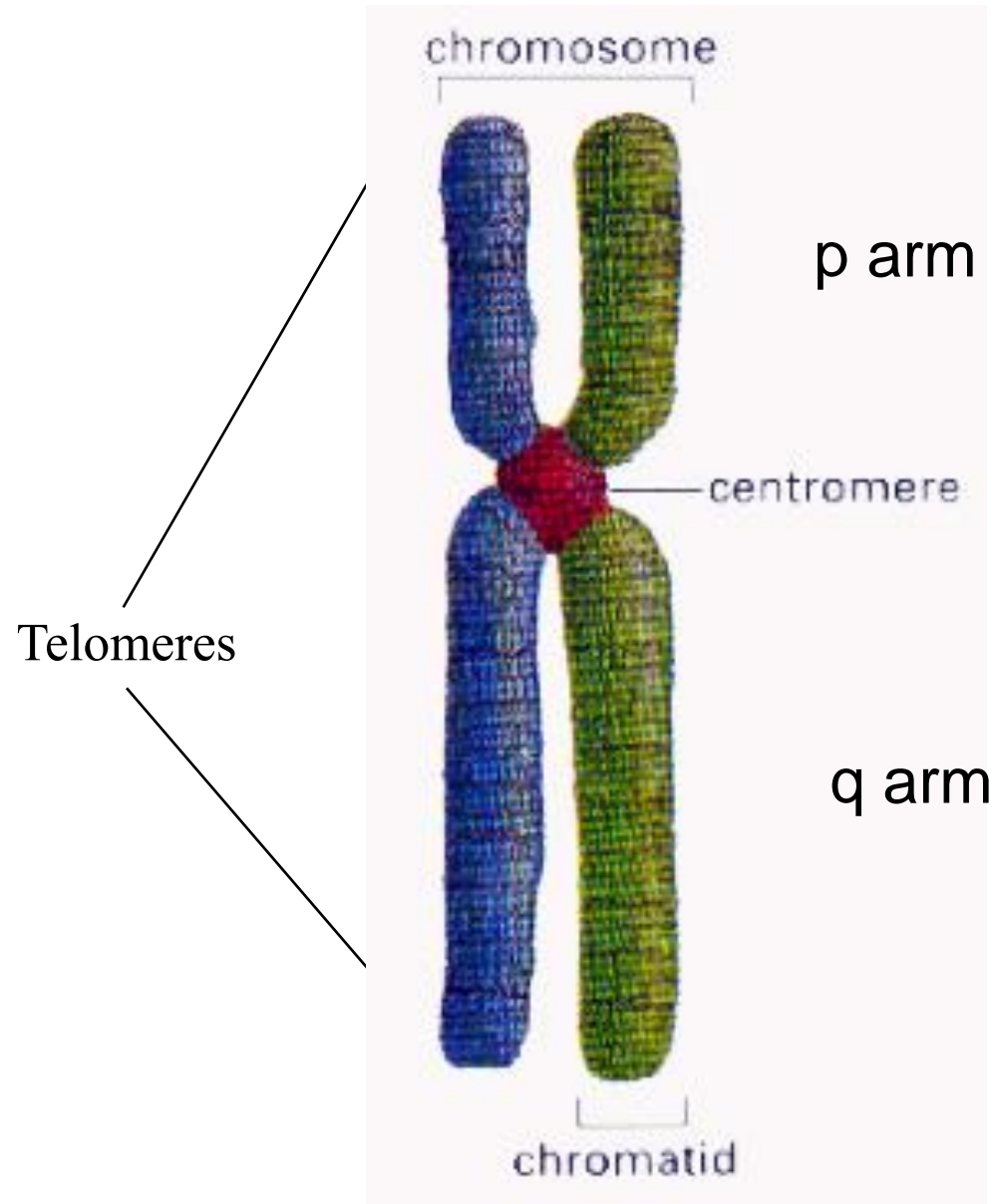




KromaTiD, Inc.

Susan M. Bailey, F. Andrew Ray, Joel S. Bedford,
Michael N. Cornforth and Edwin H. Goodwin

What is a chromosome? What is a chromatid?

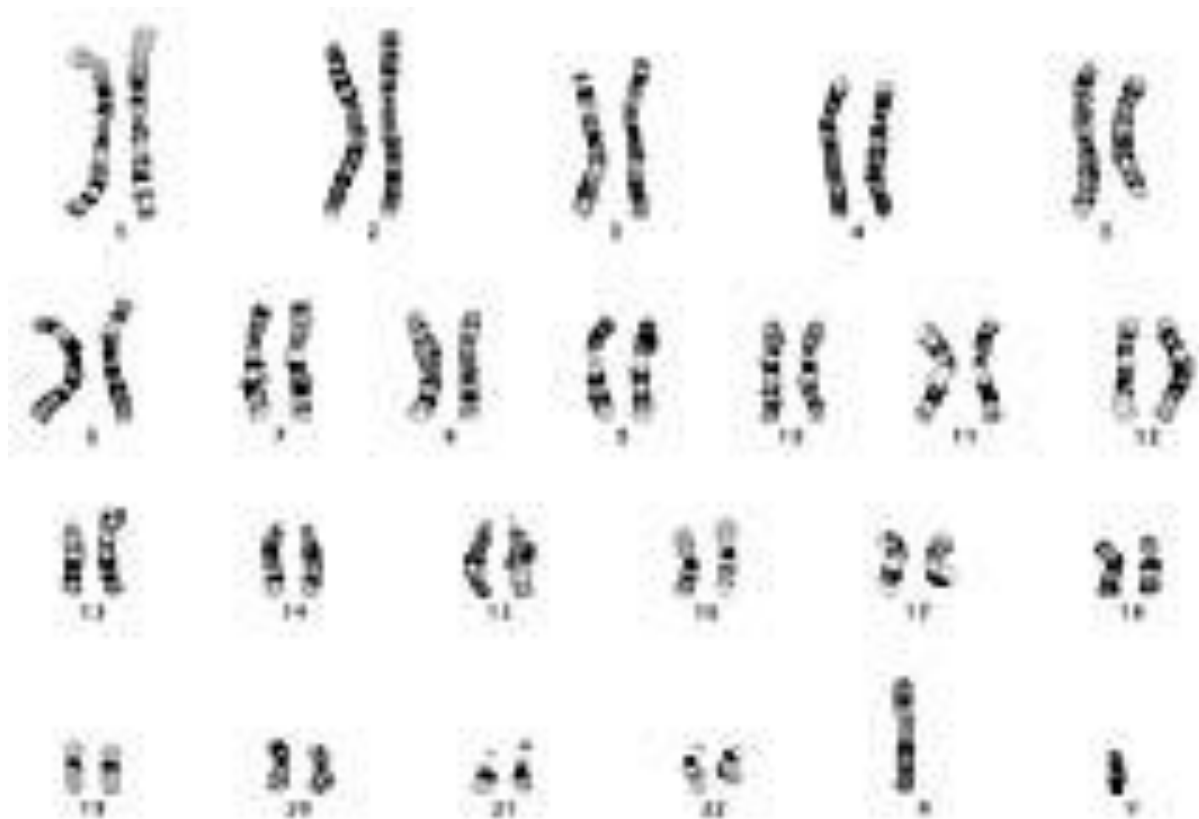




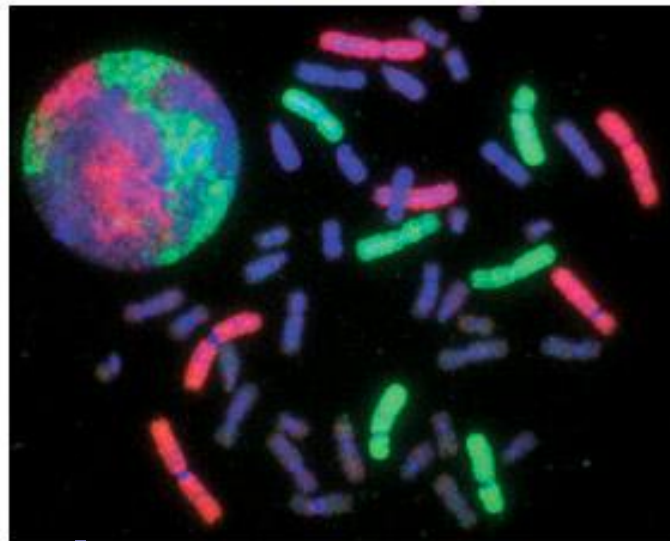
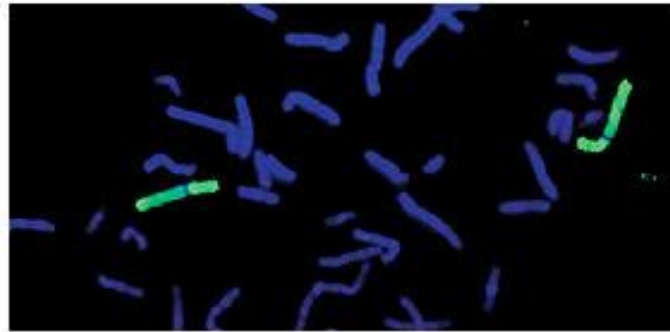
Cytogenetics – study of chromosomes

- Identification of specific abnormalities associated with a variety of disease states
 - Cancer (Ph 9:22 translocation in leukemia)
 - Down's syndrome (trisomy 21)
- Must be able to identify chromosomes

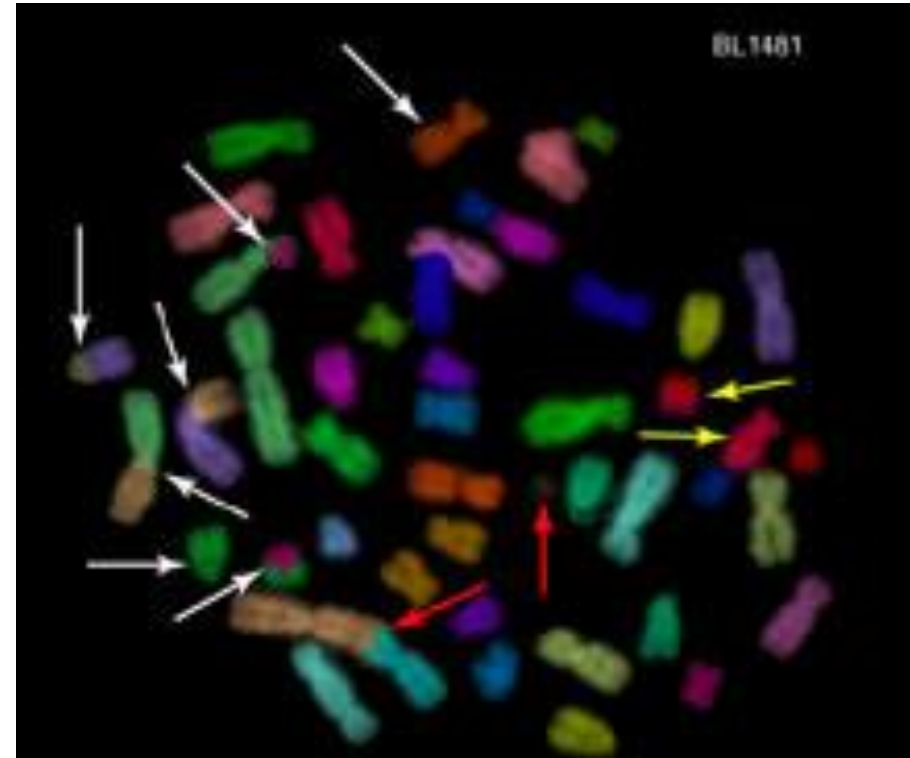
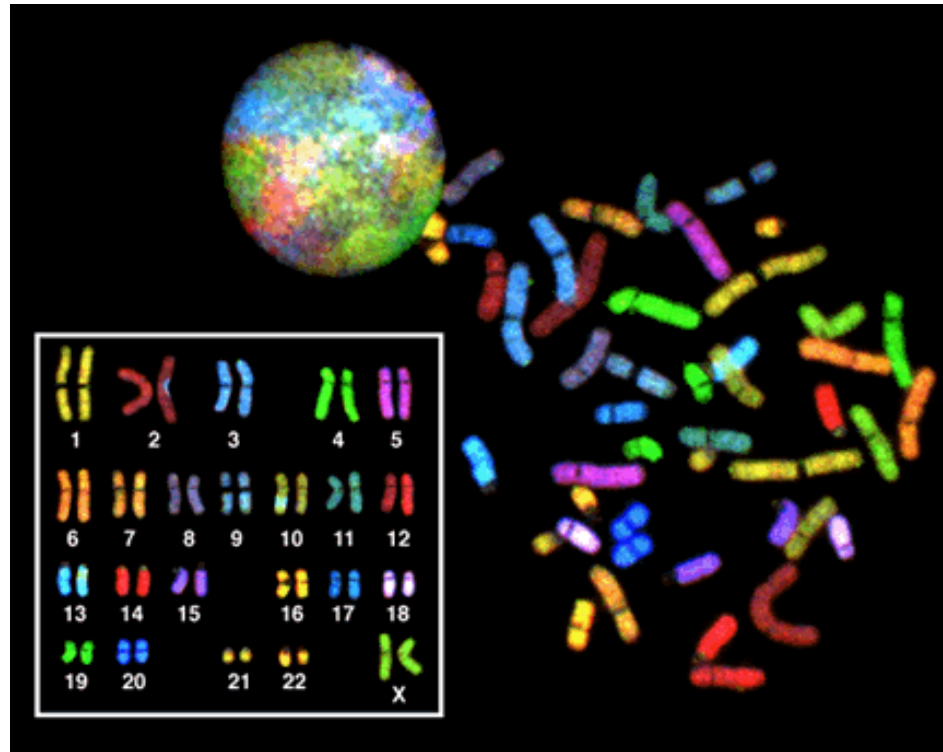
G-banded human karyotype



Whole Chromosome Paints



SKY and mFISH



M-BAND

1166

Am. J. Hum. Genet. 72:1162-1170, 2003

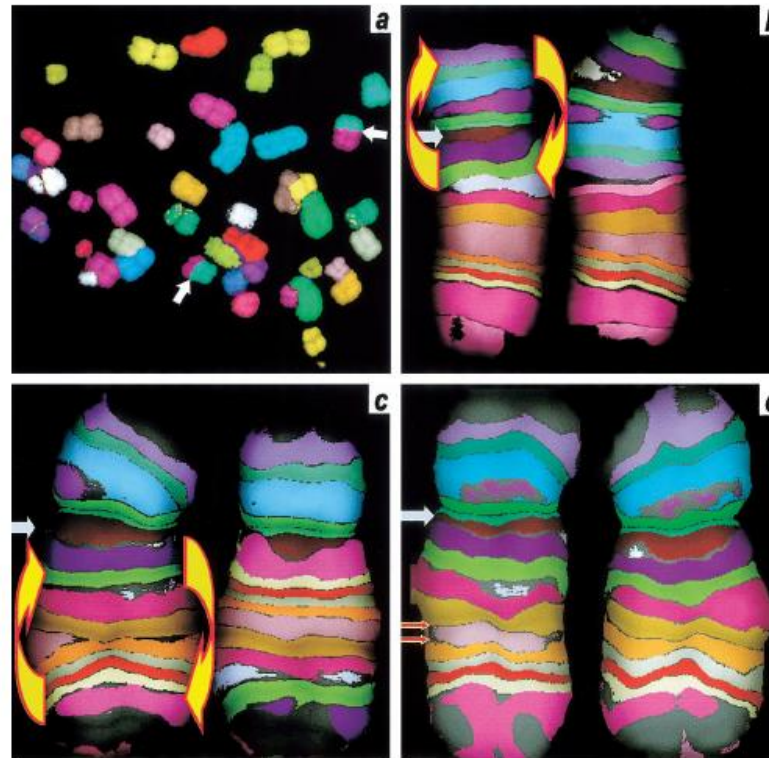
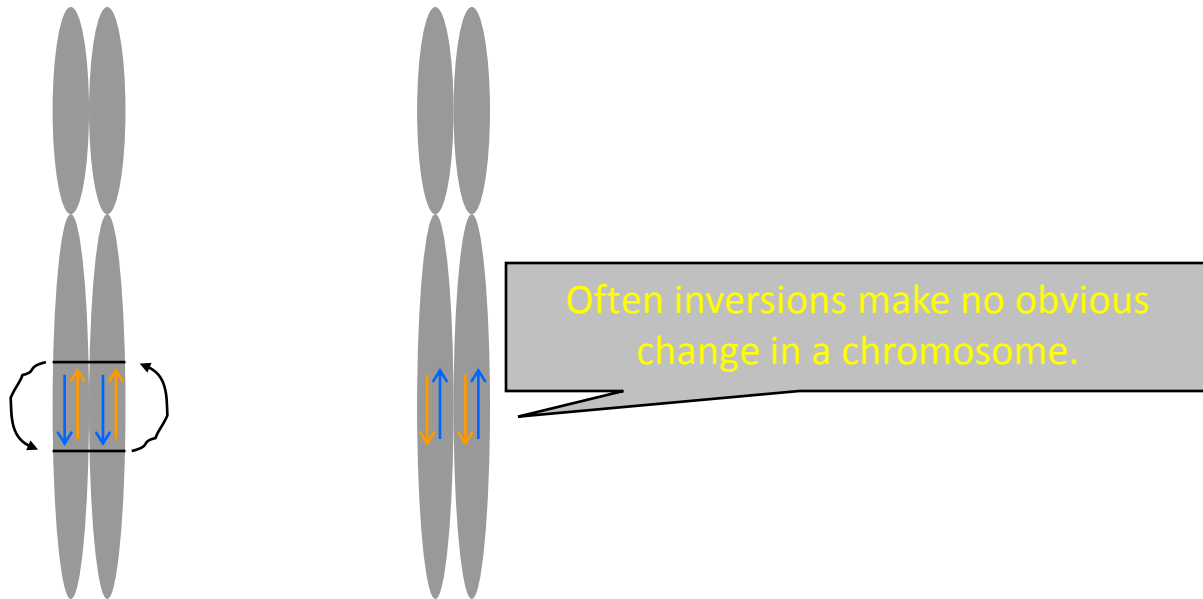


Figure 3 Stable *inter-* and *intrachromosomal* aberrations in Mayak plutonium workers (pseudocolor images). The panels correspond to the schematics in figure 1. *a*, *Interchromosomal* aberration (simple translocation) (*white arrows*), detected using mFISH. *b-d*, *Intrachromosomal* aberrations (*gray arrows*) in chromosome 5 detected using mBAND, showing centromere. Left chromosome in each pair is normal; right chromosome shows aberration. *b*, *Interarm* aberration (pericentric inversion), showing the region of the chromosome that was inverted (*yellow arrows*). *c*, *Intrachromosomal intra-arm* aberration (paracentric inversion), showing the region of the chromosome that was inverted (*yellow arrows*). *d*, *Intrachromosomal intra-arm* aberration (intra-arm deletion), showing the region of the arm that was deleted (*red arrows*).

Chromosomal Inversions

Inversions are the most difficult of all chromosome aberrations to detect; small inversions are virtually invisible to all cytogenetic methods in current use.





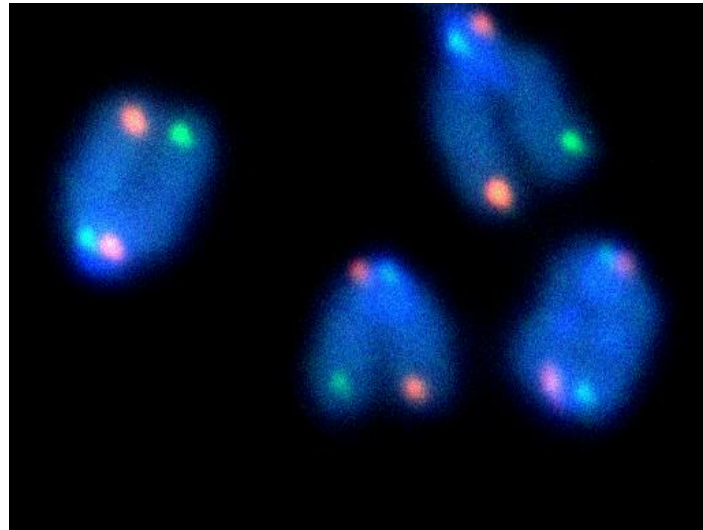
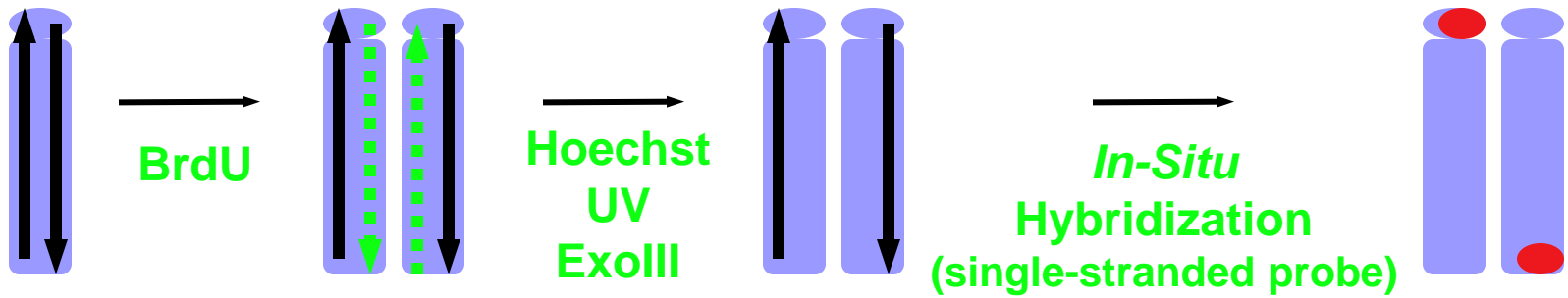
Chromosomes & Cancer

- Cytogenetics has done a lot for us -
 - More than 500 tumor-specific chromosome aberrations are known.
 - Translocations are common
 - Inversions much less so, possibly because inversions frequently go undetected.
 - As a result, many small, cryptic tumor-specific inversions await discovery.

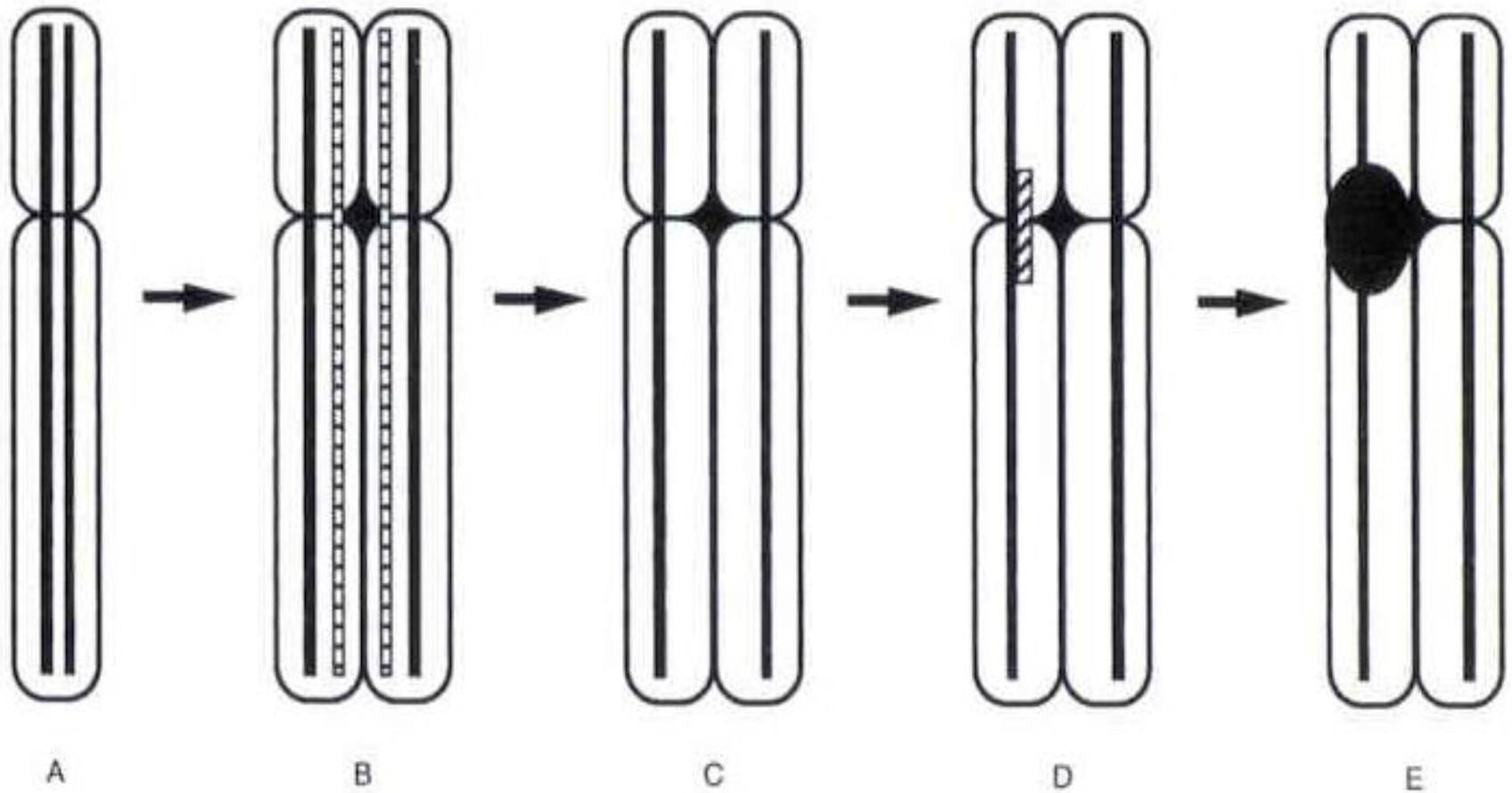
- There's a lot still to do!

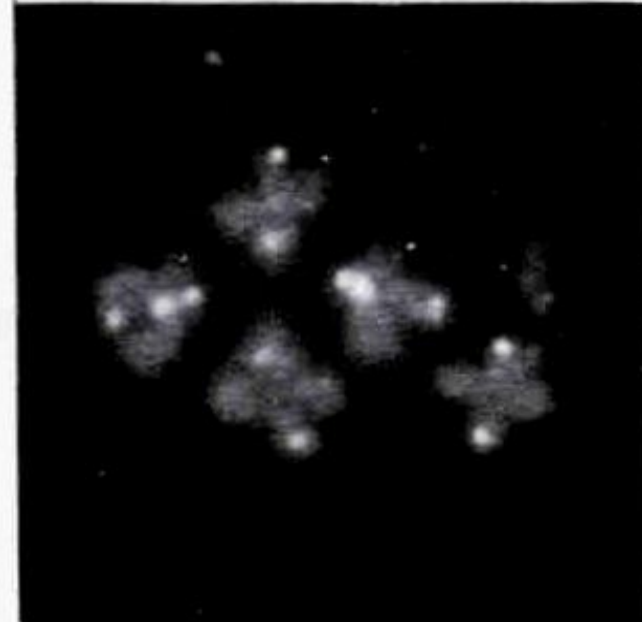
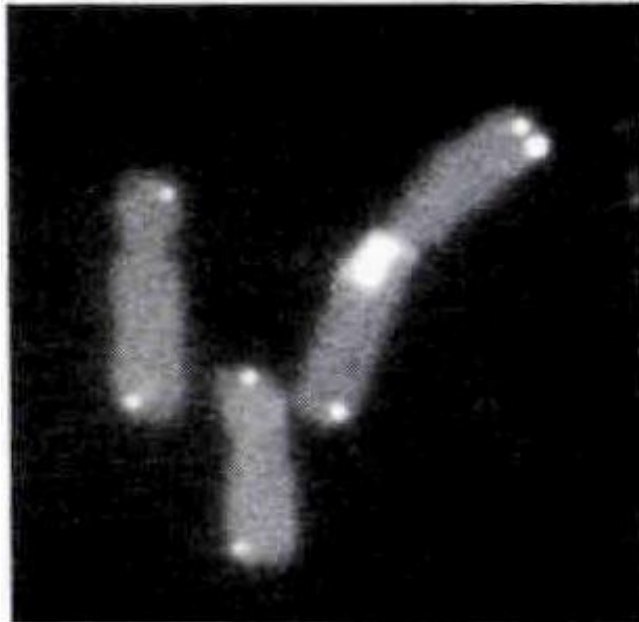
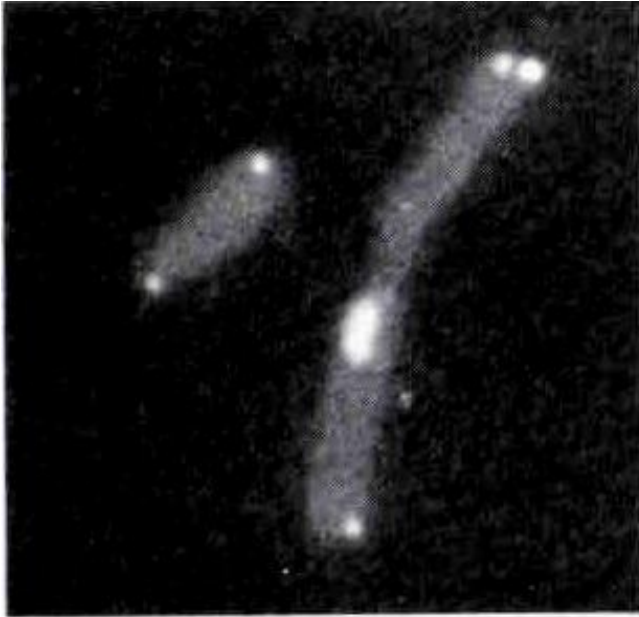
CO-FISH

Chromosome Orientation Fluorescence *In Situ* Hybridization

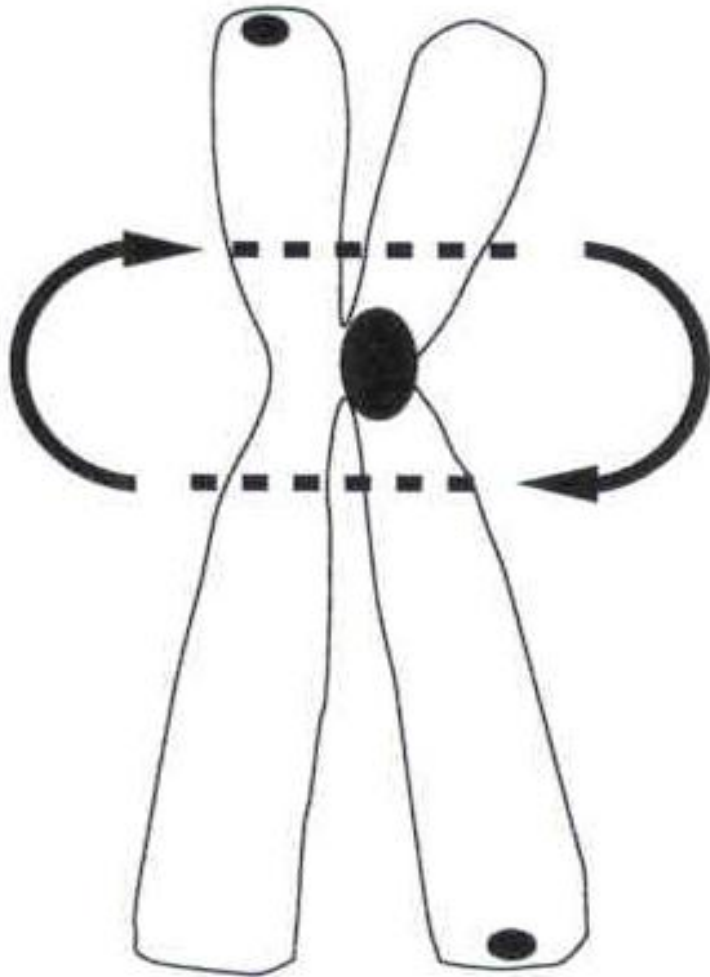


Chromosome Orientation Fluorescence *In Situ* Hybridization

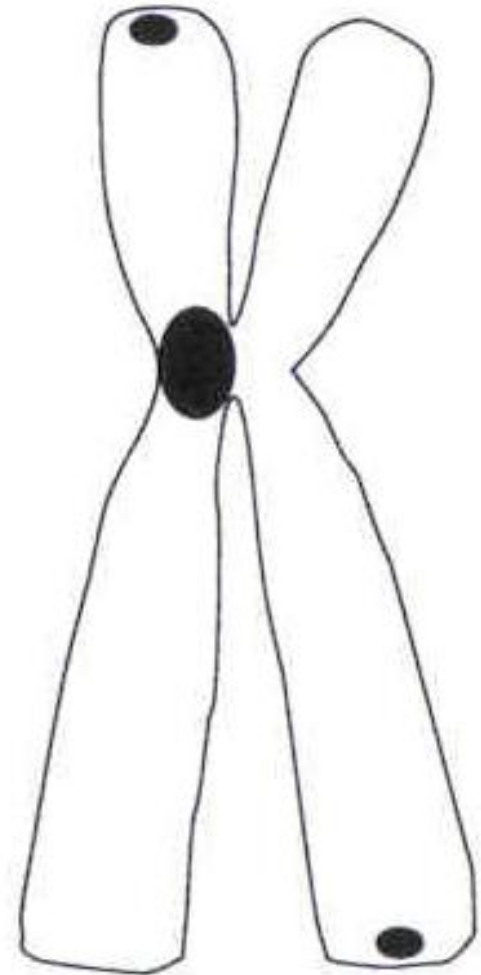




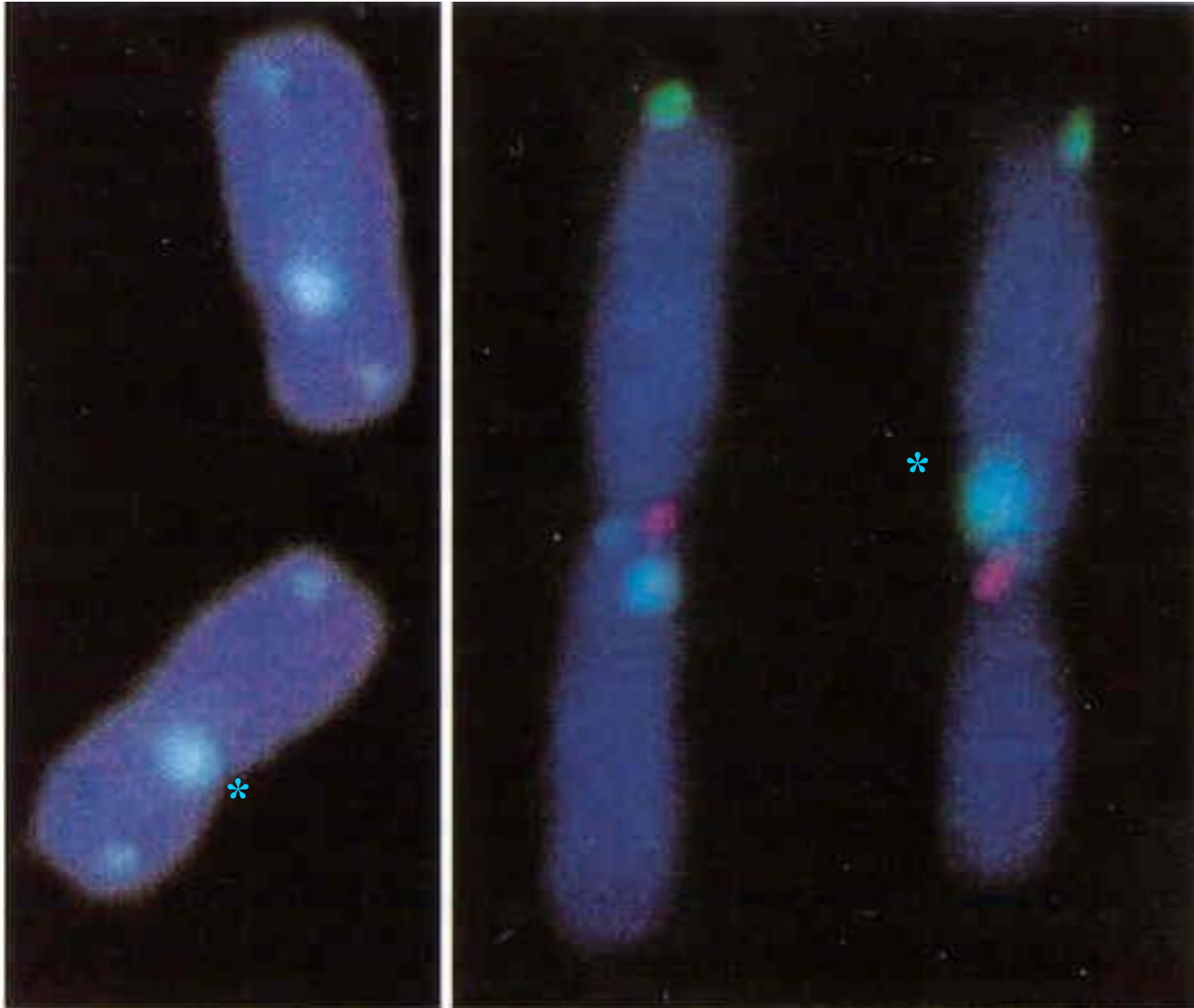
Inversion formation and CO-FISH detection – signal “flips” from one chromatid to the other



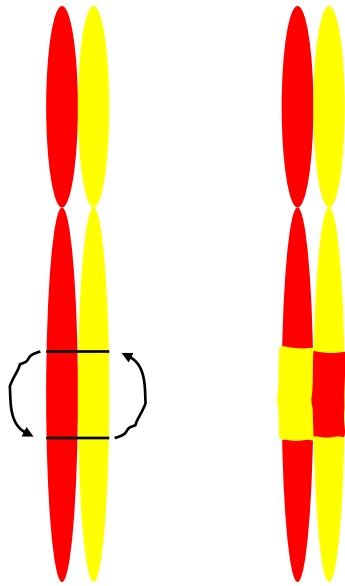
A



B



Advantages of Chromatid Paints



Ease of detection.

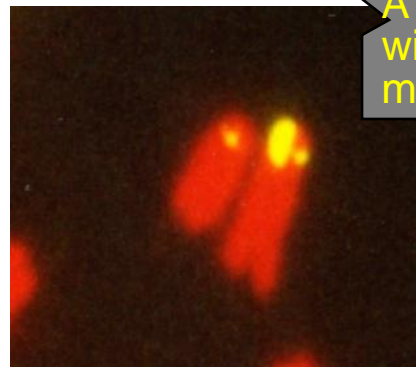
The signal switch pattern is easily identifiable.

Ease of use.

Compared to banding, much less specialized training required.

Enhanced Sensitivity.

With a high density of probe coverage, very small inversions can be detected with chromatid paints.



A small inversion within the repetitive mouse major satellite.

Chromatid Paints

- Inversions historically difficult to detect
 - many cryptic
- Increased resolution of detection
 - Disease states
 - Rec8 Syndrome (San Luis Valley, CO); parental inversion
 - Hypertension; 12p inversion
 - Radiation exposure
 - Inv10 in thyroid cancer seen in survivors of Chernobyl accident
- Development represents a milestone achievement
 - a new frontier in molecular cytogenetics

Commercial Applications

- Clinical cytogenetics
 - Cancer diagnosis and prognosis
 - Infertility diagnosis
 - Genetic counseling
 - Ethnicity studies
- Biomedical research
 - Mechanistic studies of cancer induction
- Biodosimetry
 - Nuclear power plant accidents
 - Bioterrorism
- Other species
 - Equine, canine, murine

Goals

- Augment/replace whole chromosome-specific paints with chromosome-specific chromatid paints
- Augment/replace multi-color chromosome-specific paints (SKY, mFISH) with multi-color chromatid-specific paints
 - genome-wide translocation identification
 - simultaneous and sensitive detection of inversions
- Huge market share - will surpass current and widely used chromosome paints

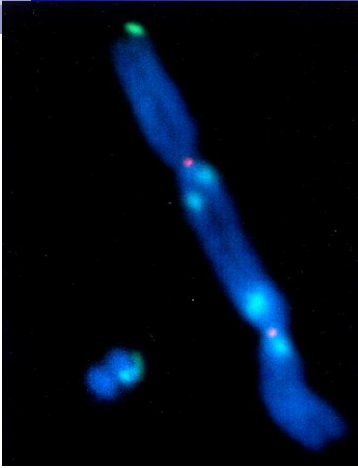


CSURF – very valuable resource

- Mark Wdowik
- Dian Kammeyer
- Christine Hardy

Facilitate -

- Tech Transfer
- File patents
- Form company
- Small business grants to develop technology



“KromaTiDz R Us”

- Edwin H. Goodwin, CEO
- Joel S. Bedford, Executive VP
- Michael N. Cornforth, VP R&D
- F. Andrew Ray, Treasurer
- Susan M. Bailey, Secretary

