Advances in Clinical Cytogenetics

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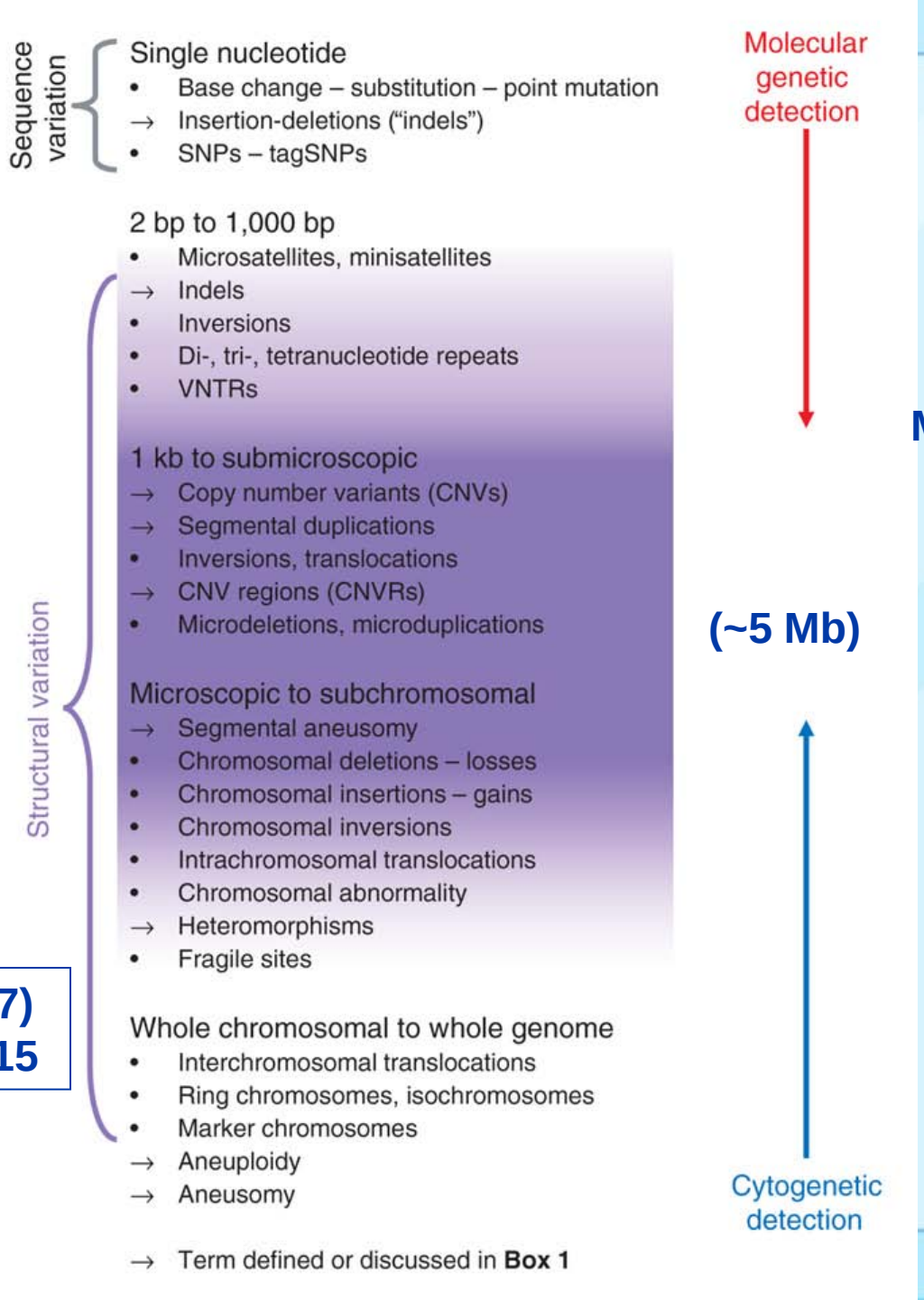
Disclaimer

"The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry (CDC/ATSDR)"

Scale of Genomic Variation

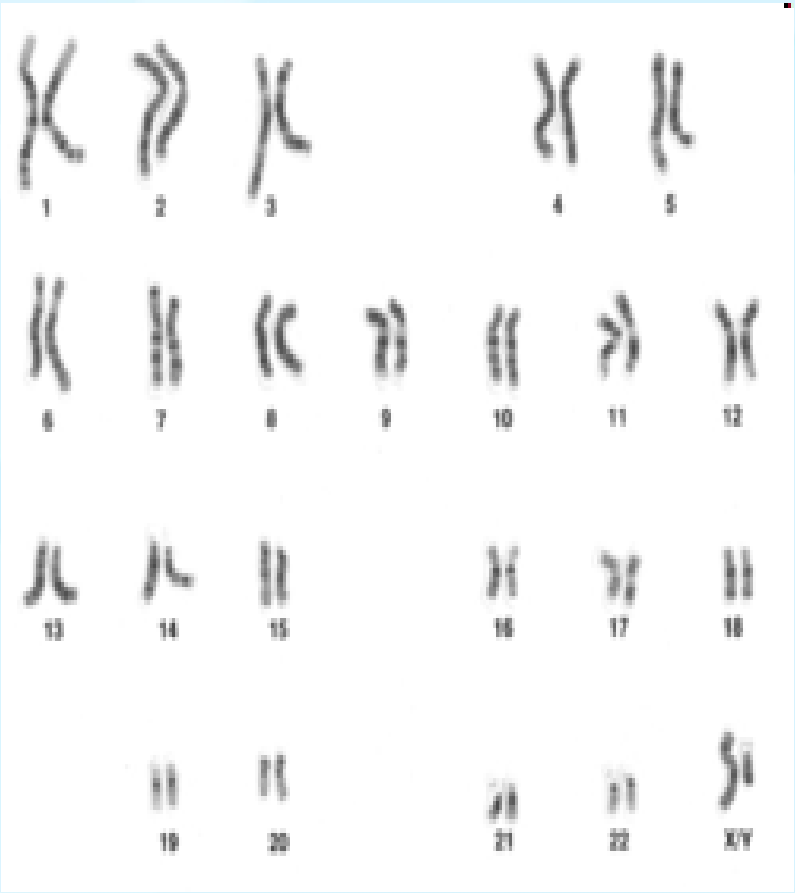


Scherer et al. (2007)
Nat Genet 39:s7-s15

Karyotyping

- 1960's - 1980
- Chromosome morphology
- Metaphase chromosomes
- Banding patterns and chromosome maps
- Translocations, deletions, insertions –

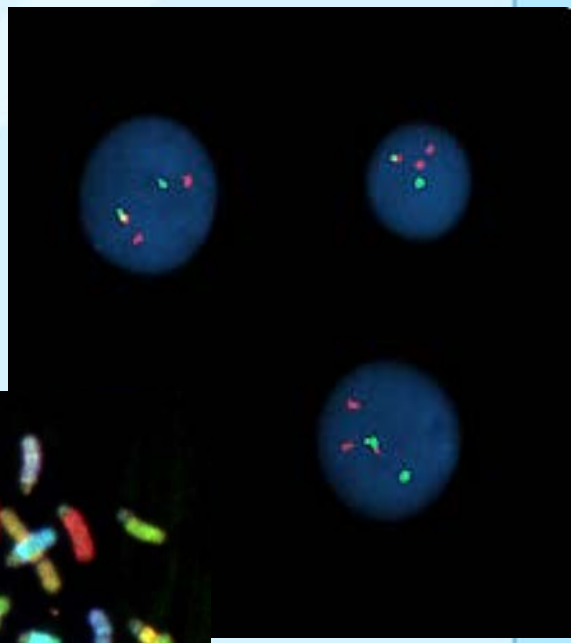
5 Mbp

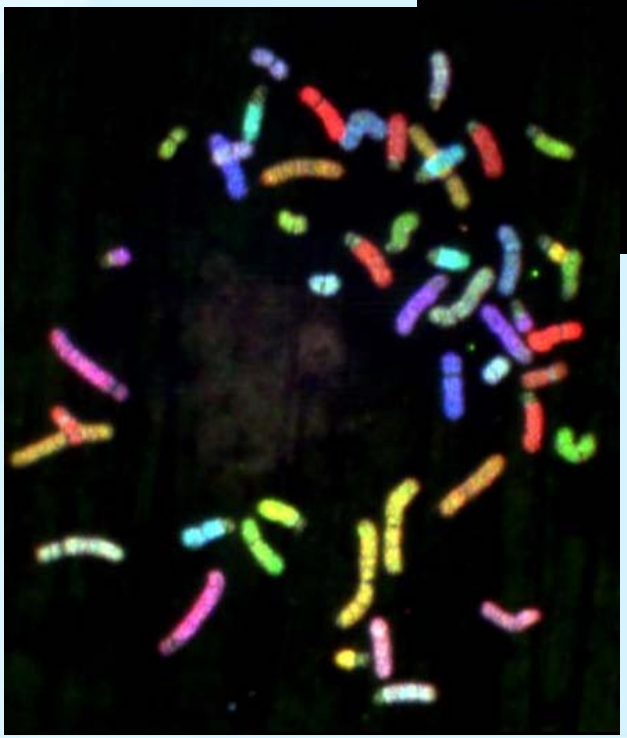


Molecular cytogenetics

- 1980's
- Fluorescent in situ hybridization probes (FISH) –sequence specific
- Interphase or metaphase
- Morphology and DNA rearrangements -

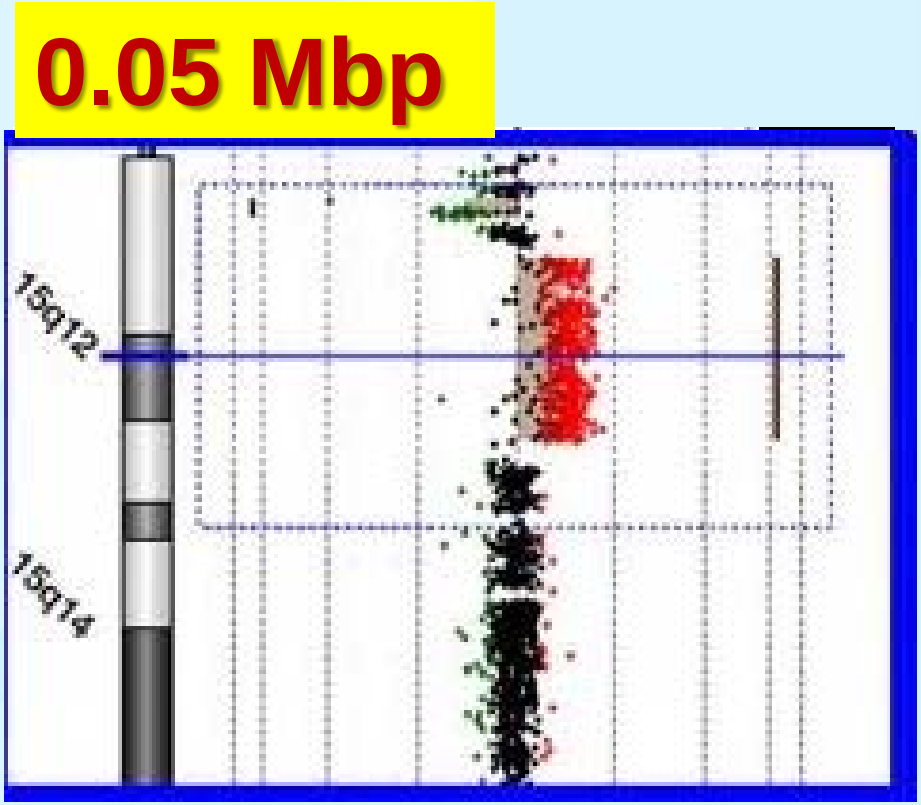
0.5 Mbp



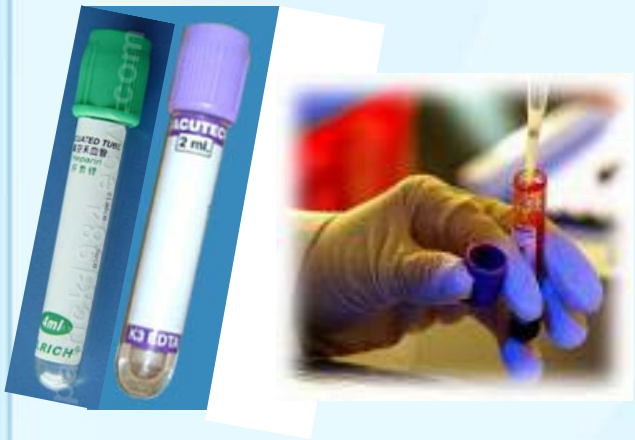


Cytogenomics

- Copy number variation (CNV) – gains or losses,
- Comparative genomic hybridization arrays (aCGH) or chromosomal microarrays (CMA)
- Single nucleotide polymorphism (SNP) arrays



Workflow for Chromosomal Microarrays



Isolate DNA

Oligo Arrays:
Agilent, Roche/Nimblegen

↓

Label DNA

↓

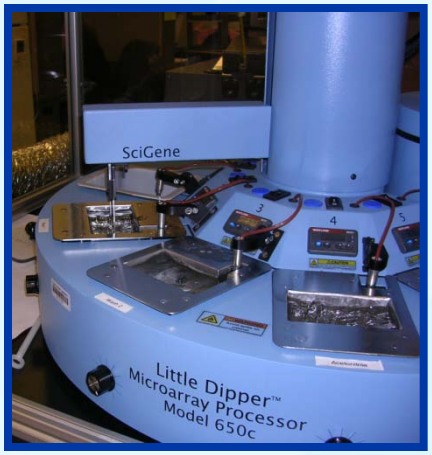
Prepare Sample
(Patient and Control or Patient Only)

↓

Hybridize DNA to Array

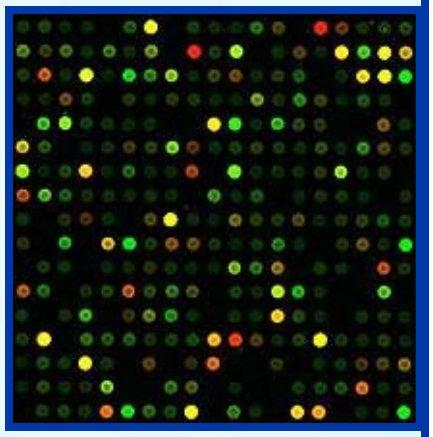
Slide courtesy of Madhuri Hegde

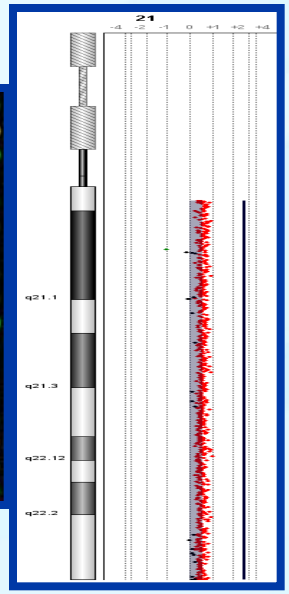
Array Processing



Wash

Scan

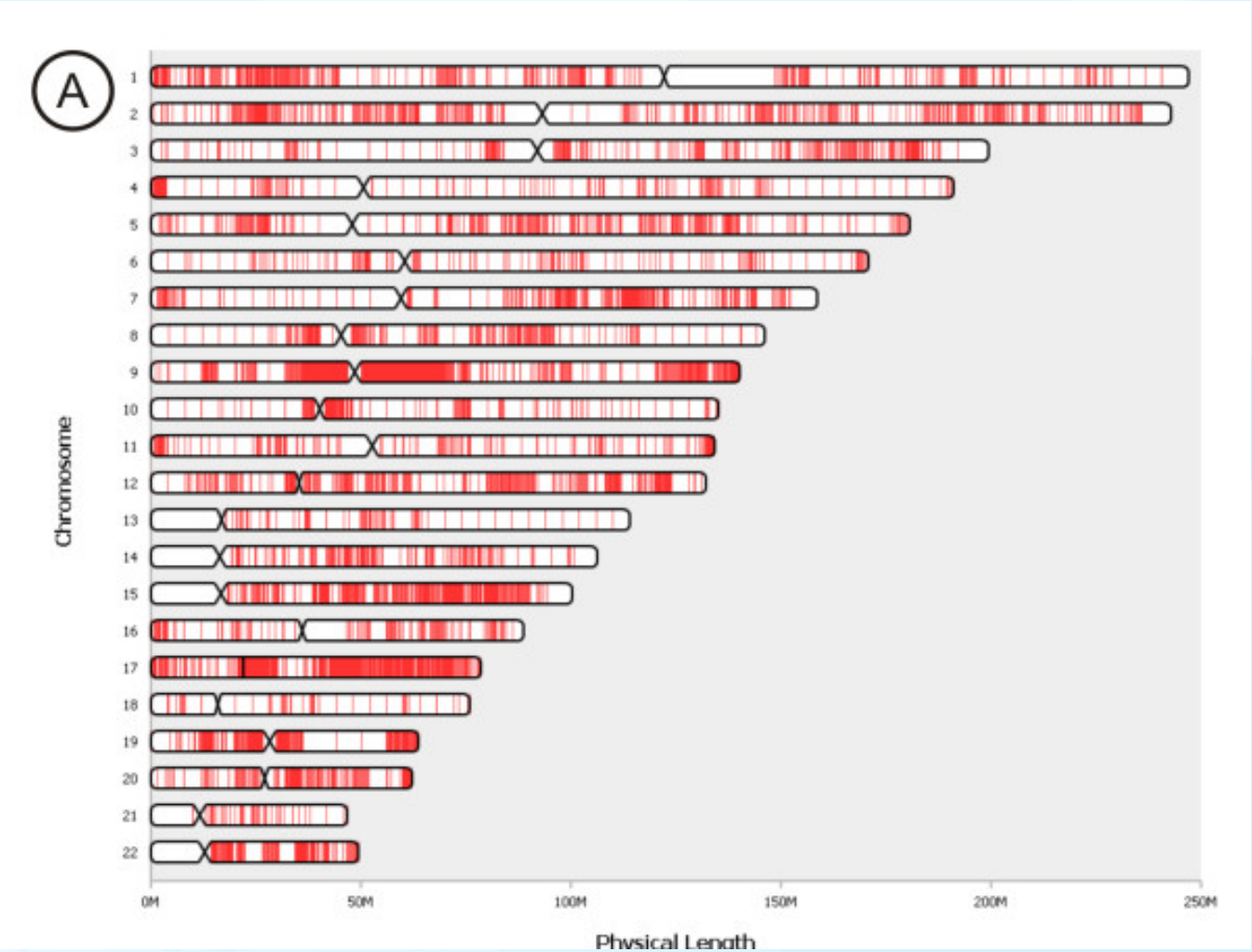




Analysis

Slide courtesy of Madhuri Hegde

CNVs on each chromosome



Forer L, et al. BMC Bioinform. 2010, 11:318
http://www.biomedcentral.com/1471-2105/11/318

Challenges

- Combined technologies of DNA and chromosomes
- All chromosomes examined at once
- Collection of huge amounts of quantitative data
- Interpretation for clinical decision-making

Questions

- Do clinical cytogenetic regulations adequately assess cytogenomic laboratory practices?
- What and where are the gaps in quality?
- How can these be addressed or remedied?