

20.109 MOD1

Genomic Instability

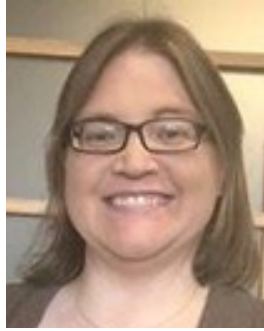
Fall 2022
Day 1

Bevin P. Engelward, *Sc.D.*
Professor of Biological Engineering

20.109 MOD1 Fall 2022 – The Fabulous Team



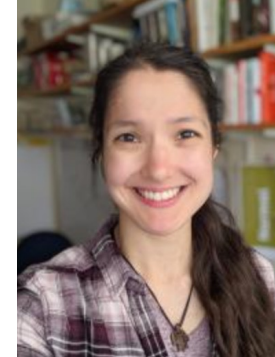
**Dr. Noreen
Lyell**
Sr. Lecturer



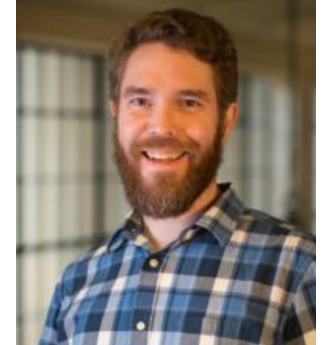
**Dr. Becky
Meyer**
Lecturer



Jamie Zhan
Instructor



Chiara Ricci-Tam
BE Communication
Lab Manager &
Lecturer



Sean Clarke
BE Communication
Lab, Lecturer



Alexander Hostetler
TA



Chyna Mays
TA



Bryan Wong
TA

Objectives of the Class

Broad Relevance of Studies of the Genome

Basics of DNA Structure-Function

Challenge of Keeping the Genome Intact & Cancer

DNA Repair

Practical Advice

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Objectives for Research Skills (Mod1)

Experimental Design

Quantitative Measurements

Controls (anticipatory experimental design)

Experimental Variability

Data Interpretation and Presentation Skills

Statistics

Critical Data Interpretation

Written & Oral Communication

Basic Laboratory Skills

Record Keeping

Sources of Error

Basic Laboratory Equipment

Mammalian Cell Culture

Immunohistochemistry

Image Analysis

Overall Course Conceptual Goals for Mod1

- Fundamental Biological Concepts of Molecular Pathways
- DNA Structure and DNA Replication
- Molecular Biology of DNA Repair
- Genomic Instability
- Inter-Individual Variation in Susceptibility to Cancer.
- Public Health
- Fundamental Engineering Concepts: Learn about harnessing engineering principles to translate an idea into a product.

Objectives of the Class

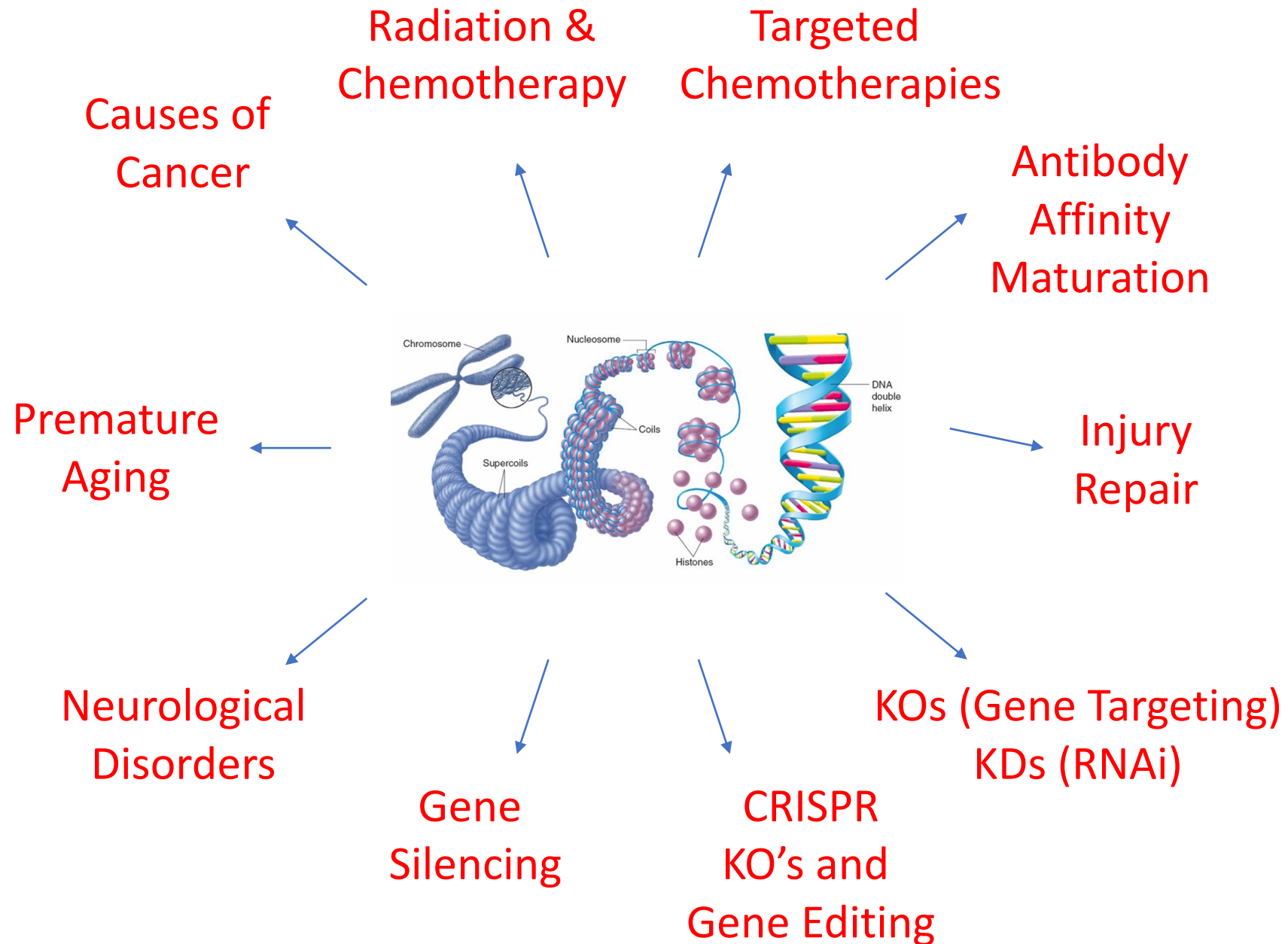
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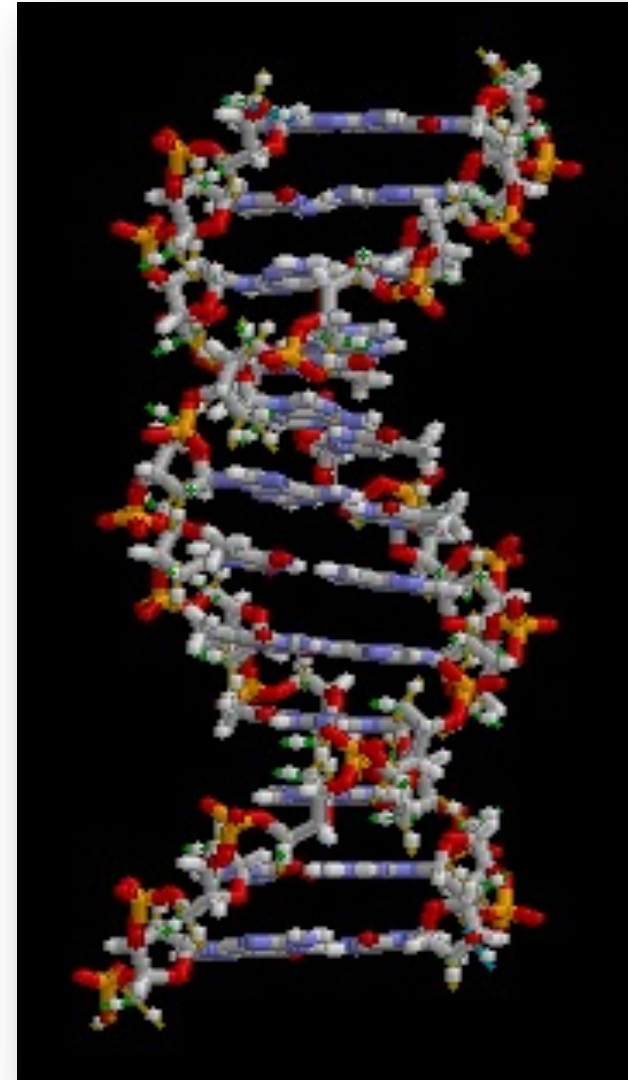
Practical Advice

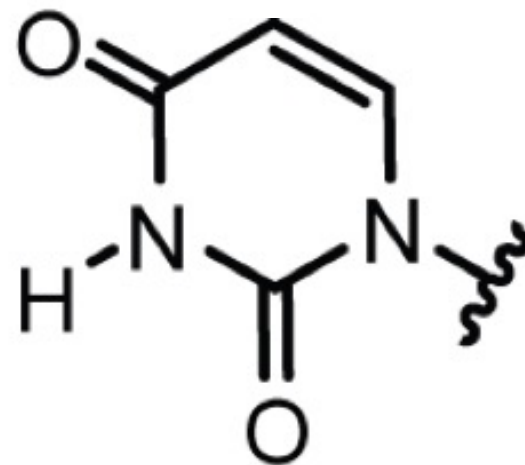
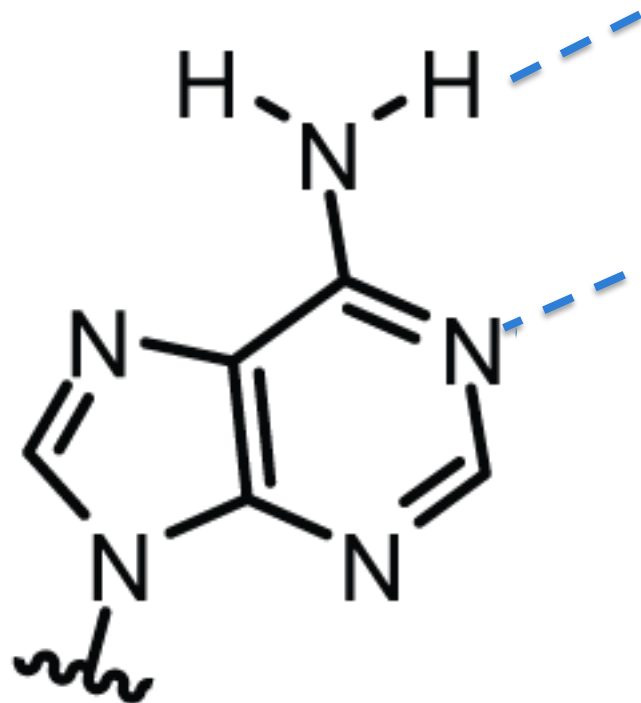
***This module is all
about the Genome....***

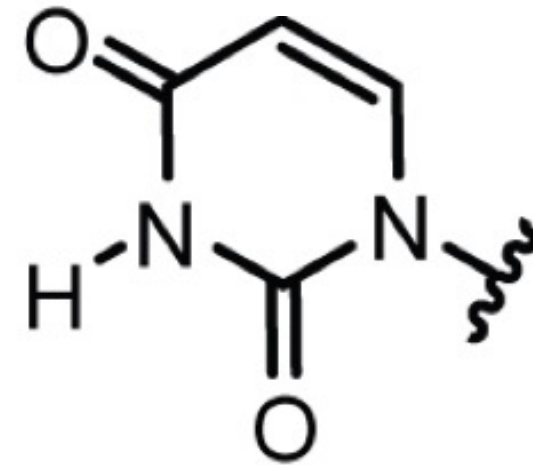
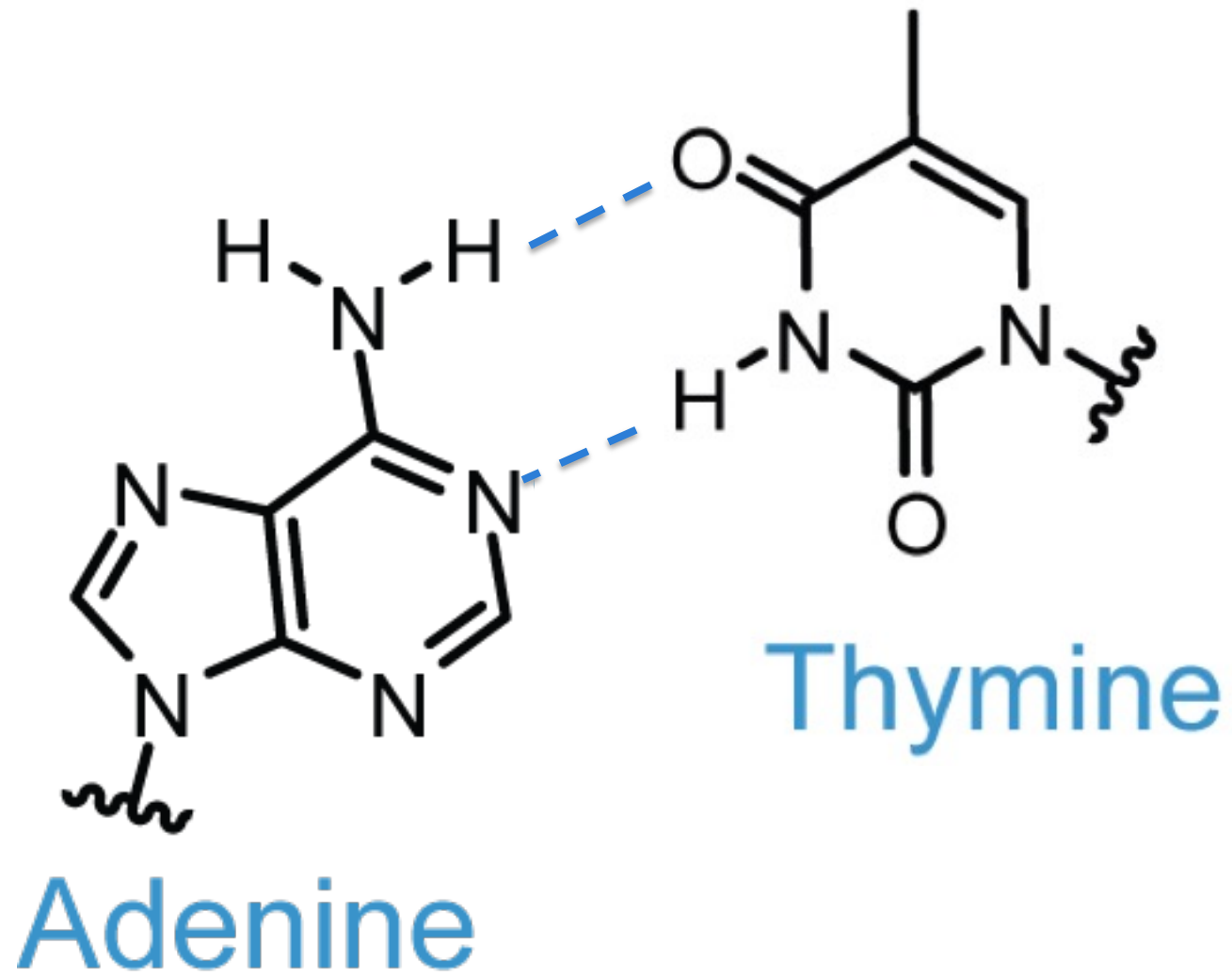
Evolution of life on Earth

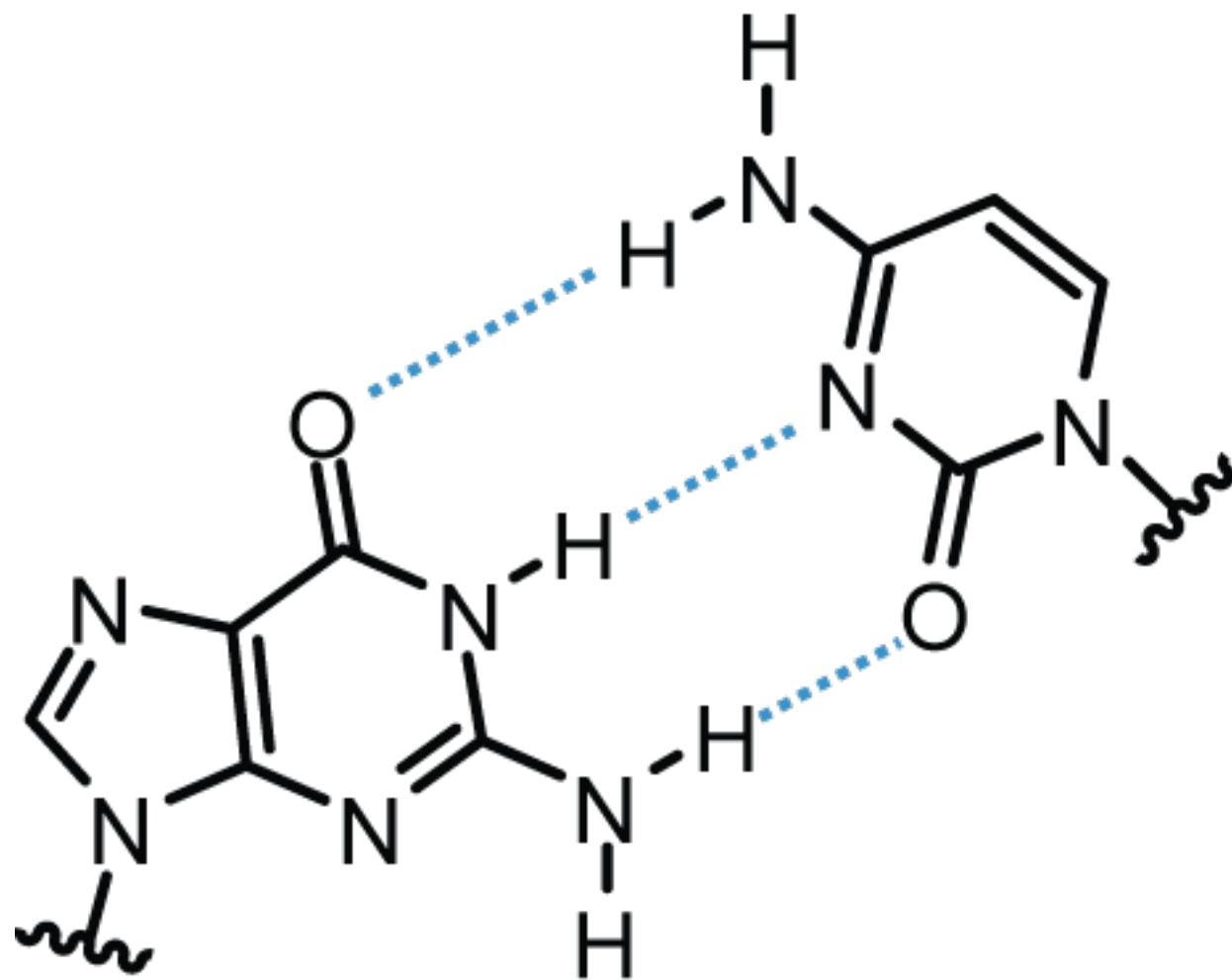


All known life forms are based on DNA

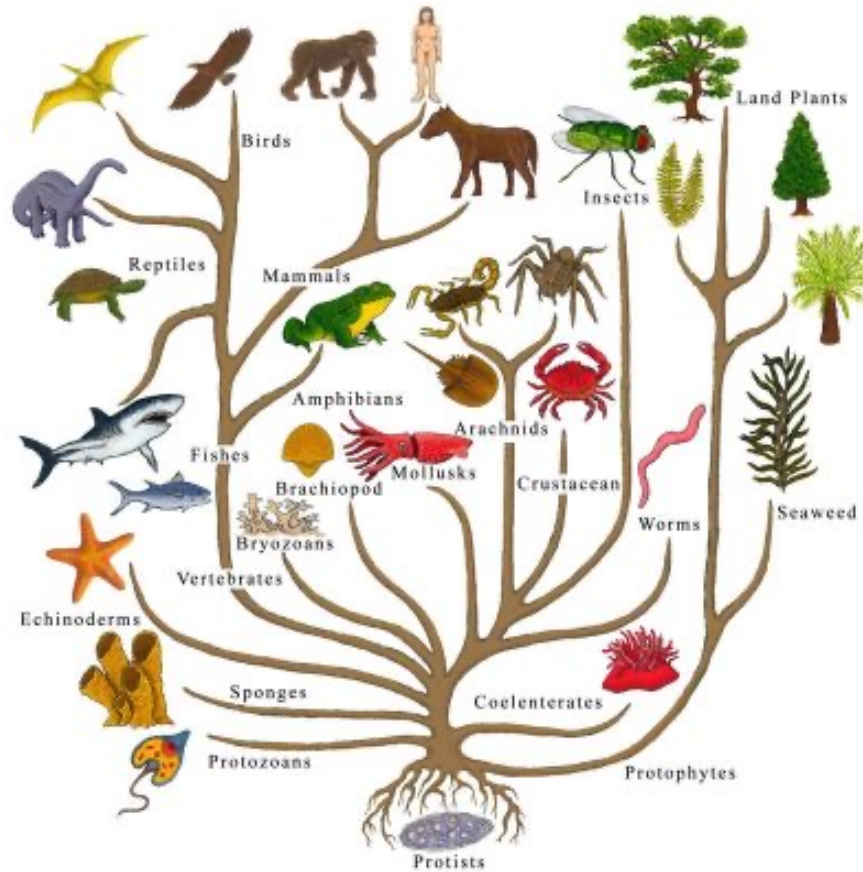






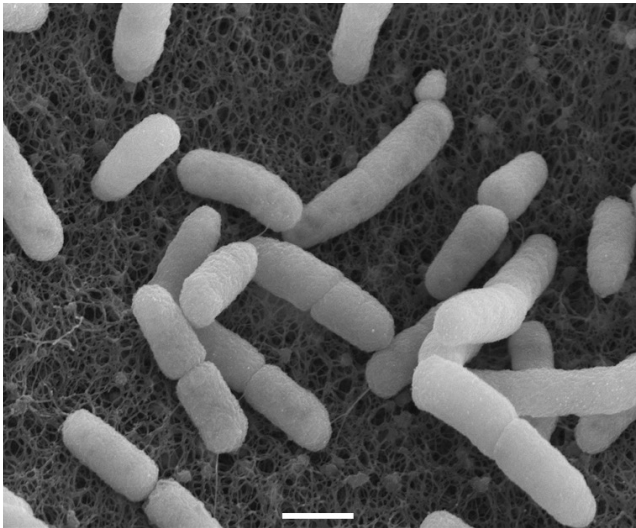


All known life forms are based on DNA



The cell is generally considered to be the basic unit of life

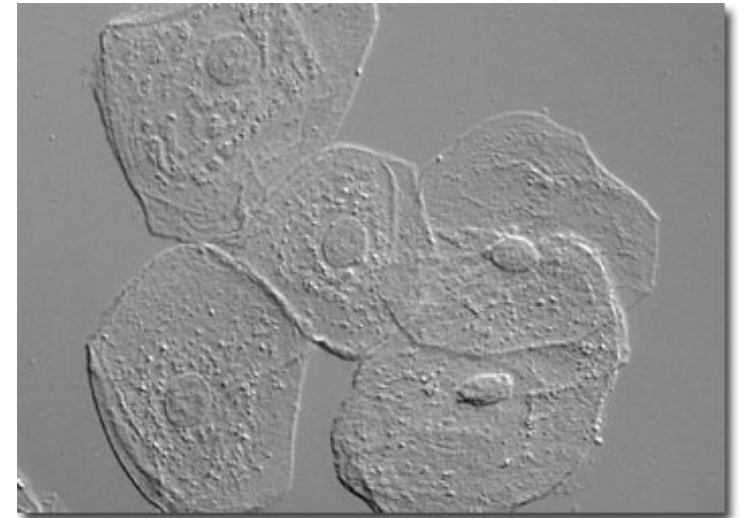
Bacteria



Archaea

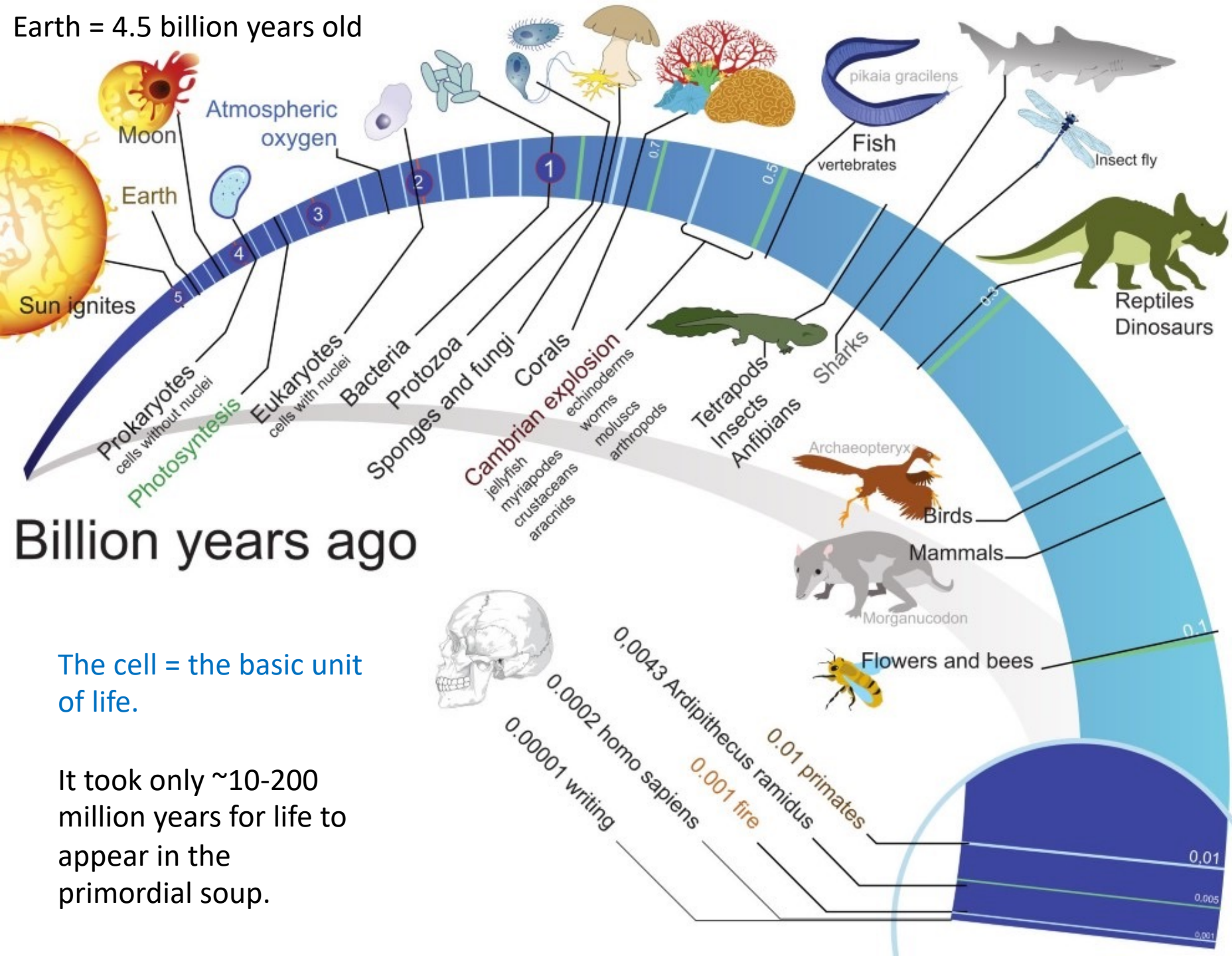


Eukaryota



The Three Domains of Life

Earth = 4.5 billion years old



From the first cell to mammals took more than 4 billion years

The cell = the basic unit of life.

It took only ~10-200 million years for life to appear in the primordial soup.



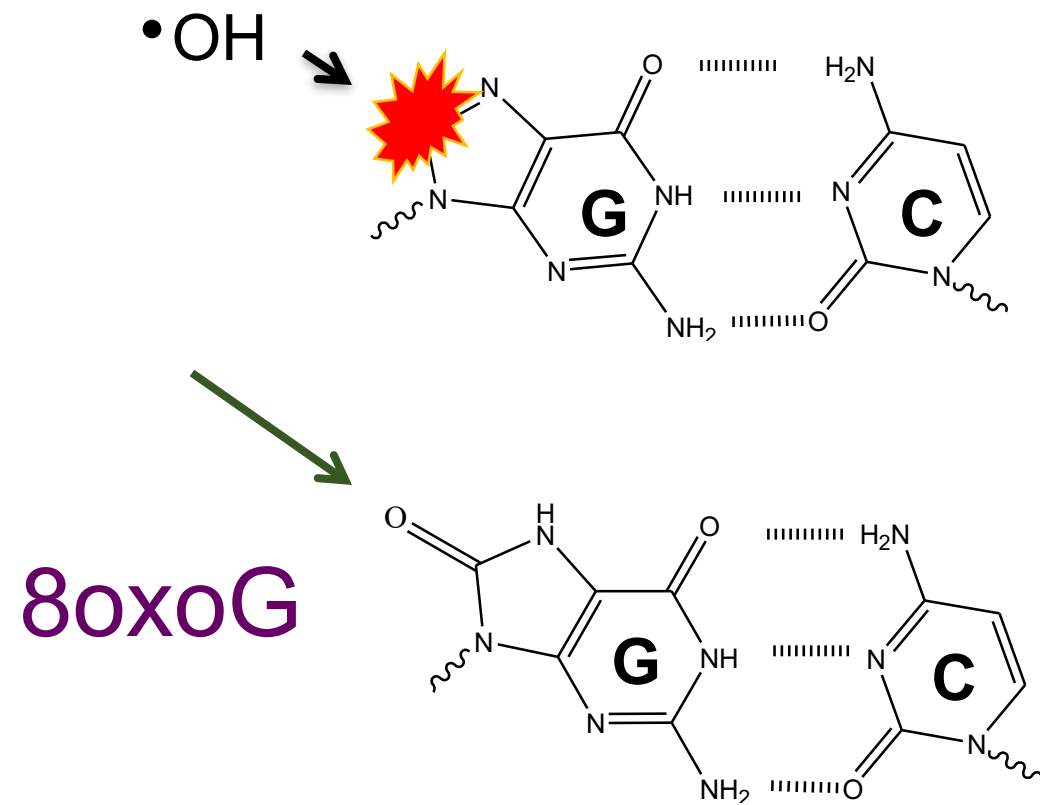
What has to happen
for life to exist?

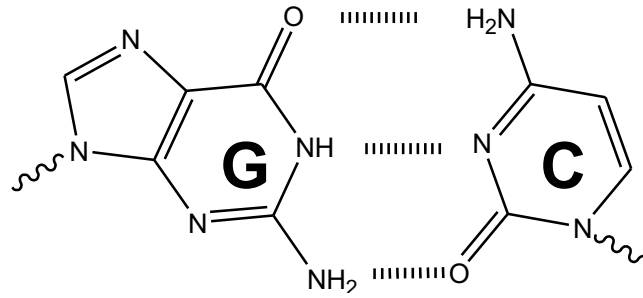


Structure is Information

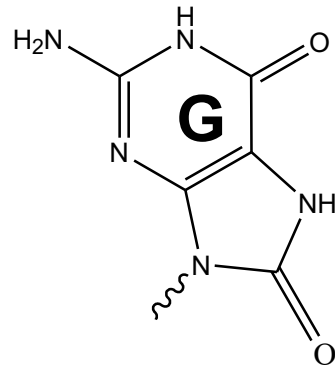
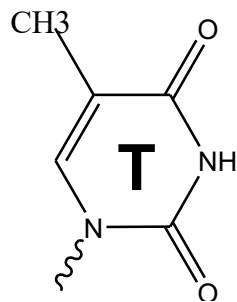
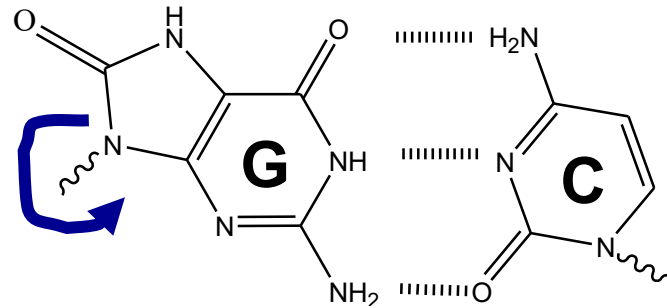
Example of 8-oxoguanine mispairing.

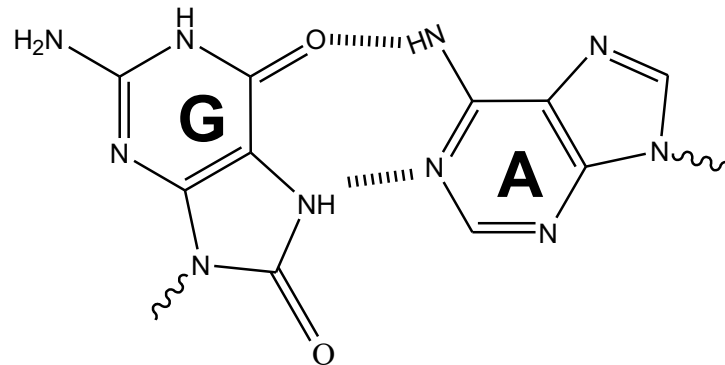
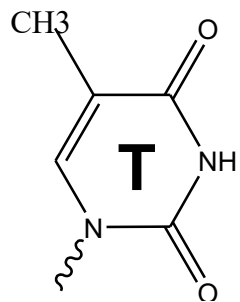
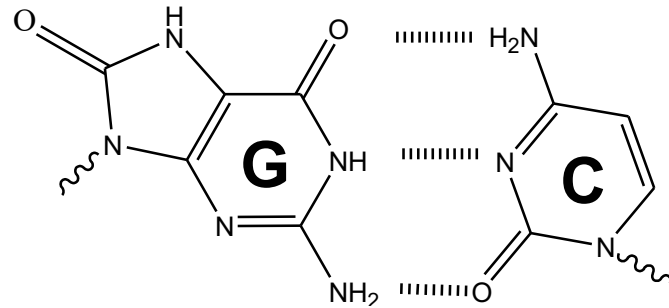
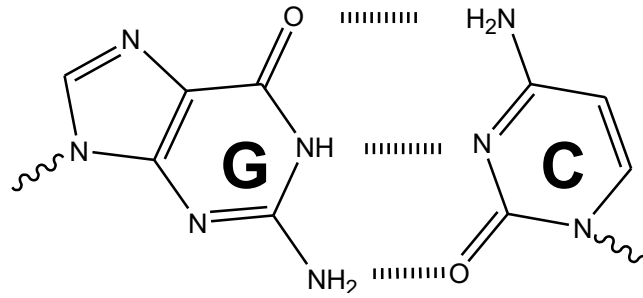
8oxoG





8oxoG





GC → TA

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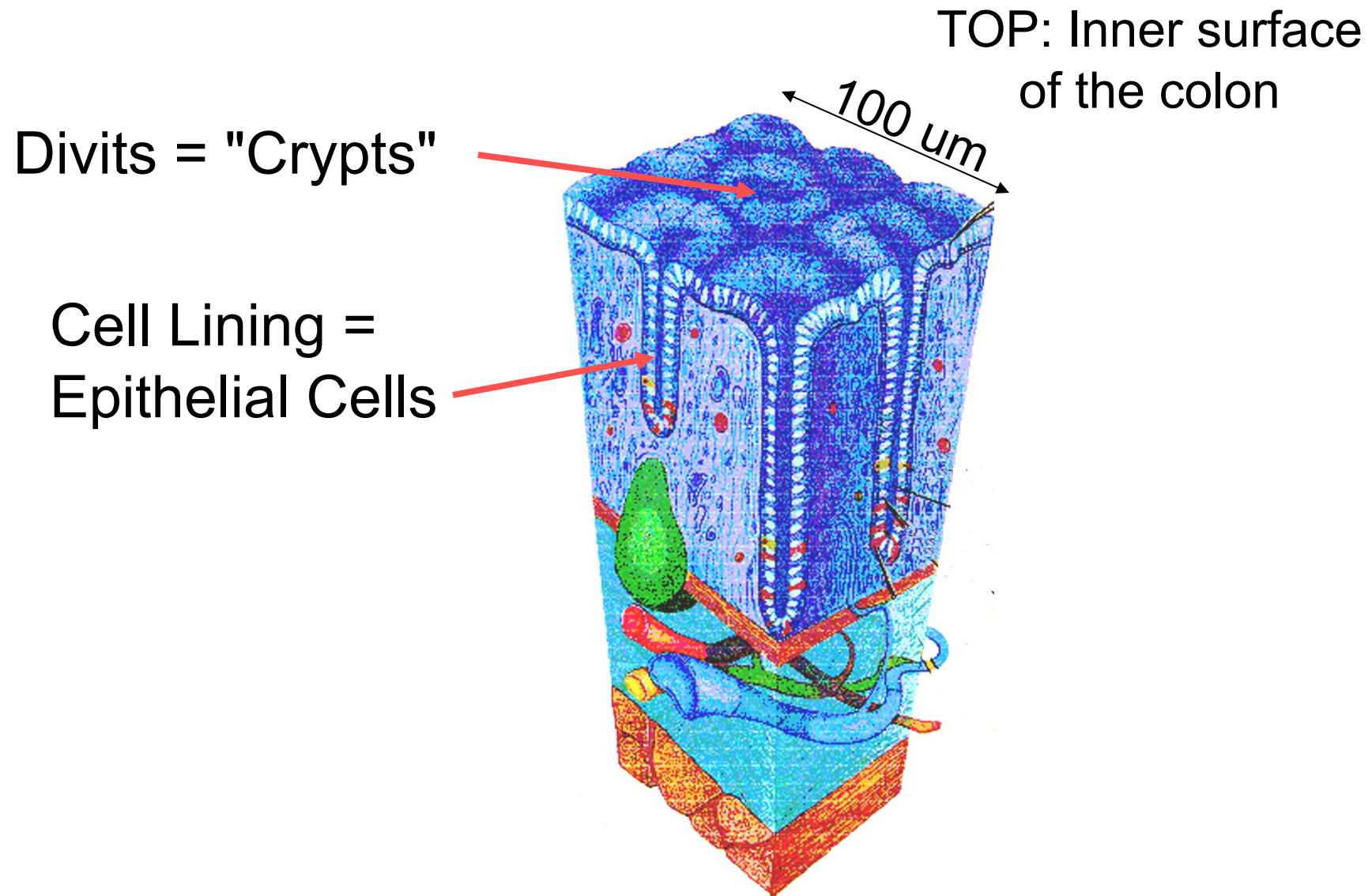
DNA Repair

Practical Advice

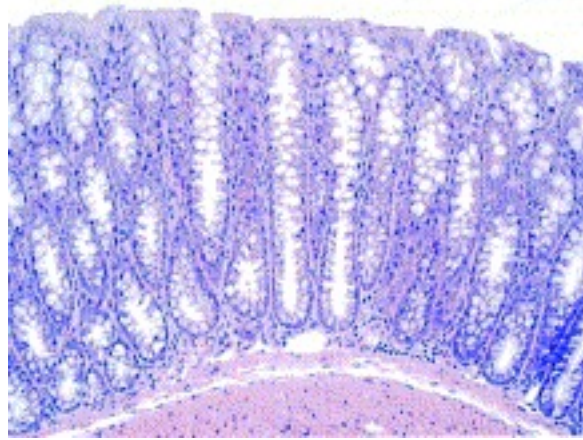
What is cancer?

Why are mutations important?

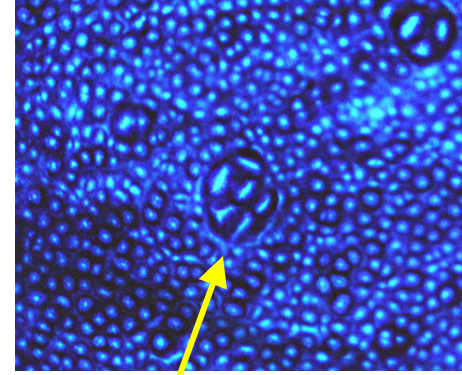
Normal Colon Tissue



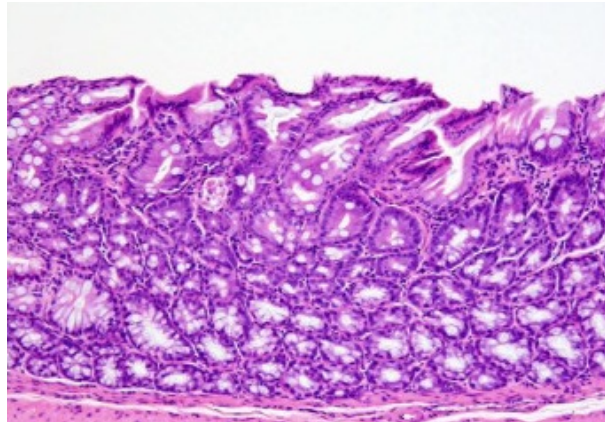
Progression



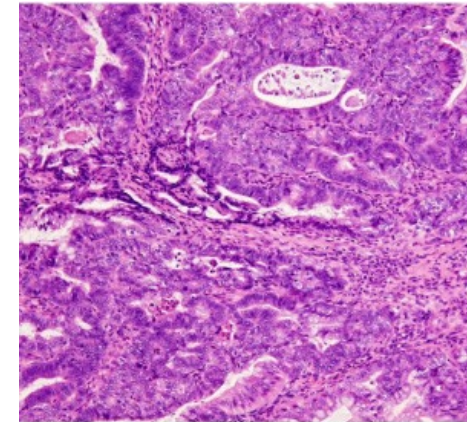
Normal Colonic Epithelium



Dysplastic Crypt



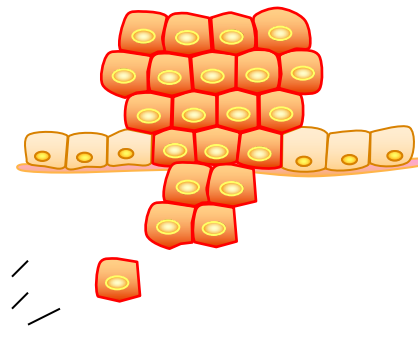
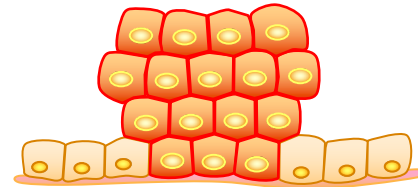
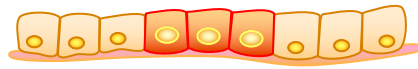
Mild Dysplasia



Cancer

What are the genetic steps?
What does a cancer cell need to be able to do?

Normal
Skin Cells



Hyperplasia



Neoplasia



Metastasis

Mutation 1



Clonal
Expansion



Mutation 2



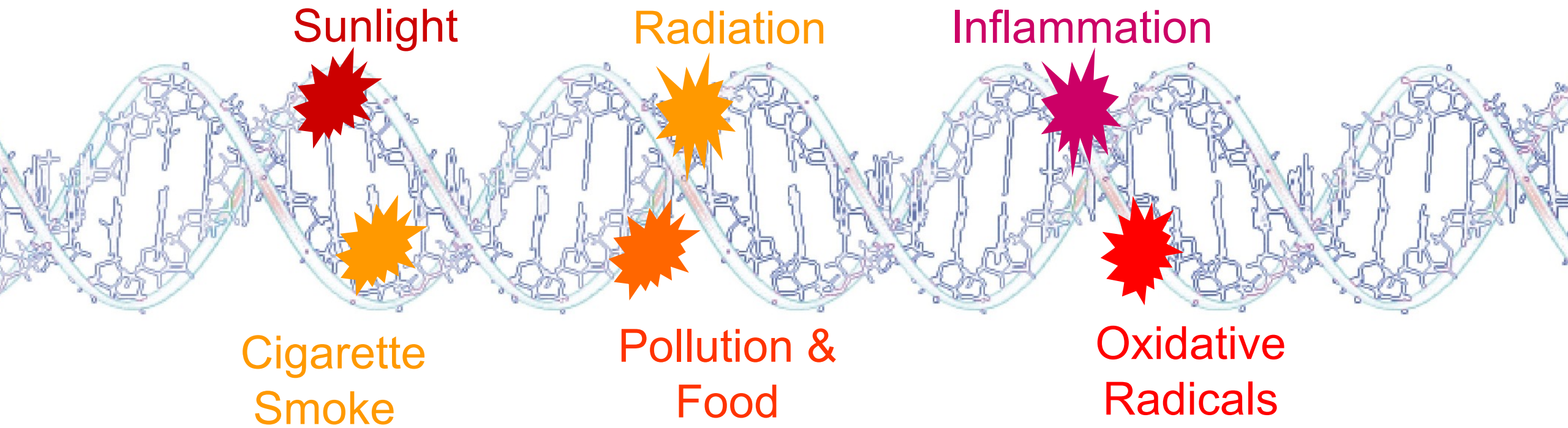
Mutation 3



Additional
Mutations



Where do
mutations come
from?



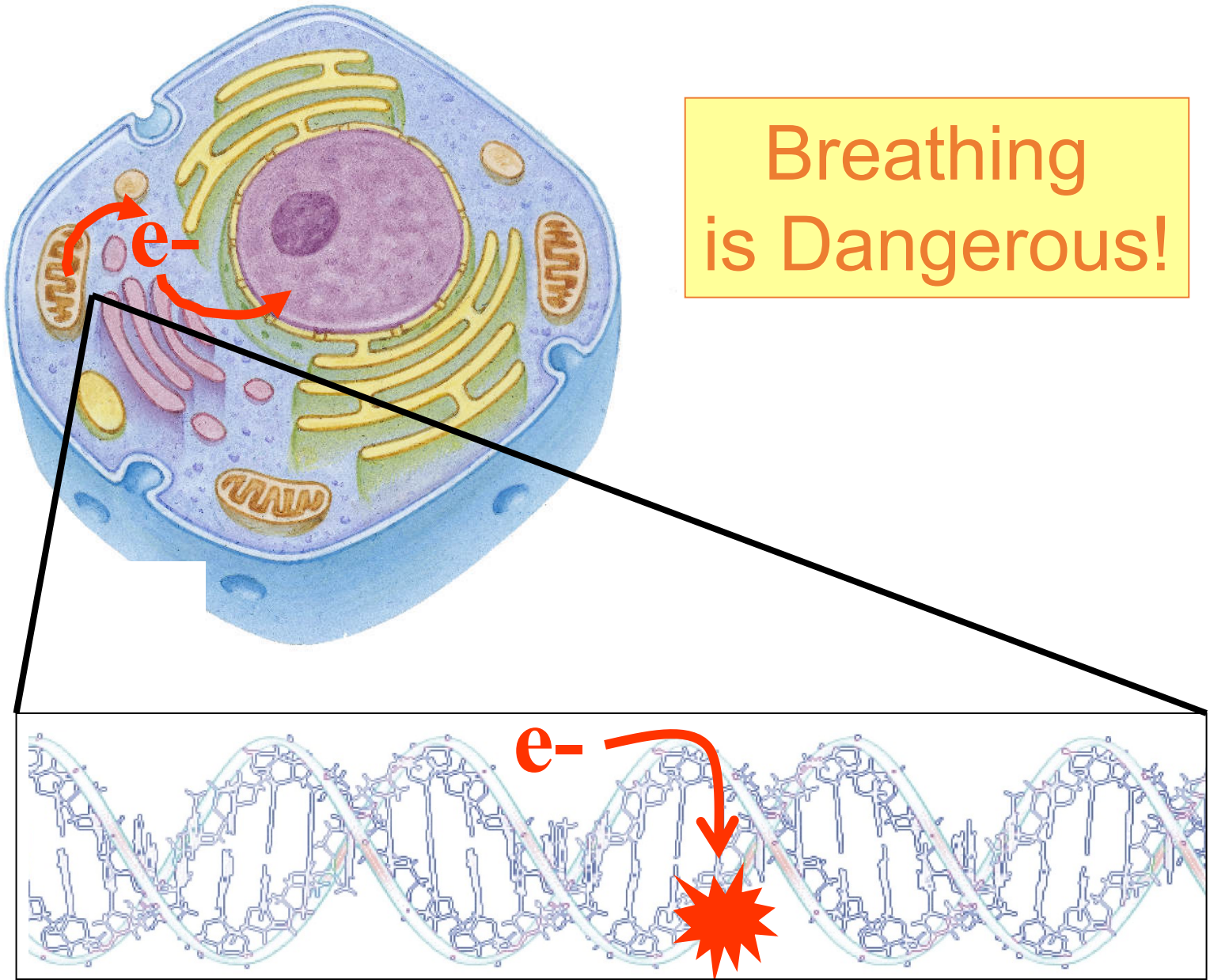
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Mutations, Toxicity, Cellular Defects

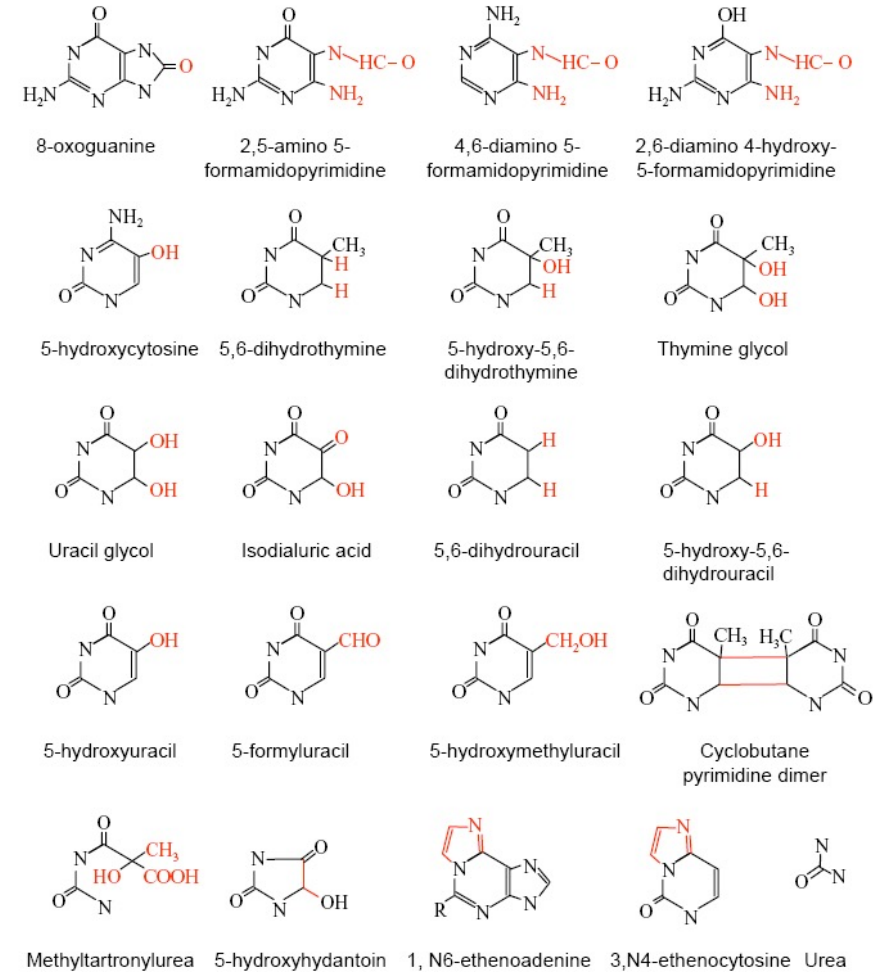
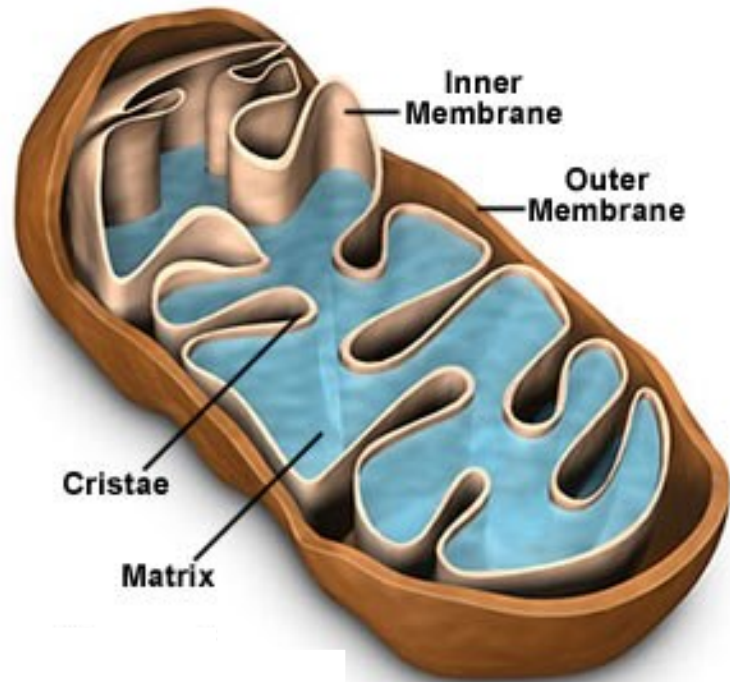
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Cancer, Aging, Heritable Diseases

Breathing
is Dangerous!



Reactive Oxygen Species Damage DNA Bases



Objectives of the Class

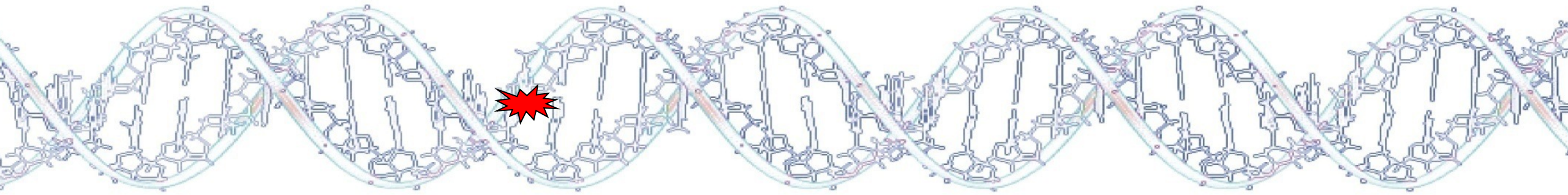
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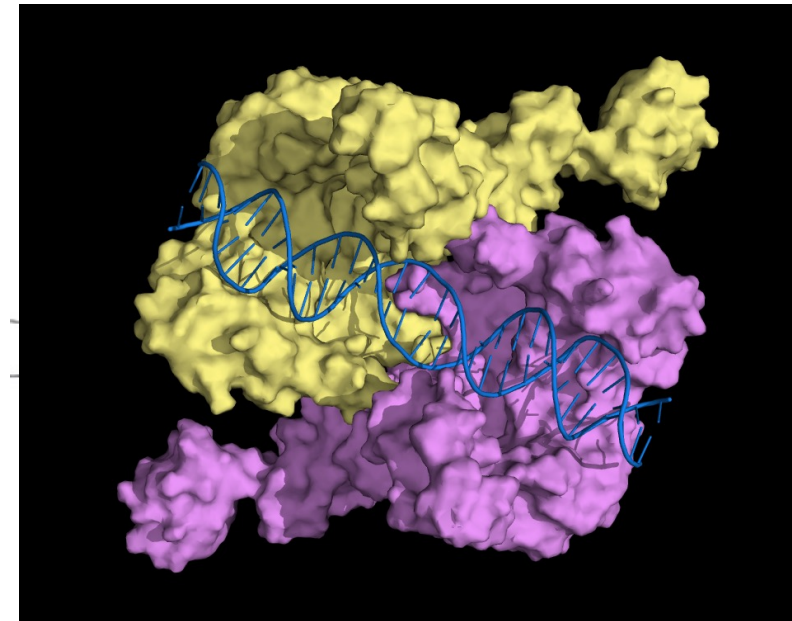
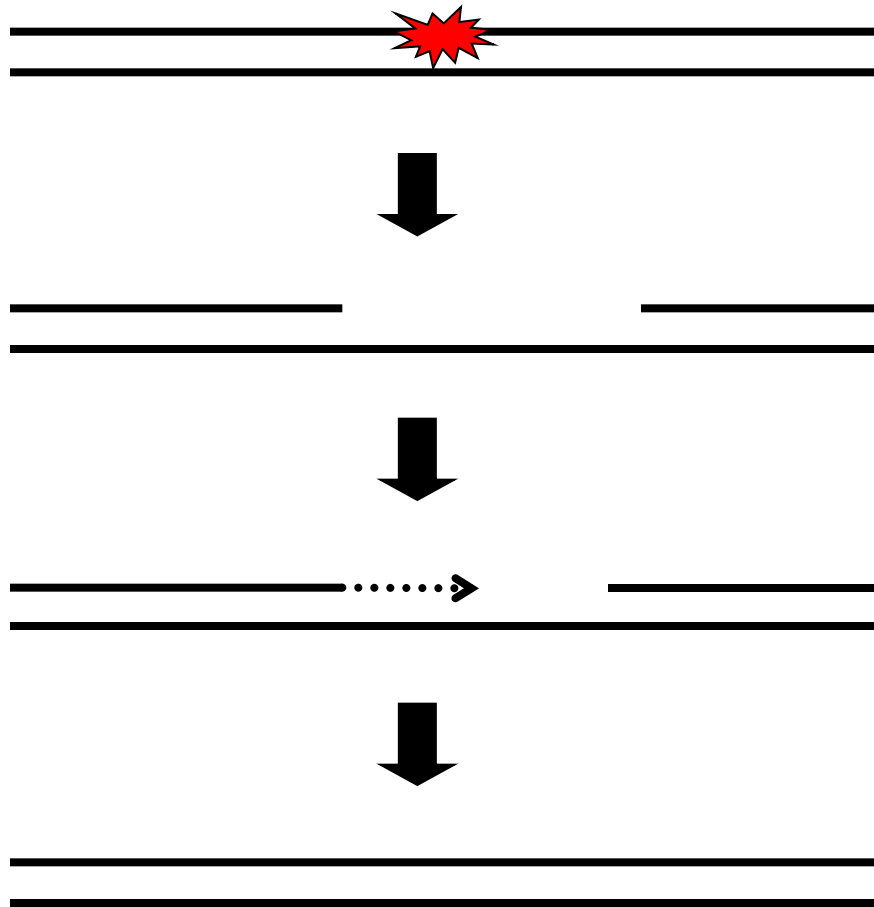
Challenge of Keeping the Genome Intact & Cancer

DNA Repair

Practical Advice



Sunlight-Induced DNA Damage can be Repaired



Nucleotide
Excision
Repair

DNA Repair impacts Risk of Cancer



People lacking repair of UV dimers have a 2000X increased risk of skin cancer.

Xeroderma Pigmentosum – A rare human disease

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Get to Know your Cells

Do they like crowding? How low can you plate your cells? What is “too crowded”?

How fast do they divide? How long does it take for them to start dividing after being split?

Are they immortal? If not, how long can you culture them?

What do they look like when they are healthy?

How often do they like to have their media changed?

Are they mycoplasma free?

Objectives of the Class

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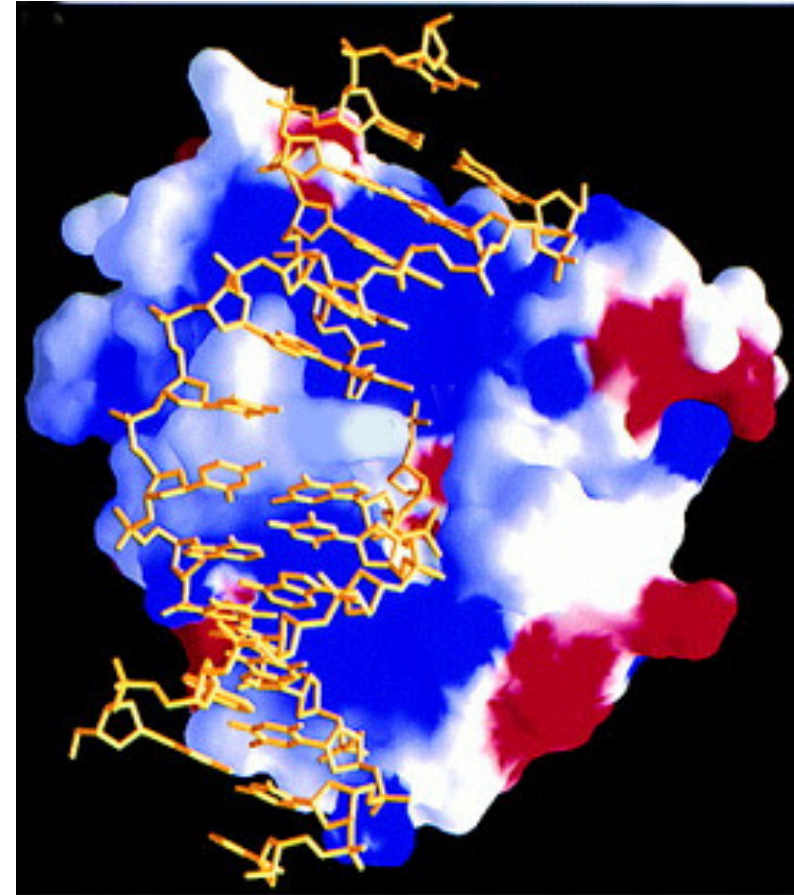
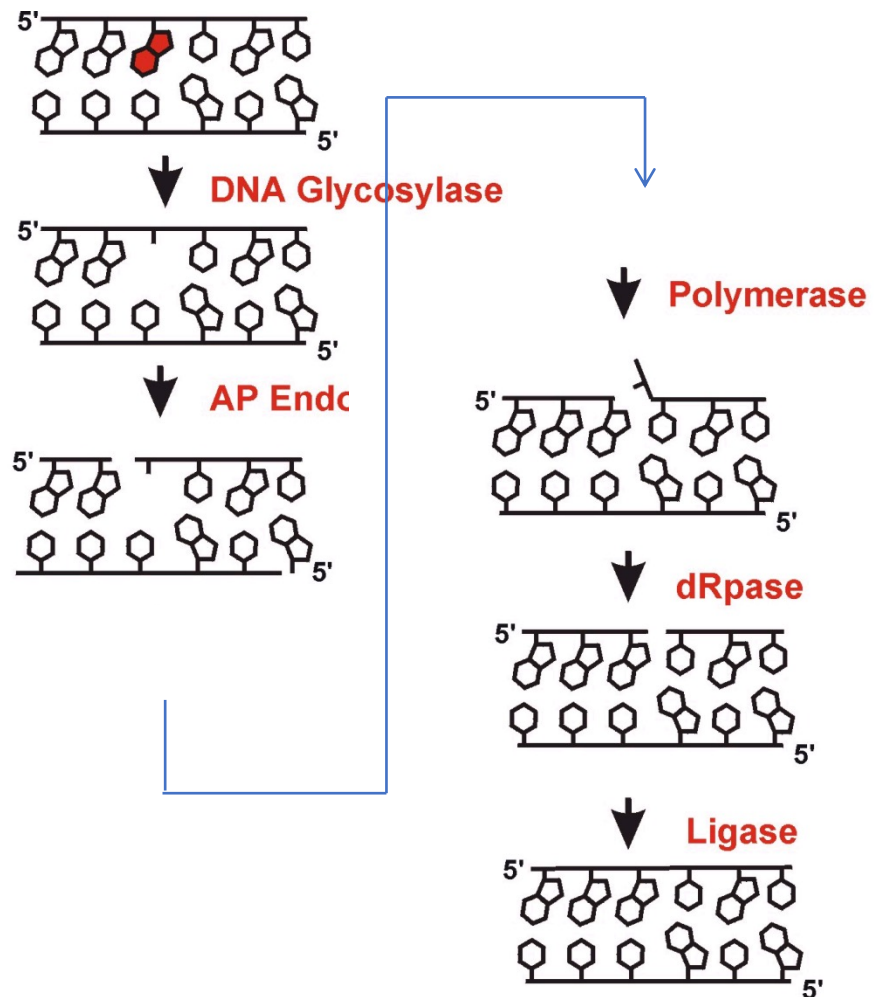
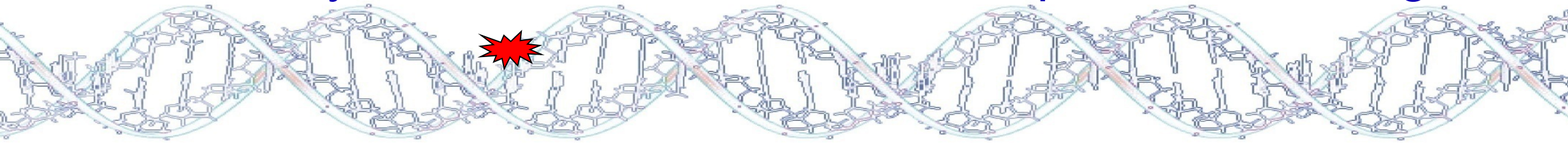
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One Way to Prevent Mutations is to Repair DNA Damage



A. Lau and T. Ellenburger; Harvard.