

# Using data discussion to promote scientific thinking in undergraduates and MSc students

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# Courses

- **A: Cancer: Molecular & Cellular Biology**
  - Final year undergraduate module
  - ~20 – 36 students
- **B: MSc in Medical Genetics**
  - 1 year taught postgraduate programme
  - Mostly overseas graduates
  - ~24 – 36 students

# Cancer: session structure

- ~ 1 hour lecture
  - Background & current status of one area of cancer biology
  - Moderately interactive
- Break
- ~ 1 hour data discussion
  - Related to lecture topic



# Discussion sessions

- Students break into groups of 4-6
- Discuss problem

# The Problems

- Real, recent research data from the lecturer's laboratory
  - Or data extracted from a research paper
- Data is presented with only experimental methods
  - Sometimes with prompts
    - What is importance of sample in lane 1?
- Students (i) evaluate (ii) interpret (iii) think about what to do next

# Student Discussions

- Students more likely to talk & give opinions in small groups without staff

# Assistance

- Lecturer (+ course coordinator) circulate to ask questions / answer queries

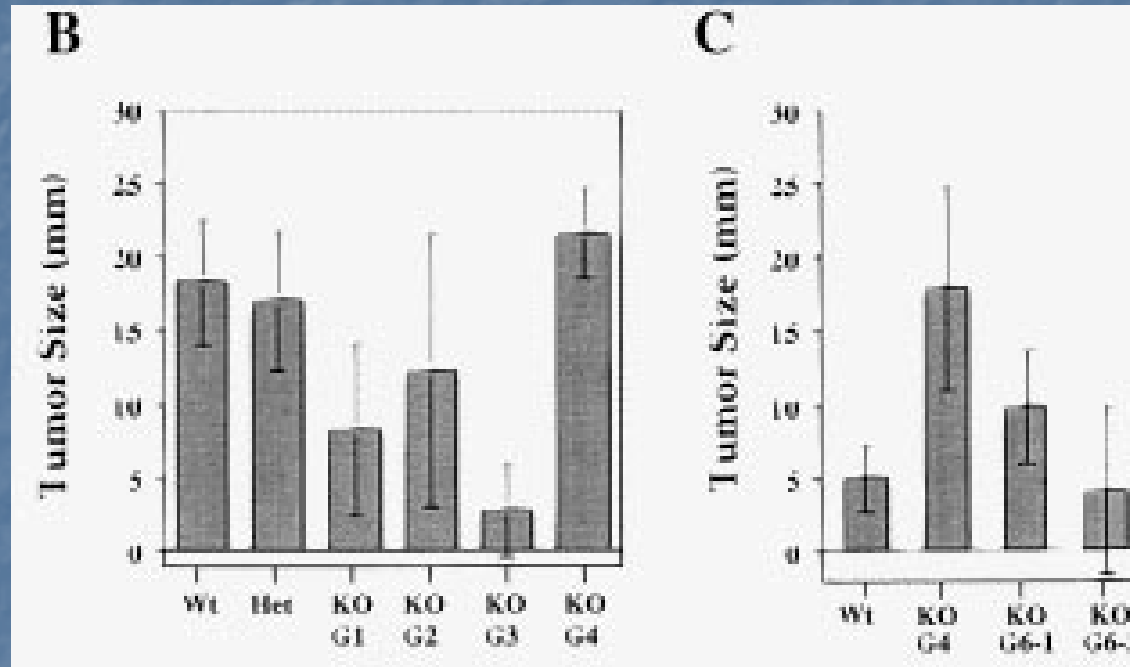


# Summarising

- After each section and at end
- Elicit & evaluate ideas from groups



# Thinking critically



Cell 91:  
25-34 (1997)

Overheard in discussions:

“...stonking great error bars !!”

“Why is wild-type different in B and C? And wild type to G4?”

# Significance

- Students often try to “over-interpret” data
- Where is the line drawn regarding significance of results?

| Transfected constructs | Relative survival rate |
|------------------------|------------------------|
| Mock transfected       | 0.01                   |
| XRCC1                  | 1.00                   |
| XRCC1 + HPV16 E6       | 0.60 ( $\pm 0.028$ )   |
| XRCC1 + HPV1 E6        | 0.83 ( $\pm 0.65$ )    |
| XRCC1 + HPV8 E6        | 0.95 ( $\pm 0.09$ )    |
| XRCC1 + HPV6 E6        | 1.04 ( $\pm 0.032$ )   |

Compiled from text in EMBO J. 21(17): 4741 (2002)

# Being critical of literature

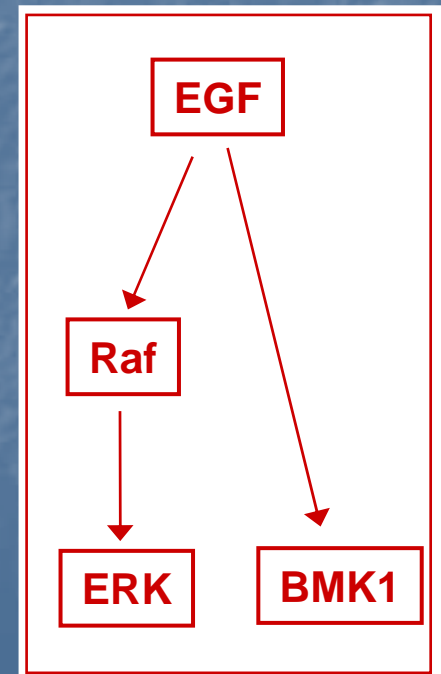
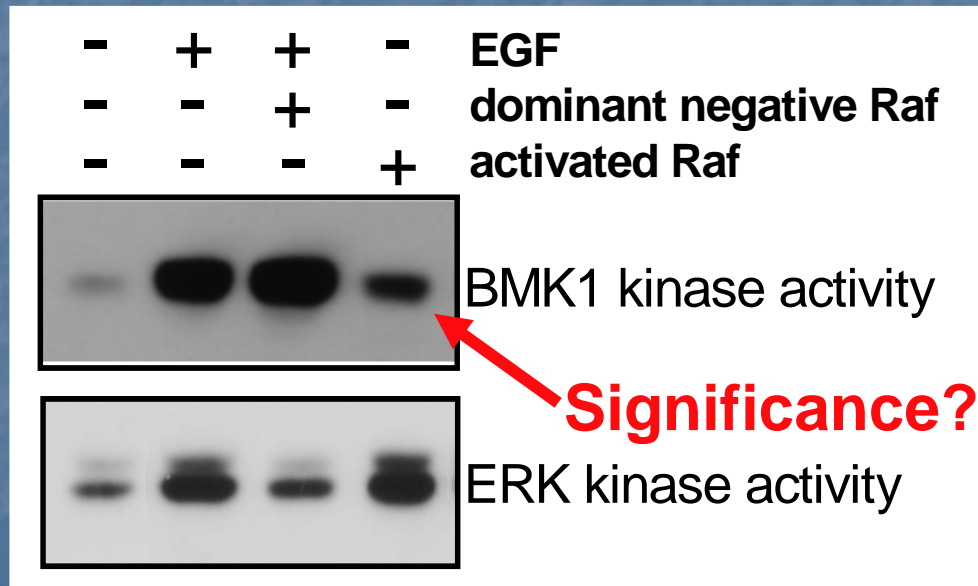
- "... made you look at data and journals in a different way, ie journals aren't all perfect."
  - "... critical appraisal ... allowed the realisation that not all papers are infallible."
  - "Made me realise that papers aren't always correct + accurate."
- All quotes from course feedback

# The mapping of signal transduction pathways

Epidermal Growth Factor (EGF) activates both ERK and BMK1 (another MAPK) in HeLa cells. Raf mutants were expressed in the cells to probe whether Raf is involved. Evaluate the results.

## Is Raf involved?

## Does EGF use the same pathway to activate ERK and BMK1?





# Extracting meaning

- You've "got to interpret for yourself and you've also got to think 'Does this mean anything?' " ETL study
- "... discussing stuff with people rather than sitting and trying to work it out for yourself. And it might give you a perspective that you wouldn't necessarily have had yourself." ETL study

ETL study: Interviews with students on Cancer course by Velda McCune & Jennifer Nisbet as part of the ESRC/TLRP Project on Enhancing Teaching-Learning Environments in Undergraduate Courses (2002/3)

# Investigating hypotheses

- Hypothesis:  
“**RKIP is a scaffolding protein**”
- Experiment 1 results
  - Interpretation: consistent with RKIP as scaffolding protein
- Experiment 2 results
  - Ditto
- Experiment 3 results
  - Inconsistent!  
RKIP is **NOT** a scaffolding protein!!!

# Investigating hypotheses

- "... three problems. And the first one ... one conclusion, the second one as well, same conclusion, and then the third one ... said that the other two were wrong. So this makes us think of all the alternative experiments that one should do to ... get an answer ..."
- "... it's not just like do one experiment – ah, yeah that's our answer ... it's all the other experiments that we should do as well to prove that."

Both quotes from ETL study



# Confidence

- "... it gives me more confidence in science ... cos I think 'oh, I just actually interpreted results, I can do this kind of thing'. It helps me think 'I'm not actually that stupid, I can see how this works'."  
ETL study



# Consolidating knowledge

- **“I remember more ... from those problem sessions than ... the lecture”** ETL study
- **“... helpful in cementing information supplied in the lecture ... and engaged the brain ...”** Course feedback
- **“... read through the problems and then you have to actually think through the lecture, or flick back through your notes and think about everything ...”** ETL study

# Summary of part A

– value of data discussion

- Consolidation of knowledge
- Being critical of data
- Interpreting data
- Proving / disproving hypotheses
- Thinking about next experiments
- Confidence in own ability
- **Learning to be a scientist**

# MSc in Medical Genetics

- Lots of different techniques are in use for diagnostics
- Students rote learn the techniques but harder for them to select the best in a given scenario
- Look at real case scenarios
  - Whole class problem sessions or group problem based learning
  - Students suggest technique(s) to use
  - See results & interpret / suggest next step



# Case study: Cytogenetics

- Seizures, epilepsy
- 46,XY
  
- Subtelomere multiprobe FISH
  - Normal result
- Subtelomere MLPA
  - Indicates 1p36 deletion
  
- How to validate MLPA result?



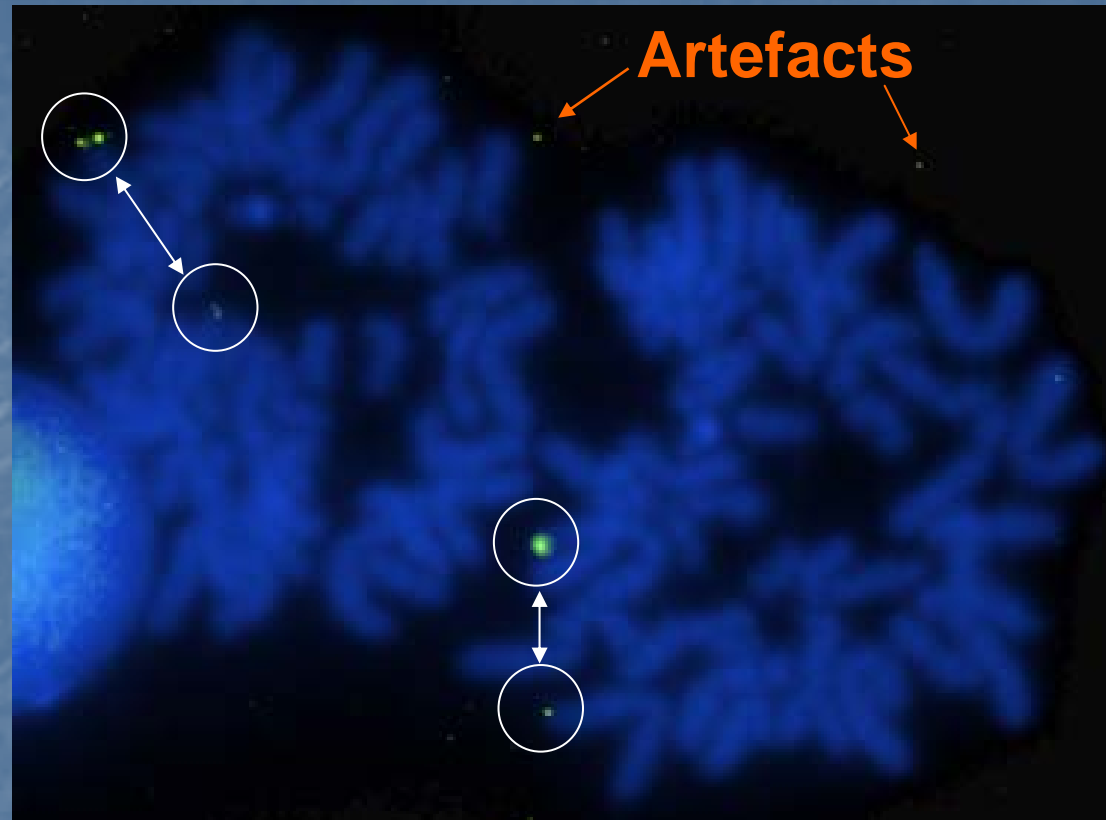
# Validation methods

- Use a different MLPA kit?
- Microsatellite study?
- FISH with specific probes from that region?
- Microarray CGH?
- Several methods could be used

# FISH with RP11-465B22



**Most cells:**  
signal on only one  
chromosome 1

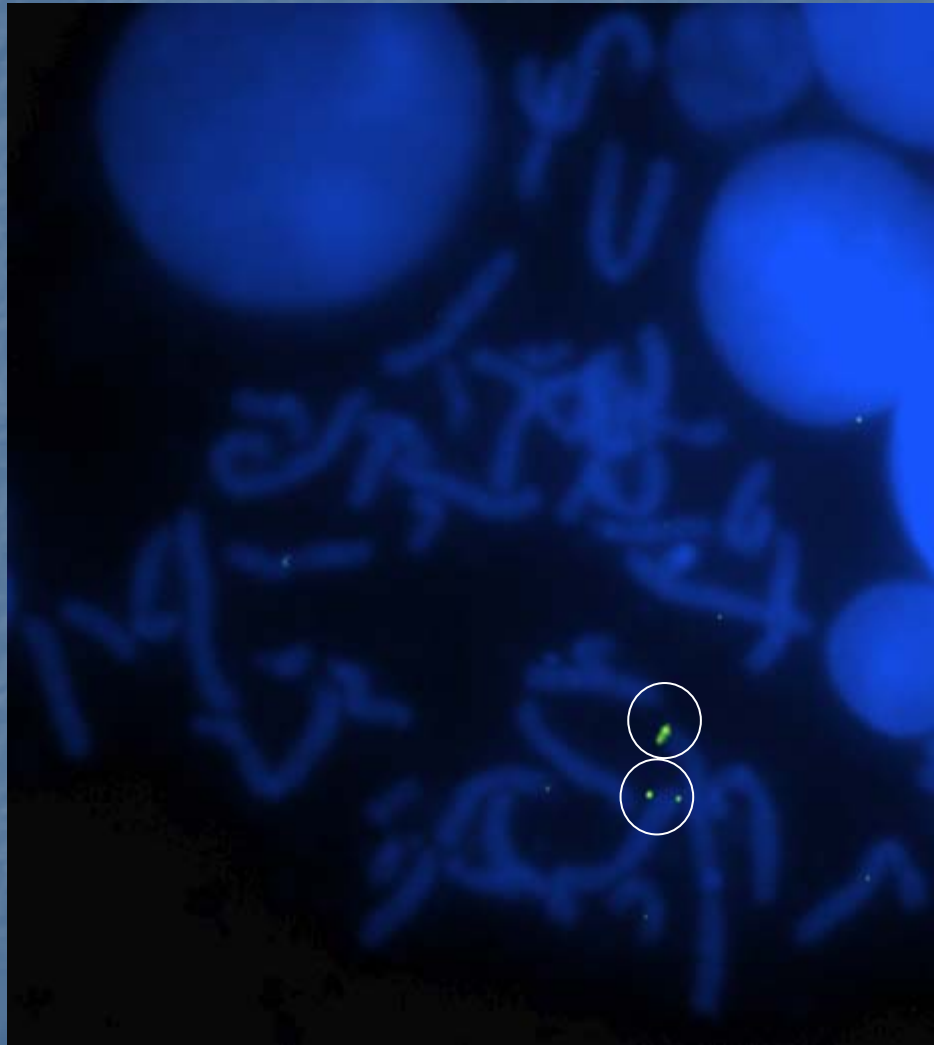


**Some cells:**  
strong signal on one c'some 1,  
weak signal on other c'some 1

→ Breakpoint is **within** probe sequence

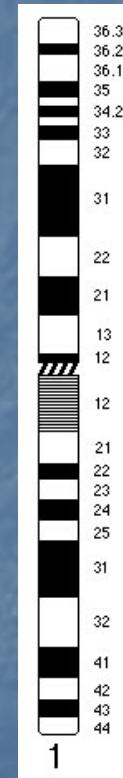
# FISH with RP11-58A11

Signal on both chromosomes 1

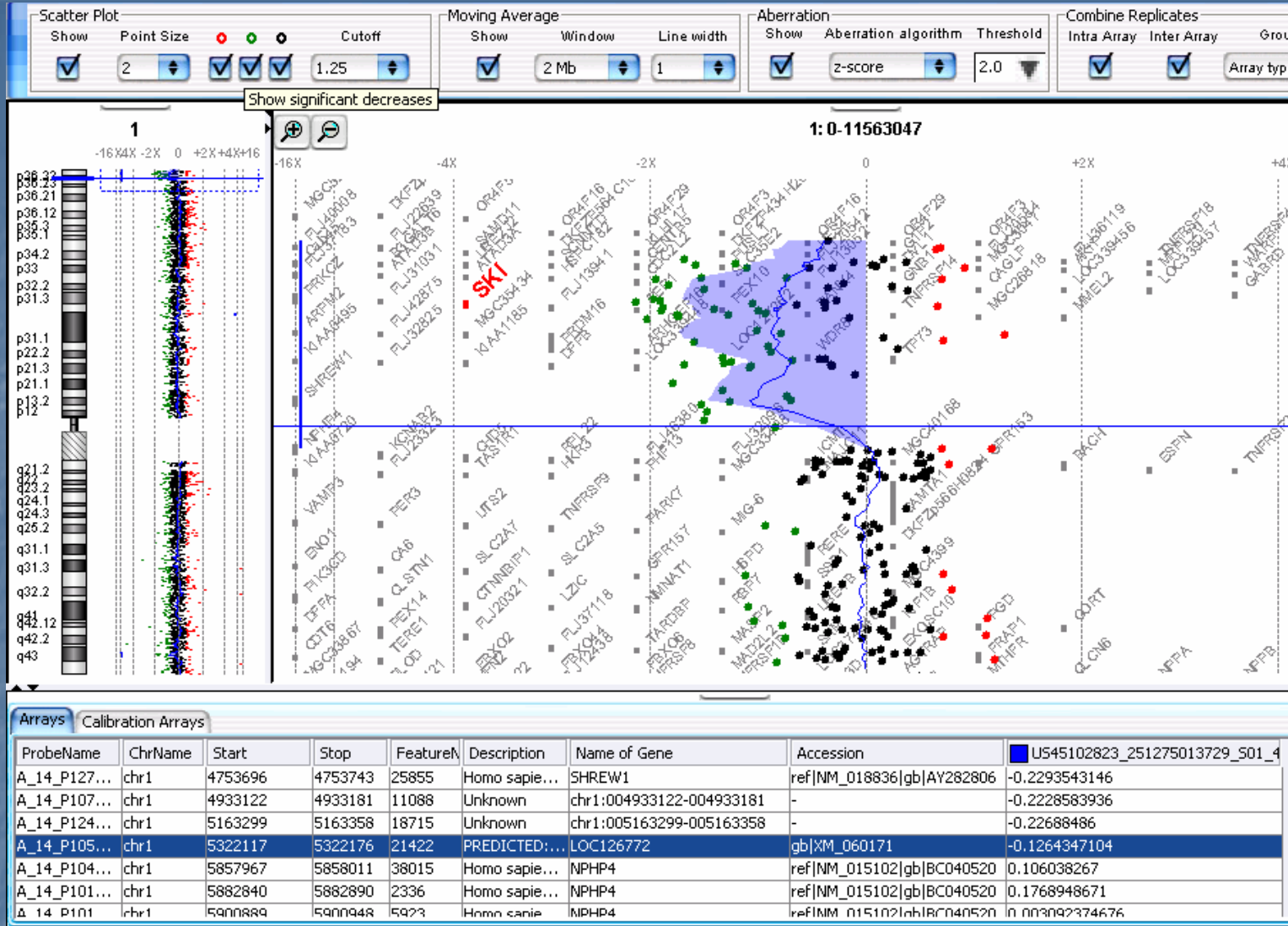


RP11- 465B22

RP11-58A11



Breakpoint is proximal to this probe sequence



**Microarray data: deletion from 1.089934 Mb to 5.322176 Mb (4.232242 Mb deletion)**

**Having confirmed deletion – what next?**



| >> LITERATURE & DATABASES                                | Heilstedt et al 2003<br>DECIPHER NOTES | DECIPHER<br>0 - 5.2Mb | Our Patient<br>1 - 5.3Mb | Redon et al 2005<br>Patient E<br>0 - 2.5Mb | al 2005<br>Patient F<br>2.9- 10Mb |
|--|--|-----------------------|--------------------------|--|-----------------------------------|
| CLINICAL FEATURES: 1p36 deletion                         |  |                       |                          |  |                                   |
| Developmental delay                                      | 100% <i>100</i>                        | +                     | +                        | +  | +                                 |
| Hypotonia (distal 2Mb)                                   | 82% <i>100</i>                         | +                     | +                        | +  | +                                 |
| Large ant.fontanelle (dist 2Mb)                          | 85%                                    | +                     | -                        | ?  | ?                                 |
| Impaired hearing (dist 2.5Mb)                            | 82%                                    |                       | -                        | -  | +                                 |
| Cardiac defect   | 43% <i>40</i>                          |                       | -                        | -  | Ebstein anomaly                   |
| Cardiomyopathy (distal 3Mb)                              | 23% <i>23</i>                          |                       |                          |  |                                   |
| Microcephaly/Brachycephaly                               | 60%                                    |                       | +                        | -  | +                                 |
| Deep set eyes  | 80%                                    | +                     |                          | +  | +                                 |
| Flat nose/nasal bridge                                   | 77%                                    |                       |                          | +  | -                                 |
| Flat mid face  |  |                       | +                        | +  | +                                 |
| Pointed chin   | 67%                                    | +                     | -                        | +  | +                                 |
| Overt clefting (distal 4Mb)                              | 17% <i>20-40</i>                       |                       | -                        | -  | -                                 |
| Seizures (? <i>KCNAB2</i> 5.97-6.08Mb)                   | 58%<br><i>&lt;72</i>                   | +                     | +                        | +  | -                                 |
| Ophthalmologic abnormalities:<br>hypermetropia;nystagmus | 67%;13%                                |                       | ++; +                    | -  | -                                 |

Case from Norma Morrison et al, Duncan Guthrie Institute

DatabasE of Chromosomal Imbalance and Phenotype in Humans using Ensembl Resources

Heilstedt et al (2003) Am J Hum Genet 71:1200-1212; Redon et al (2005) J Med Genet 42:166-171

# PBL format case study

- **Groups are given clinical case scenario**
  - On basis of information provided they can request various diagnostic tests
  - If they are able to justify the test (and the cost) they are given the results
- **After two weeks of “testing” they provide a report including their diagnosis and suggested management for various members of the family**

# Summary of part B

– value of case studies

- Requires students to **select** sensible sequence of techniques or investigations
  - Students should justify their choice
  - They see the results
  - Interpret & decide how to proceed
- Progression of ideas



# Overall Summary

- Data discussions and case studies provide students opportunity to develop skills in
  - Critical analysis and evaluation of data
  - Applying their knowledge to real problems
  - Communication of ideas and building on each other's ideas
  - Planning a logical sequence of investigation(s)
- Discussion sessions provide *intrinsic feedback* for the skills being developed



# Acknowledgements

- Interviews with students (ETL study):  
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  - ESRC/TLRP Project on Enhancing Teaching-Learning Environments in Undergraduate Courses
  - <http://www.tla.ed.ac.uk/etl/>