Genetics update and implications for (General) Practice

May 12th 2018
Women’s Health Symposium
Clearwater Estate

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Topics

• NZ Clinical Genetics delivery
• New Technologies
  – Array CGH case
  – Genomic Medicine
• Direct to Consumer Testing

Questions and answers throughout
Delivery of Clinical Genetics in NZ

- National clinical genetics service
- Three hubs, extensive outreach
- Healthpathways

Private referrals
- Auckland (Clinical Genetics Auckland via Fert Associates)
- Christchurch (Children’s Specialist Centre / Fertility Associates)
- Wellington
Array Comparative Genome Hybridisation (aCGH)

- Resolution x20 best karyotype
- Copy number variants “CNVs”
  - Pathogenic
  - Benign familial variants
  - VUCS
- Parental studies and literature can be helpful
- First line investigation for intellectual disability and congenital anomalies
- NB variable penetrance, susceptibility locus
A chromosomal tale

- Severe intellectual disability
- Autism
- Karyotype normal (2003)
- Absent uterus

Karyotype: `ish del(14)(q11.2q11.2)(RP11-659J20).arr 14q11.2(20,608,216-23,061,615)x1 dn`

Final Result: Approximately 2.5Mb de novo pathogenic deletion detected

Parental studies
- normal array and FISH
- de novo

Recurrence risk ~ zero
A chromosomal tale

• Paternal uncle
• Short
• Moderate intellectual disability IQ 66
• Round face, mild dysmorphism

- Array
  - 46,XY,dup (14)(q11.2q11.2)


Final Result: Approximately 3.4Mb pathogenic duplication detected
A chromosomal tale

Result: Balanced intrachromosomal insertion detected
Genomic Medicine is here

July 4th 2017 BBC Radio 4 Today Programme, 0800 news

- Chief Medical Officer → genomic dream must be realised within 5y
- All patients should have genetic testing to transform treatment
- Starting with cancer
- Drugs matched to patients and disease, side effects reduced

- Life changing answers for patients / families
- Need for rapid increase in genomics literacy for healthcare practitioners
Genomic Medicine is here – but what is it?

Next generation sequencing of DNA
- Parallel sequencing of thousands of gene fragments simultaneously
- Fast, precise and efficient
- Massive amount of data
- No limit to amount of DNA we can sequence
- Buy one, get lots free

Challenge now is interpretation
Genomic Medicine is here – what will change?

- Cancer – somatic mutations guide treatment, germline...?familial
- Rare diseases – 1 in 17, new diagnostic options, monitoring, ?familial
- Infectious disease – pathogen genomes, guide treatment
- Common complex disease – more tailored advice, diet, CVS risk, DM
- Pharmacogenetics – predict efficacy, dosage and safety, new drug targets
- ELSI – Ethical, legal, social, institutional – consent (esp children), risks and benefits, privacy, data storage, AI
- ART – boundaries of practice continue to expand both in managing infertility and in increasing chance of a healthy baby
Genomic Medicine and Fertility

- Many more diagnoses now made – familial implications
- Pre conception testing
  - known common disorders – CF, FraX, SMA (NZD$595)
  - all carrier status?
  - ethnicity based?
  - susceptibility loci?
- Fetal genetic screening
  - current - common chromosomal disorders, high risk genetic disorders
  - prompted by fetal anomalies
  - future - ?susceptibility loci
Genomic Medicine and Fertility

- Increasing utilisation free fetal DNA for prenatal screening
  - NIPS: Non Invasive Prenatal Screening
  - Free fetal DNA (ffDNA) – detectable from 5/40
  - High or low risk result for T21/18/13 and sex chromosome aneuploidies
  - Private only – NZD$700
  - “Non call” around 3% (20% above 95kg)
  - In time – specific mutation screening / microduplications etc

- NIPS @ national screening unit – to follow……
Genomic Medicine – who will do it?

Advent of NGS – no limit to DNA sequencing
Multi-gene panels, mendeliome, exomes, genomes
Limits now in bioinformatics / interpretation

Combination approach
Genomics Health Alliance NZ (GHANZ)
National equity of access
Geneticist supported mainstreaming
Increased access to a geneticist
Increase genomics literacy
Educating funders in cost benefits
(Geneticist for cascade testing – esp predictive)

Goal
Right patient
Right test
Right time
Right interpretation
Genomic Medicine – how can I upskill?

Genomics Education Programme

January 2016

Dr Imran Rafi
Dr Judith Hayward

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Genomics in mainstream medicine

General practice and genomics

Clinicians have always personalised patient management. There is a growing momentum to improve this further through the integration of genomic information into clinical care. This will incorporate powerful new tools through which clinicians can further tailor healthcare, improving disease prevention, prediction, diagnosis and treatment.
Get to know you. Health and ancestry start here.

- Reports on 240+ health conditions and traits
- Discover your lineage, find relatives and more
- Get updates on your DNA as science advances

$99

What your DNA says about you.
Find out things like your body metabolizes caffeine quickly, or if you're at a higher risk for diabetes. The more you know about your DNA, the more you know about yourself.

Carrier status
Find out if your children are at risk for inherited conditions, so you can plan for the health of your family.

Health risks
Understand your genetic health risks. Change what you can, manage what you can't.

Drug response
Arm your doctor with information on how you might respond to certain medications.

order now

Show mum what she’s really made of!

Get AncestryDNA for AU$99* until May 13.
Goal
Right patient
Right test
Right time
Right interpretation

? does this “result” relate to this patient
? does it fit with phenotype – personal or family history of breast / ovarian cancer
? If it does – do we need to confirm just mutation or re-sequence the whole BRCA2 gene
? If not – do we need to do anything
? who pays – clinician time and testing
? insurance
? screening
Genomic Medicine – take home messages

• Be aware of the changes in practice genomic medicine will create
• Consider re-referral families with rare disorders and no clear diagnosis
  – New technologies
  – Recurrence risk sibs / extended families and ART
• Consider opportunities to further upskill in genomic medicine (that’s you)
• Get to know your local geneticist (that’s me)
• Watch out for direct to consumer testing
Genetic Health Service Referrals

The Genetic Health Service NZ – South Island Hub is based at Christchurch Hospital and provides outreach clinics to centres throughout the South Island.

Referral

Send referrals by:

- ERMS: Genetics > Genetics Referral, or
- Fax to (03) 379-1343, or
- Email genetic.servicenz@cdhb.health.nz, or
- Post to Genetic Health Service NZ – South Island Hub, Christchurch Hospital, PO Box 4710, Christchurch 8140.

http://www.genetichealthservice.org.nz/