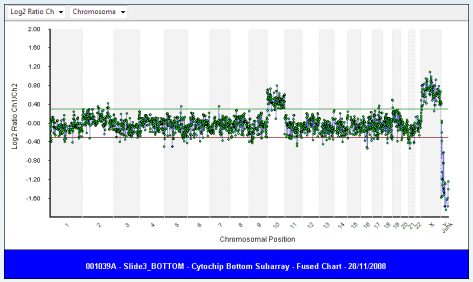
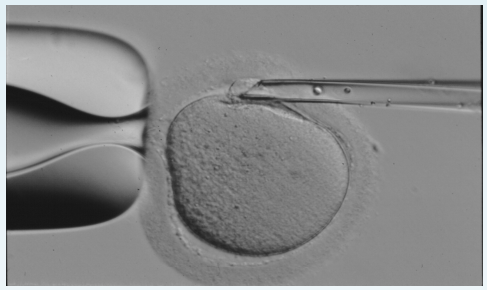
The use of arrays in PGD
A summary



Joyce Harper



Chair ESHRE PGD Consortium
UCL Centre for PGD

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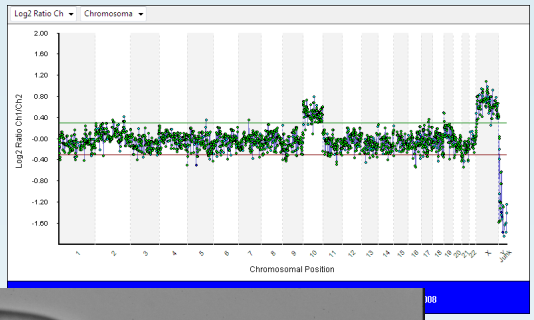
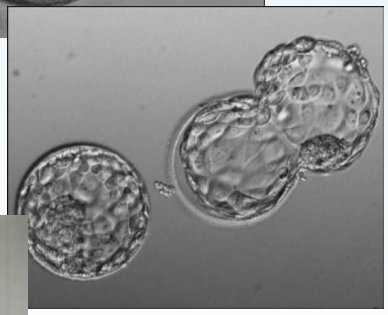
Summary

- Three questions for PGS
  - Validation (and which type of array?)
  - When to biopsy?
  - Is PGS a valid procedure?
- ESHRE PGS task force
- Conclusion





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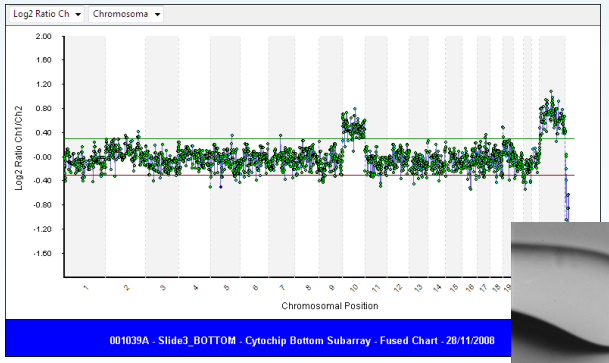
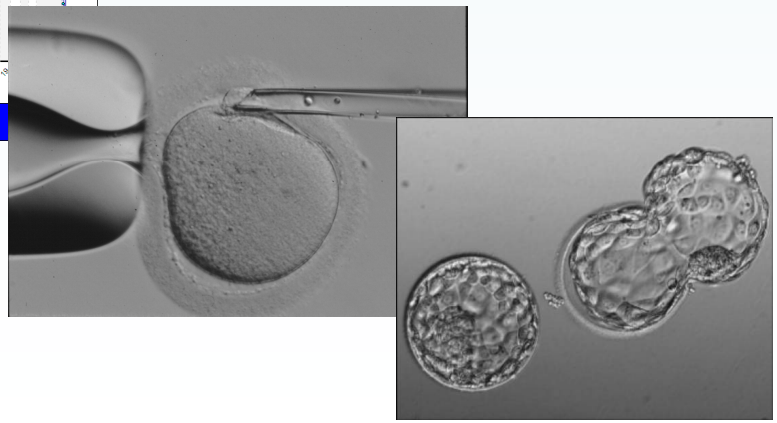
Three questions for PGS

- Have the array platforms been validated?
- What stage should PGS be performed?
- Is PGS going to increase the delivery rate?





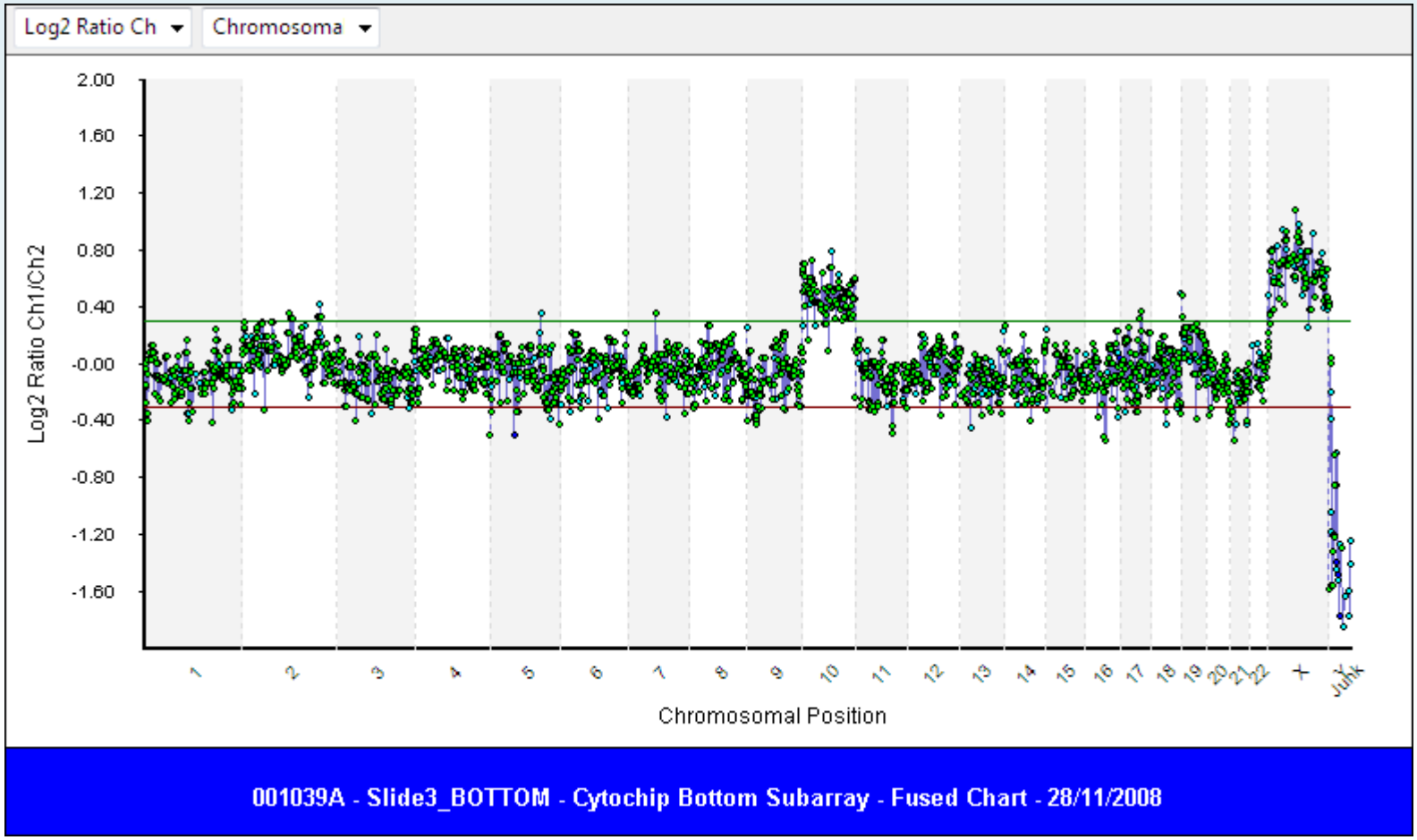
Validation of arrays

- Single aneuploid cells
- PBs and/or trophectoderm
- How many cells to analyse?
- Inter and intra observer
- Run samples on more than one type of array
- EQA arrays

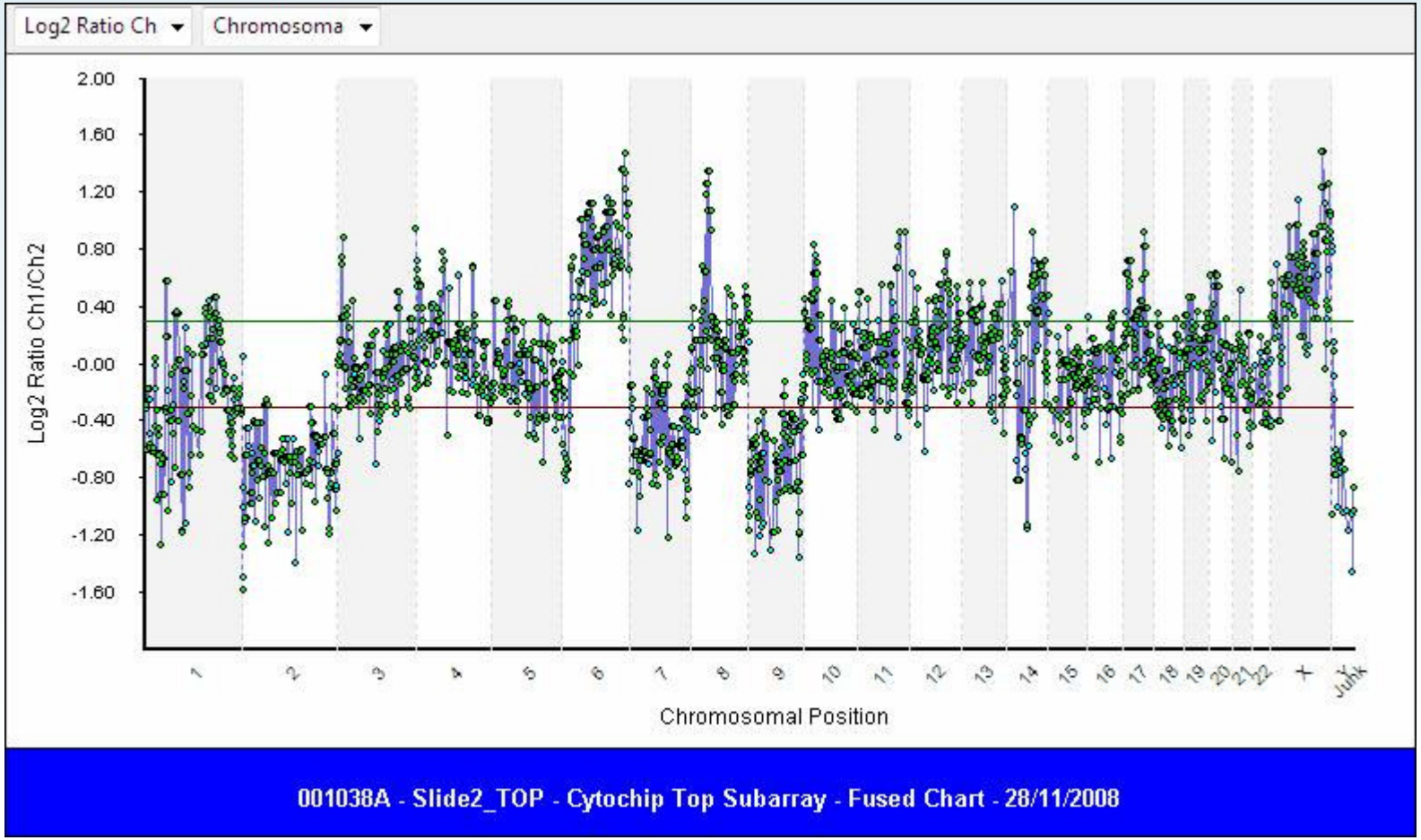
Validation

- Has to be done on a number of single cells from known aneuploid cell lines
- Epithelial cells; controls and cancer lines
- Four cancer lines with variety of aneuploidies
- GenomePlex
- BlueGnome 24sure array

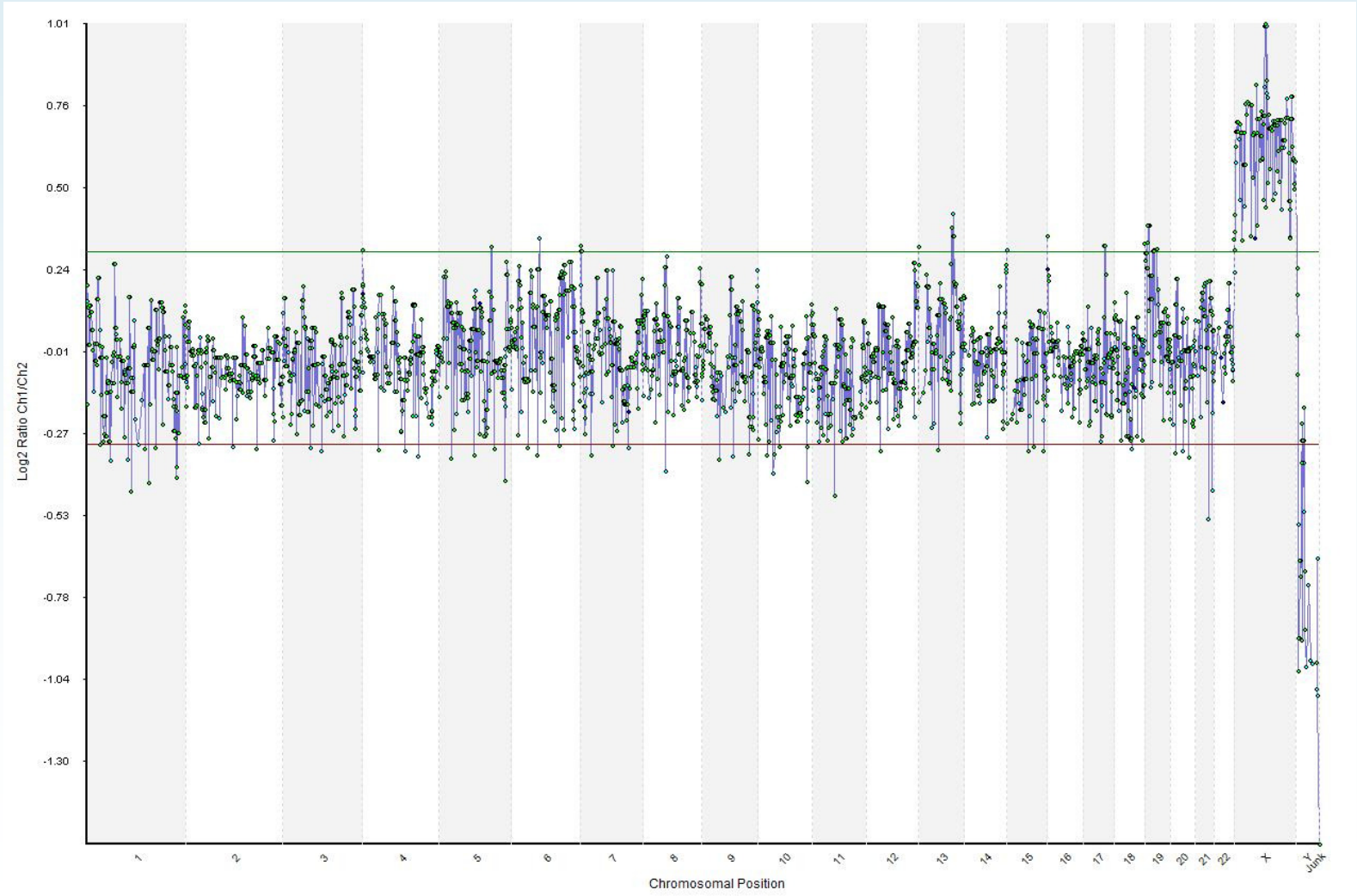
Trisomy 10 cell line



Monosomy for chromosomes 2, 7 and 9 and trisomy 6



Normal female

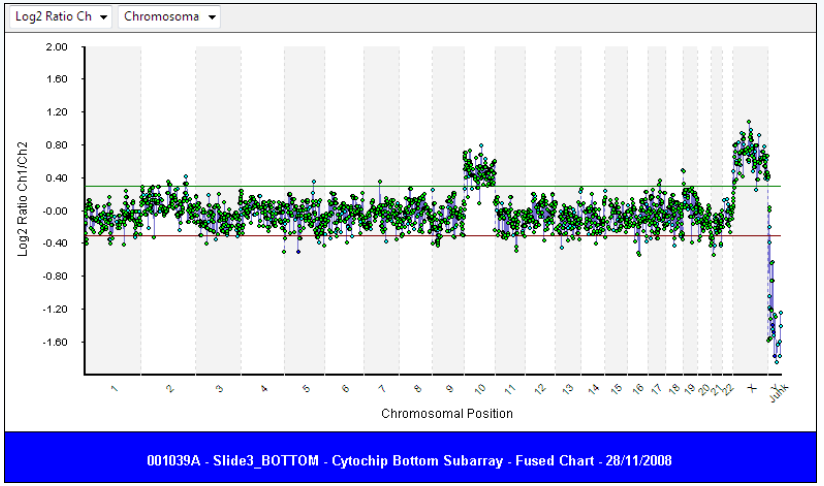


Summary of results

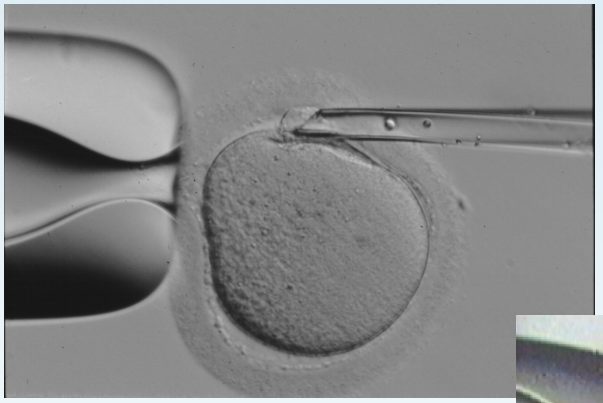
- 40 single cells
- 39/40 successful amplification
- 39/39 successful array
- 9 normal cells
  - All normal
- 30 abnormal cells
  - 28 confirmed abnormal results
  - 2 unassigned

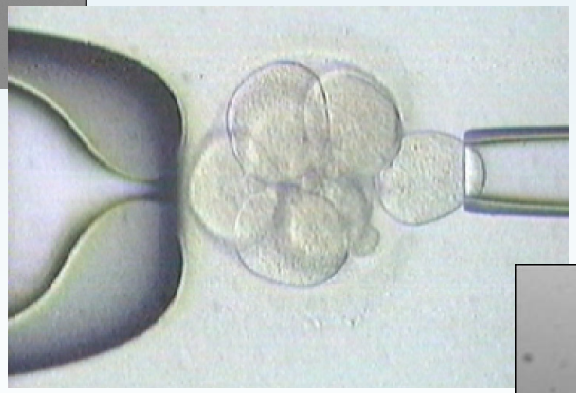
Which type of array?

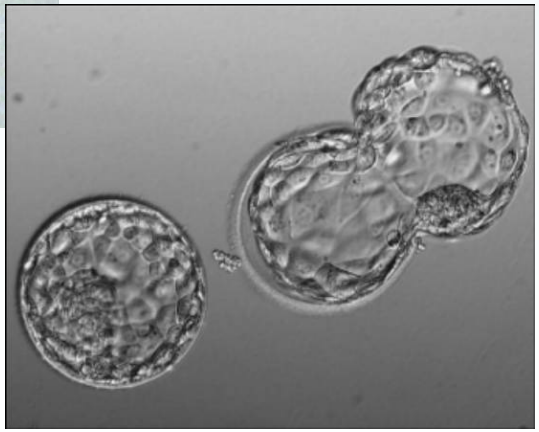
- SNP
  - Ethical concerns
  - Monogenic and chromosomes
  - Longer protocol
- Array CGH
  - Just chromosomes
  - Shorter protocol



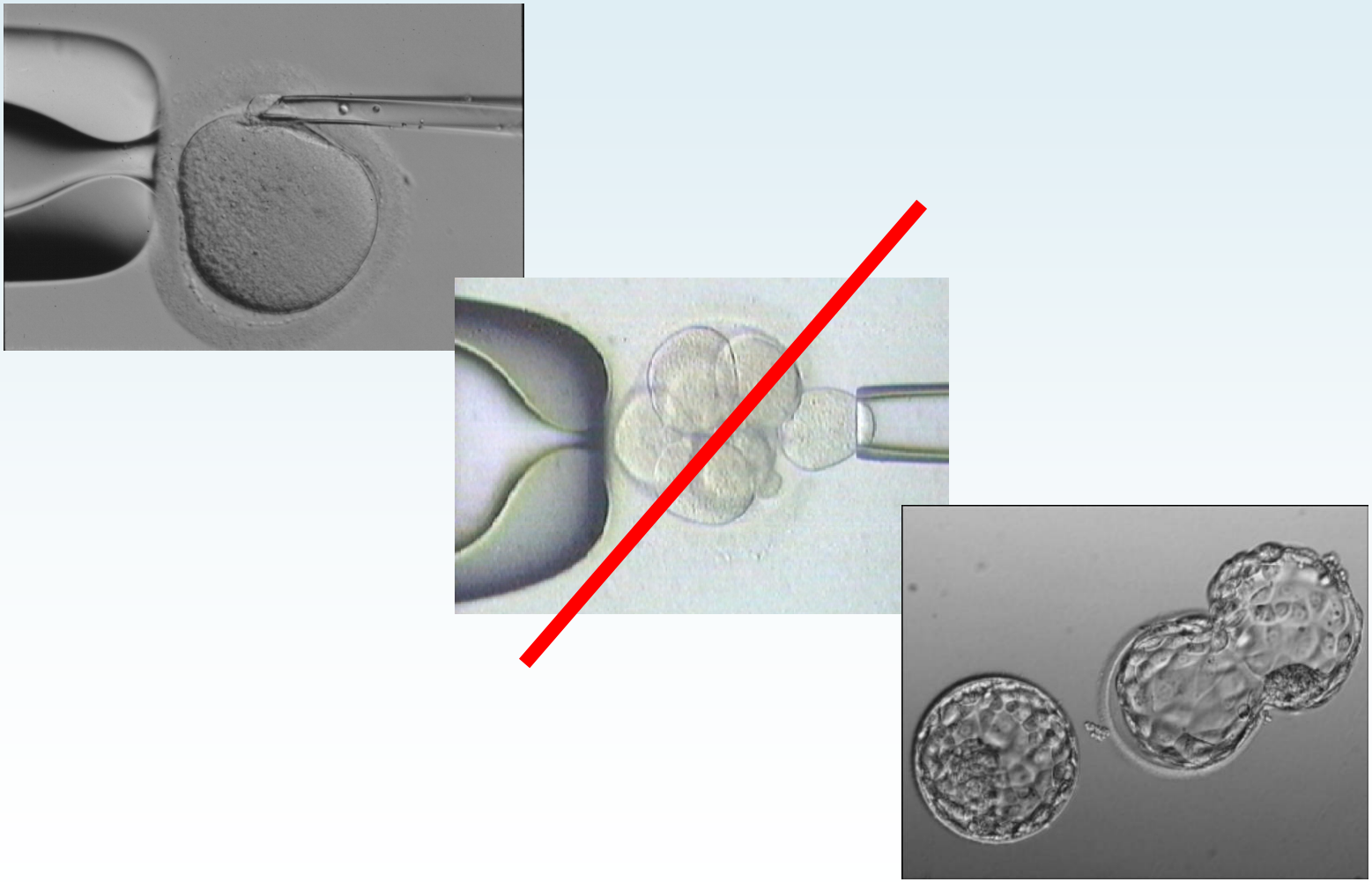
When to biopsy?







When to biopsy?



Is PGS a valid procedure?

- Poor prognosis patients
  - Staessens et al, 2004
  - Stevens et al, 2004
  - Debrock et al, 2007
  - Mastenbroek et al, 2007
  - Hardarson et al, 2008

- Good prognosis patients
  - Staessens et al, 2007
  - Meyer et al, 2007
  - Jansen et al, 2008
  - Mersereai et al. 2008

ESHRE PGS task force

- Can polar body biopsy and array CGH improve the delivery rate of patients with advanced maternal age?

ESHRE PGS task force

- Set up in 2007
- ESHREs first involvement in a clinical trial
- Assess efficacy of PGS for advanced maternal age using polar body biopsy and analysis of 24 chromosomes (array)
- Two stages – pilot and randomised controlled trial

Pilot study

- Feasibility study
  - Can analysis of both polar bodies be completed within a time period that allows for fresh transfer?
  - Ensure reliable identification of the chromosomal status of an oocyte in at least 90% of polar body biopsy attempts
  - Test the feasibility of a multicentre randomized trial based on the technology used in the pilot study
- Two centres with polar body biopsy and PGS experience
  - SISMER, Bologna, Italy (Cristina Magli, Luca Gianaroli)
  - University of Bonn, Germany (Markus Montag, Hans van der Ven)
- Both polar bodies and untransferred zygotes analysed using 24sure with no age restriction
  - BlueGnome, Cambridge, UK
- Data analysed by third party
  - Sjoerd Repping, Academic Medical Centre, Amsterdam
- Starting September 2009
- Present data ESHRE Rome 2010

BlueGnome

24sure™

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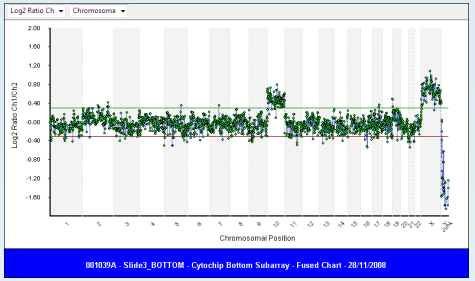
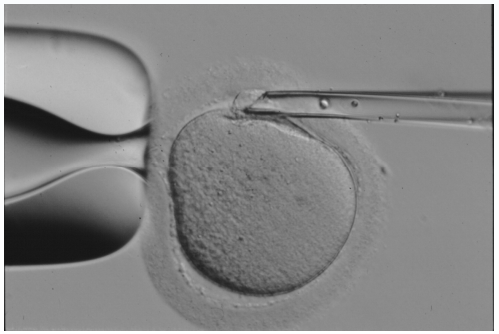
Randomised controlled trial

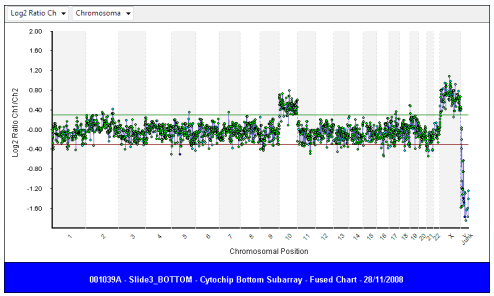


- If pilot shows technology is feasible –
- RCT
- Multi-centre
- At least six centres in different EU countries
- Advanced maternal age
- Polar body biopsy allows
  - Fresh transfer
  - Less invasive biopsy
  - Hopefully more reliable than cleavage or blastocyst biopsy (mosaicism)
- If trial shows that PGS improves delivery rates – will be major step in IVF treatment

Conclusion

- Biology and technology
- Validate arrays
  - SNP arrays – ethical concerns
  - Array CGH
  - BOBs
- Choose appropriate time to biopsy
  - PBs
  - Blastocyst
- RCT using arrays to determine affect on delivery rates
- Can we use arrays for translocations, etc?





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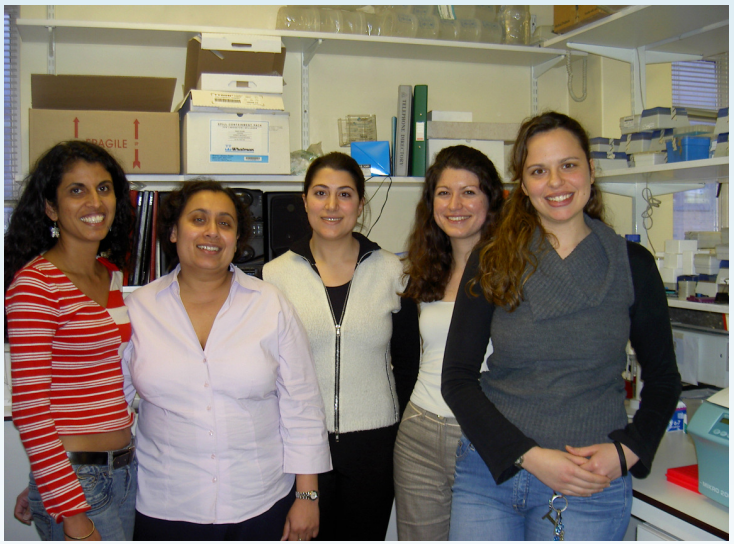

ESHRE PGS task force

- Joep Geraedts
- Cristina Magli
- Sjoerd Repping
- Catherine Staessen
- Paul Devroey
- John Collins
- Veerle Goossens

Luca Gianaroli
Markus Montag
Andreas Schmutzler
Katerina Vesela
Alan Handyside
Joyce Harper

Thanks to all participants and speakers

See you in Rome

- Evaluations
- Focus in Reproduction