characterised by multiple genetic mutations.

- Identifying the spectrum of mutations in a patient’s cancer cell may provide a means for diagnosing the specific subtype of cancer involved.
**Stratification**
- Demographics
- Clinical features
- Histology
- Biomarker etc

**Personalisation**
- Patient preference
- Other clinical features
- Medication history etc
Multiple causes of genomic alterations

- Modifier genes
- Response to DNA damage
- Not everyone with an altered gene develops cancer

- Carcinogens
- Hormonal/reproductive factors
Diagnosis

- Cancer is an interplay between genes and environment

- 1 major gene alteration or a combination of factors which influence risk and diagnostic factors

- The genome of the patient and the genome of the cancer influence the treatment decisions
Autosomal Dominant Inheritance

Parents

Gametes

At conception

Affected
Affected
Unaffected
Unaffected
Multi-Step Carcinogenesis (eg, Colon Cancer)

Loss of APC  

Activation Loss of K-ras  

Loss of 18q  

Loss of p53  

Other alterations  

Normal epithelium  

Hypermethylated epithelium  

Early adenoma  

Intermediate adenoma  

Late adenoma  

Carcinoma  

Metastasis  

ASCO
Why is genomic information different?
To personalise treatment and surveillance we can use genomic information...

- From a person:
  - To sub-classify their disease
  - To assess their susceptibility
  - To predict their response to drugs
  - To choose the best treatment

- From a person’s cancer:
  - To make a prognosis
  - To target therapy to its genomic profile

- From an infective organism:
  - To diagnose the type of infection
  - To choose appropriate treatment
  - To track epidemics
100,000 Genome Project UK

Personal Genome Project Canada (PGP-C)
The first human chromosome sequence

Climate change
Thermohaline trigger

Intermolecular energetics
Good vibrations

Impacts of foreseeable science
Supplement with this issue

New on the market
Lasers
VAST GENE STUDY RAISES HOPE FOR COLON CANCER DRUG

New cancer drugs aim to block broken genes

New drug is “greatest advance” for basal cell skin cancer

A GENETIC TEST COULD HELP PREDICT BREAST CANCER ...

Mail Online

NHS patients are refused ‘too expensive’ prostate cancer drug
Human genome may reveal key to healthy life

Scientists claim they will be able to unravel the secrets of how to live a healthy life from the human genome ahead of the 10th anniversary of the completion of the first draft of the 'book of life'.

**PM: genome project will transform cancer care next four years**

NHS to sequence DNA of 40,000 patients over

**The guardian**

**Government backs massive new £300m gene sequencing project**

**Independent Friday 08 August 2014**

UK to sequence 100,000 human genomes by 2017

The author has posted comments on this article **Kounteya Sinha**, TNN | Jun 7, 2014, 05.10AM IST
Media Hype

*The Guardian*
Women are unfairly denied Herceptin by the NHS

*The Globe and Mail*
Health minister reaches out to cancer patient refused Herceptin

*The Telegraph*
Breast cancer sufferers denied two drugs on NHS
HER2

- HER2 is a protein in a group known as ‘epidermal growth factor receptor’
  - Everyone has HER2 in their body naturally

- Amplification or over expression of HER2 is a biomarker and target for treatment
HERCEPTIN
(monoclonal antibody trastuzumab)

- Only works when there are a proliferation of HER2 receptors

- Has a wide range of very serious side effects including: heart damage, infusion reactions leading to shortness of breath and allergic response
NICE condemn breast cancer women to death while fatties jump the queue for gastric bands
Cancers where targeted therapy is used

- Melanoma
- Breast
- Lung
- Colon
- Ovary
- Different types of leukemia
Treatments that work on specific cancers – melanoma

- About 90% of mutations found in *BRAF* in patients with melanoma are due to one particular tumour-causing mutation. This change in one copy of the gene leads to its being activated constantly, and not responsive to the usual control in the MAPK (ERK) pathway.

- Molecular modelling experiments, which took into account the shape of the enzyme, led to the design of a compound (PLX4032) which is a highly specific inhibitor of the mutated enzyme.

- One example where this has been successful is vemurafenib (Zelboraf) although the side effects in 10% of patients are problematic.
Using genomic information to develop new treatments - an example of drug-protein interaction

The existing drug interacts effectively with the protein:

1. Gene
2. Protein
3. Interacting
4. Drug

Due to an alteration in the gene, the existing drug cannot interact with the changed protein:

1. Altered gene
2. Altered protein
3. Not interacting
4. Drug

Information about the altered protein is used to develop a new drug:

1. Altered gene
2. Altered protein
3. Interacting
4. New drug

The new drug interacts effectively with the altered protein:

1. Altered gene
2. Altered protein
3. Interacting
4. New drug
A cancer growth blocker blocks the growth factors that trigger the cancer cells to divide and grow. Scientists are looking at different ways of doing this such as:

- Lowering levels of the growth factor in the body
- Blocking the growth factor receptor on the cancer cell
- Blocking the signals inside the cell that start up when the growth factor triggers the receptor
Types of anti angiogenesis treatment

There are different types of drugs that block blood vessel growth, including:

- Drugs that block blood vessel growth factor
- Drugs that block signalling within the cell
- Drugs that affect signals between cells
Drugs that block blood vessel growth factor

- Some drugs block vascular endothelial growth factor (VEGF) from attaching to the receptors on the cells that line the blood vessels. This stops the blood vessels from growing.

- A drug that blocks VEGF is bevacizumab (Avastin). It is also a monoclonal antibody.

Drugs that block signalling within the cell

- Some drugs stop the VEGF receptors from sending growth signals into the blood vessel cells. These treatments are also called cancer growth blockers or tyrosine kinase inhibitors (TKIs).

- Sunitinib (Sutent) is a type of TKI that blocks the growth signals inside blood vessel cells. It is used to treat kidney cancer and a rare type of stomach cancer called gastrointestinal stromal tumour (GIST).

Drugs that affect signals between cells

- Some drugs act on the chemicals that cells use to signal to each other to grow. This can block the formation of blood vessels. Drugs that work in this way include thalidomide and lenalidomide (Revlimid).
Monoclonal Antibodies
Types of Monoclonal Antibodies

Trigger the immune system

- Rituximab (Mabthera) for non Hodgkin lymphoma (NHL) and some types of leukaemia
- Alemtuzumab (MabCampath) for Chronic lymphocytic leukaemia (CLL)

Block signals telling cancer cells to divide

- Trastuzumab (Herceptin) for breast cancer and stomach cancer
- Bevacizumab (Avastin) for advanced bowel cancer, breast cancer and some other cancers
- Cetuximab (Erbitux) for advanced bowel cancer or in trials for other cancers
- Panitumumab (Vectibix) for advanced bowel cancer
- Pertuzumab (Perjeta) for breast cancer
Other therapies in Clinical Practice and in Phase II & III Trials

- Therapeutic vaccines
- Synthetic lethality
- Armed antibodies
How genomic information is reducing adverse drug reactions

- Adverse drug reactions are one of the leading causes of death among hospitalised patients. In one prospective study, adverse drug reactions accounted for 1-in-16 hospital admissions. The annual cost to the NHS has been estimated at £466m.

- Greater understanding of how genomic variations can affect how our bodies respond to medication is helping to avoid adverse drug reactions in patients.
Adverse drug effects can arise because of the ways in which a drug:

- moves around the body (pharmacokinetic effects); or
- interacts with the body (pharmacodynamic effects).

Both can be influenced by common variations in the genome.

The effect of more than 100 drugs is influenced by genetic variation.

- codeine
- carbamazepine
- azathioprine
- warfarin
- flucloxacillin
Genomic testing for patients requiring the HIV / AIDS drug Abacavir has reduced the risk of hypersensitive reactions to near zero.

Some patients suffer a hypersensitivity reaction to Abacavir that can be fatal. As genomic studies have discovered that the sensitivity is related to a specific genetic alteration, testing is now carried out before prescribing this drug.

This has reduced the risk associated with being hypersensitive from between 5%-10% to near zero.
New developments

- Genomic testing can be used to pinpoint which gene is responsible for an inherited condition, identify the genetic variants involved in an increased or decreased likelihood of developing a common condition, or how a person responds and reacts to drugs.
New developments

- New, faster DNA sequencing technologies will make personal genomic information available in other NHS care pathways; for instance, through the UK’s 100,000 Genomes Project involving patients with cancers, rare diseases and infections.

- Commercial genomic testing is already available online. Some tests may include health-related results about carrier status for inherited conditions and how a person might respond to particular classes of drugs.
So out with the old and in with the new

1953 DNA structure discovered by Francis Crick and James Watson

July 12th 1957 the Surgeon General links smoking with lung cancer

The Reports of the Surgeon General

The 1964 Report on Smoking and Health
1977 ‘Sanger method’ for DNA sequencing

1982 First cancer-causing DNA change identified
Knowing Your MEDICAL FAMILY TREE Can SAVE YOUR LIFE

Your mother's smile,
Your father's eyes...

But have you also inherited...
DIABETES?
CANCER?
ALZHEIMER'S?
2001 First draft of the human genome

December 13, 2005 NIH launches comprehensive effort to explore genomic alterations in human tumours

2007 The first genome-wide association studies (GWAS) in cancer

Nov 2011 Cancer Research UK launches the Genomics Initiative
The Future?

- Treatments focused on the individual and that individuals cancer with less side effects and no adverse reactions

- Treatments which make permanent alterations to the cancer genome and the growth and spread of the cancer

- Personal health messages which identify those requiring monitoring and those at greatest risk
Cancer Nurses of the future?

So Thank You, Goodbye and..........
Any questions?

www.geneticseducation.nhs.uk