MCB142/ICB163 Overview

Instructors:

Professor Sharon Amacher
Professor Abby Dernburg
Professor Monty Slatkin

GSIs:
Kristin Camfield
Nat Hallihan
Hana Lee
Christine Preston
Richard Price
Kate Smallenburg
Joel Swenson

MCB142/ICB163 Overview

Course policies, instructor information, and other salient information are all available through the course website:
http://mcb.Berkeley.EDU/courses/mcb142/

- **Prerequisites**: Biology 1A, 1AL, and 1B, or consent of instructor.
  Recommended: Chemistry 3A-3B or equivalent.
- **Textbook**: Hartwell *et al.*, Genetics: From Genes to Genomes. Third Edition.
- Exam dates: **Oct 6 @ 6-8 pm**, **Nov 6 @ 7-9pm**, and **Dec 19 @ 8-11am.**
  We are aware of conflicts with Physics 8A/B; please let us know of others.
- No make-up exams (see web site).
- You must attend the section for which you are enrolled
  (If you want to change sections, it must be done through BearFacts.)
- Wait list and Concurrent Enrollment: we hope to accommodate everyone, but it will probably take at least until the end of next week for the dust to settle.
- DSP students: please contact the DSP office as soon as possible to let them know that you are registered for this course.

Inheritance means that some traits are predictable

Identical twins reared apart show remarkable similarities in personalities and preferences

Twist of Fate: Twins Reared Apart 133

Body postures of reared apart twins from the Minnesota Study, taken on the first assessment day. Without instruction from researchers, the three identical twin pairs (top row) naturally assumed similar standing positions, in contrast with the three fraternal twin pairs (bottom row) who posed differently. PHOTO COURTESY OF THOMAS J. BOUCHARD, JR.

MCB142/ICB163 Lectures

- This week (Lectures 1 & 2) - <u>Dernburg</u>
  (Monday 9/1: Labor Day)
- Sept 3 - 26 (Lectures 3-13) - <u>Amacher</u>
- Sept 29 - Oct 24 (Lectures 14-25) <u>Dernburg</u>
- Oct 27-Nov 3 (Lectures 26-29) <u>Amacher</u>
- Nov 5 - Dec 10 (Lectures 30-44) <u>Slatkin</u>

Quiz and midterm dates on syllabus posted on course website!
http://mcb.Berkeley.EDU/courses/mcb142/

MCB 142/ICB 163, Fall 2008 © Abby Dernburg

MCB142/ICB163 Overview

Genetics is a *quantitative, problem-solving* branch of biology.

It is not a set of facts or formulas that can be memorized.

Thus... skipping problem sets and cramming for quizzes and midterms will not serve you well in this course.

The instructors will assign reading and problems that emphasize the concepts that they hope you will take away.

If you do the problems early and often, and seek help from your instructors and GSIs when you don't understand, you will likely do very well on quizzes and exams.

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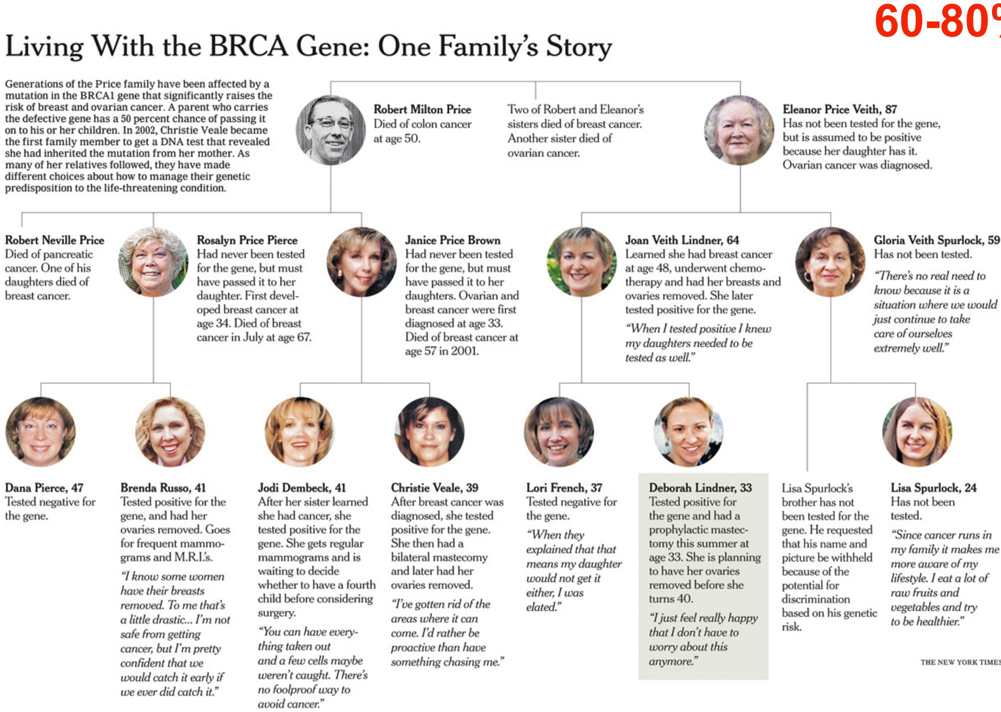
"Cancer Free at 33, but Weighing a Mastectomy"

Deborah Lindner, 33, did intensive research as she considered having a preventive mastectomy after a DNA test.

The New York Times, Sunday, Sep. 16, 2007

60-80%



The New York Times, Sunday, Sep. 16, 2007

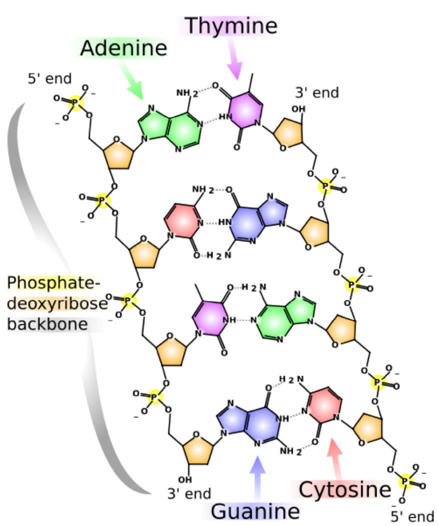
Generations of the Price family have been affected by a mutation in the BRCA1 gene that significantly raises the risk of breast and ovarian cancer. A parent who carries the defective gene has a 50 percent chance of passing it on to his or her children. In 2002, Christie Veale became the first family member to get a DNA test that revealed she had inherited the mutation from her mother. As many of her relatives followed, they have made different choices about how to manage their genetic predisposition to the life-threatening condition.

The New York Times, Sunday, Sep. 16, 2007

Take-home messages from today's lecture & from Hartwell *et al.*, Chapters 1 & 4

- ⋆ All living organisms (at least on Earth) are closely related.
- ⋆ DNA molecules encode the biological information fundamental to all life forms.
- ⋆ Biological function emerges primarily from protein molecules.
- ⋆ Genomes are organized into *chromosomes*, which are enormous strands of DNA packaged by proteins.
- ⋆ The size of an organism's genome and the number of chromosomes are not related to each other.
- ⋆ Organism complexity is not related in an obvious way to the size or even the gene content of a genome.
- ⋆ Mitosis and meiosis are the key chromosome division mechanisms that enable faithful transmission of the genome.

Information encoded in DNA generates functional diversity



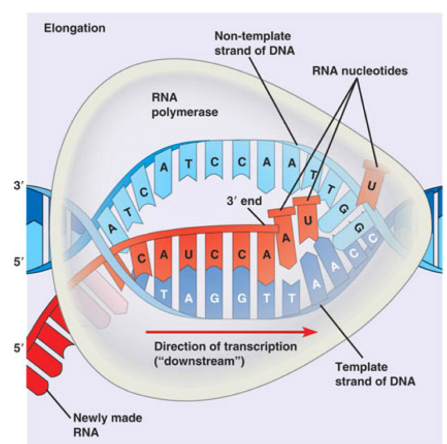
Four bases form the nucleotide building blocks of DNA:

- ✴ G (guanine)
- ✴ A (adenine)
- ✴ T (thymine)
- ✴ C (cytosine)

DNA is a double stranded helix composed of A-T and G-C complementary bases.

The DNA sequence "encodes" the amino acid sequence of the proteins that are made. Regulatory information in the DNA specifies when and where the synthesis occurs.

To make a protein from a gene, the DNA sequence is first *transcribed* into single-stranded RNA by an RNA polymerase. The product of this is a *messenger RNA* (*mRNA*). mRNA is then *translated* into a protein by a ribosome.



First letter \ Second letter	U	C	A	G	Third letter
U	UUU Phe UUC Phe UUA Leu UUG Leu	UCU Ser UCC Ser UCA Ser UCG Ser	UAU Tyr UAC Tyr UAA Stop UAG Stop	UGU Cys UGC Cys UGA Stop UGG Trp	U C A G
C	CUU Leu CUC Leu CUA Leu CUG Leu	CCU Pro CCC Pro CCA Pro CCG Pro	CAU His CAC His CAA Gln CAG Gln	CGU Arg CGC Arg CGA Arg CGG Arg	U C A G
A	AUU Ile AUC Ile AUA Ile AUG Met	ACU Thr ACC Thr ACA Thr ACG Thr	AAU Asn AAC Asn AAA Lys AAG Lys	AGU Ser AGC Ser AGA Arg AGG Arg	U C A G
G	GUU Val GUC Val GUA Val GUG Val	GCU Ala GCC Ala GCA Ala GCG Ala	GAU Asp GAC Asp GAA Glu GAG Glu	GGU Gly GGC Gly GGA Gly GGG Gly	U C A G

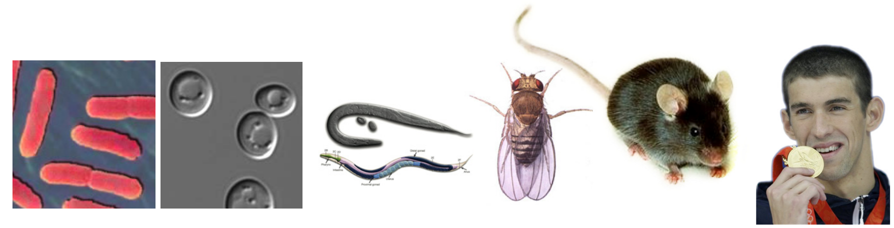
Universal genetic code

Amino acid sequences determine the 3D structures and functions of proteins

Hemoglobin β chain

Lactate dehydrogenase

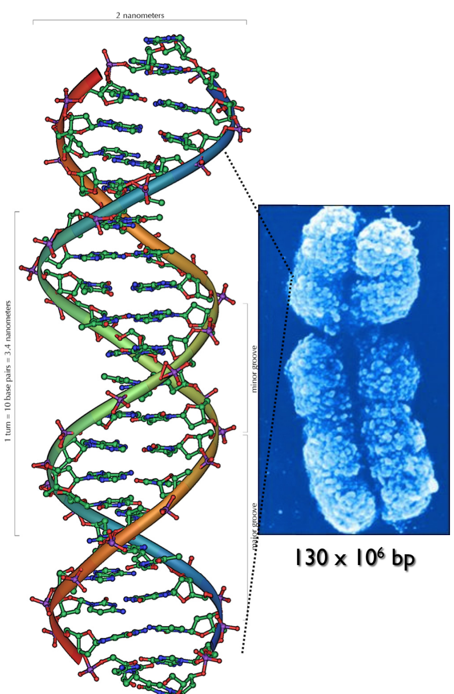
Neither the number of genes nor the size of the genome correlates directly with the complexity of an organism



Organism	bacterium *Escherichia coli*	Baker's yeast *Saccharomyces cerevisiae*	nematode *Caenorhabditis elegans*	fruit fly *Drosophila melanogaster*	mouse *Mus musculus*	human *Homo sapiens*
Genome size	4.5 Mb	13 Mb	97 Mb	230 Mb	3,000 Mb	3,000 Mb
Number of genes	4500	6200	20000	14000	20,000-30,000	20,000-30,000

Some plants (e.g., oriental lilies) and animals (e.g., salamanders) have more than 50-fold more DNA per cell than humans

Inside the cell, DNA is packaged into chromosomes



130 x 10^6 bp

20 bp

Chromosomes contain a lot of DNA and are highly compacted!

Human genome ~3000 Mbp
= 3 x 10^9 base pairs, arranged in 23 chromosomes

Average chromosome size = (3 x 10^9 ÷ 23)
= 130 x 10^6 bp

1 turn of the helix (10 bp) => 3.4 nm (3.4 x 10^{-9} m)

1 bp => 0.34 nm = 3.4 x 10^{-10} m

Linear length of DNA in one chromosome:
(130 x 10^6 bp) x (3.4 x 10^{-10} m/bp) = 4.4 x 10^{-2} m
= 4.4 cm

Cell nucleus is only ~5-10 microns (10^{-6} m) in diameter!

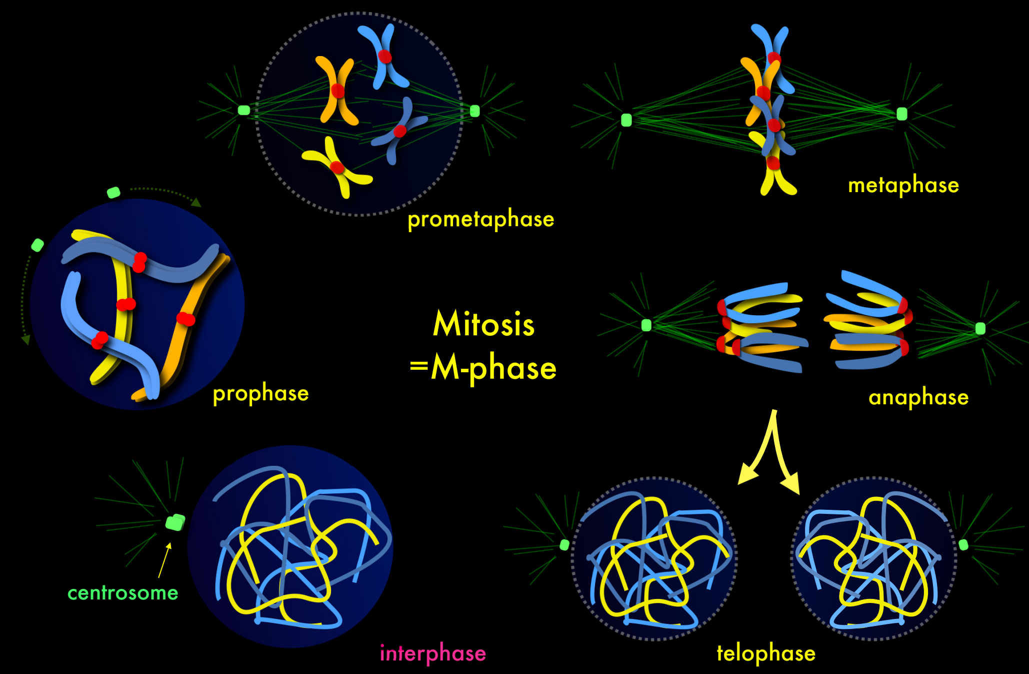
This means that chromosomes must be compacted about 5,000-fold relative to their DNA length to fit in a nucleus.

Chromosomes contain protein of about the same mass as their DNA content.

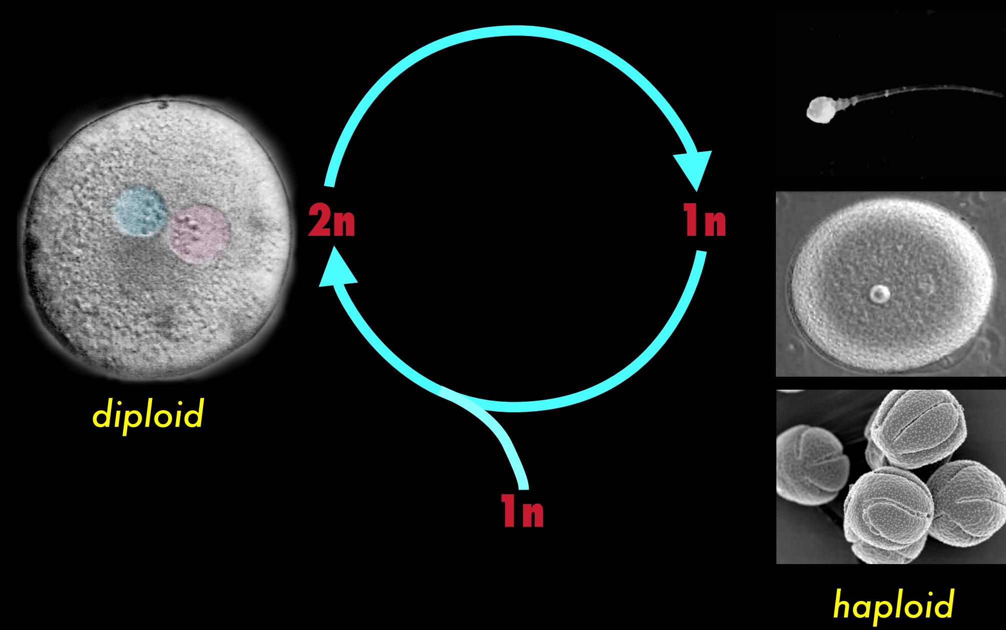
The number of chromosomes in a genome varies considerably, even among related species

Organism	*n*	2*n*
Drosophila melanogaster	4	8
Drosophila obscura	5	10
Drosophila virilis	6	12
Pisum sativum - Mendel's peas	7	14
Caenorhabditis elegans - a nematode roundworm	6	12
Parascaris univalens - a parasitic roundworm	1	2
Carasius auratus -Goldfish	47	94
Canis domesticus - Dogs	39	78
Homo sapiens - Humans	23	46

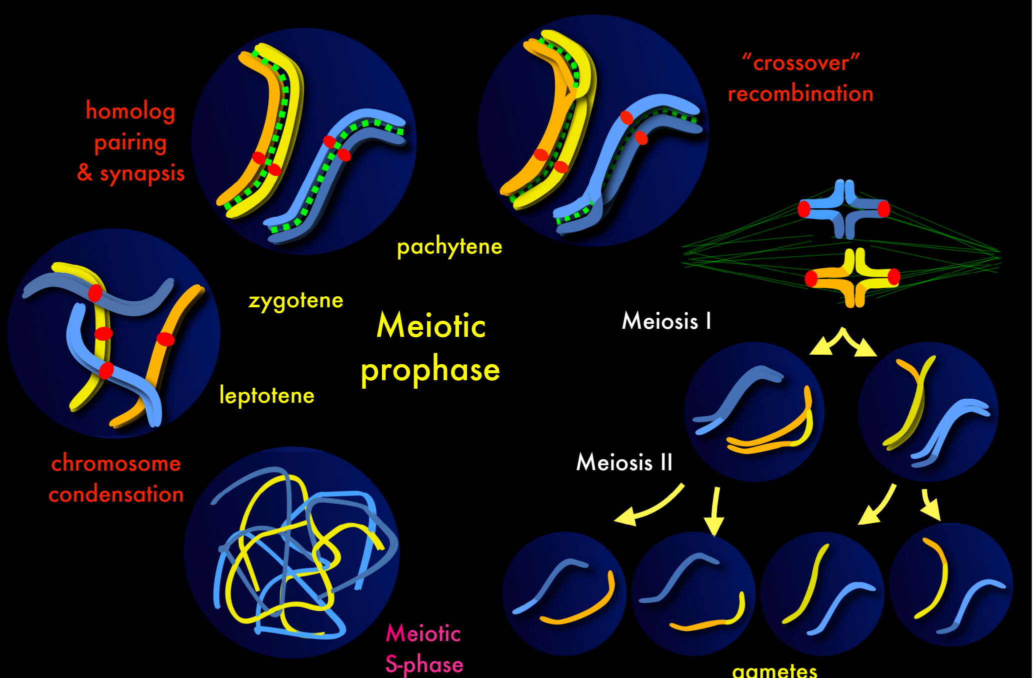
Mitosis is the mechanism by which dividing cells partition their chromosomes to produce genetically identical daughters



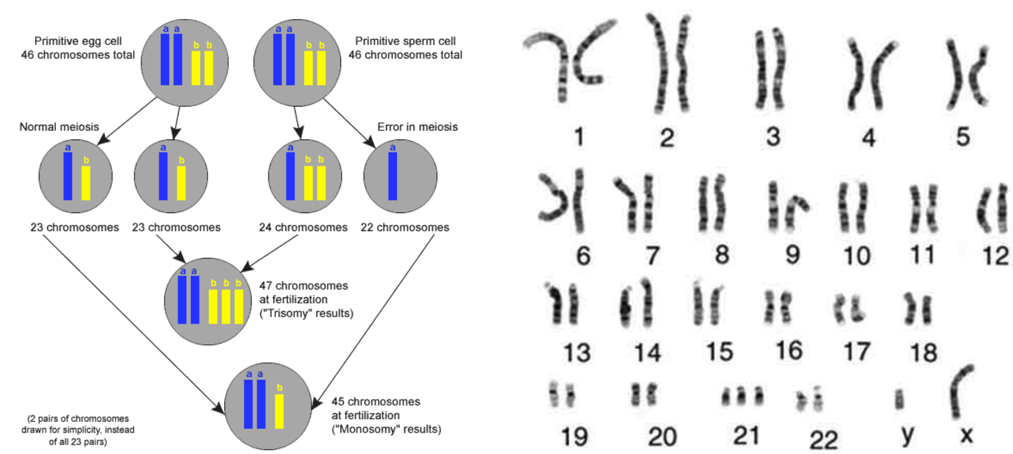
Sexual reproduction relies on MEIOSIS



Chromosome segregation during meiosis is accomplished through *homolog pairing, synapsis,* and *recombination*



Errors in meiotic chromosome segregation ("*nondisjunction*") result in *aneuploidy*, leading to chromosomal birth defects



Amniocentesis reveals a male fetus carrying 3 copies of chromosome 21
Trisomy 21 = Down Syndrome

Humans show an extraordinarily high occurrence of meiotic chromosome missegregation.

TO ERR (MEIOTICALLY) IS HUMAN: THE GENESIS OF HUMAN ANEUPLOIDY

Terry Hassold and Patricia Hunt

Aneuploidy (trisomy or monosomy) is the most commonly identified chromosome abnormality in humans, occurring in at least 5% of all clinically recognized pregnancies. Most aneuploid conceptuses perish *in utero*, which makes this the leading genetic cause of pregnancy loss. However, some aneuploid fetuses survive to term and, as a class, aneuploidy is the most common known cause of mental retardation. Despite the devastating clinical consequences of aneuploidy, relatively little is known of how trisomy and monosomy originate in humans. However, recent molecular and cytogenetic approaches are now beginning to shed light on the non-disjunctional processes that lead to aneuploidy.

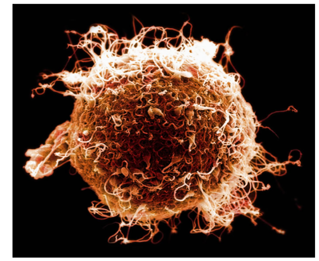
Humans have an extraordinarily high occurrence of meiotic chromosome missegregation.

A typical human female produces approximately 450 mature eggs over the course of her lifetime.

Eggs are big cells, requiring a serious investment of energy.

A typical human male produces about 60 million mature sperm per milliliter (cm^3) of ejaculate.

(In 1940 it was 113 million)



Would you guess that male or female meiosis is more error-prone?

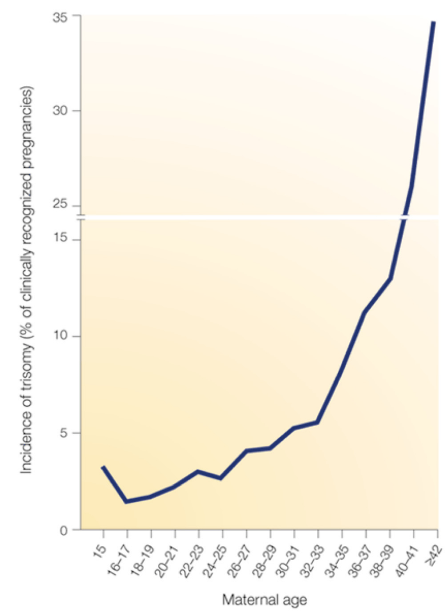
Most human aneuploidy is maternal in origin

Table 2 | **The origin of human trisomy**

		Origin (%)				
Trisomy	**No. of cases**	**Paternal MI**	**MII**	**Maternal MI**	**MII**	**Post-zygotic mitosis**
2	18	28	–	54	13	6
7	14	–	–	17	26	57
15	34	–	15	76	9	–
16	104	–	–	100	–	–
18	143	–	–	33	56	11
21	642	3	5	65	23	3
22	38	3	–	94	3	–
XXY	142	46	–	38	14	3
XXX	50	–	6	60	16	18

(MI, meiosis I; MII, meiosis II.)

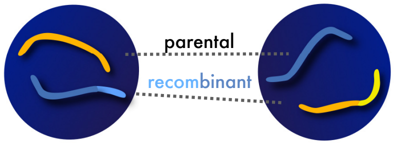
The incidence of human aneuploidy is strongly dependent on the age of the mother. This "maternal age effect" is not understood.



Nature Reviews | Genetics

Things worth understanding about meiosis (eventually):

- Offspring, or progeny, inherit a mixture of ***recombinant*** and ***parental*** chromosomes.



- Recombinant chromosomes carry new combinations of ***alleles***, resulting in *genetic diversity*

- Each pair of chromosomes segregates independently of all other pairs.

- This ***independent assortment*** will take on new significance (hopefully) when we discuss Mendel's discoveries on Friday

- We will revisit these issues in more detail in subsequent lectures