

Epigenetics

... tweaking your genetic destiny



Tim Herman

What is Epigenetics?

Epigenetics is the study of how your behaviors and environment can cause ***changes that affect the way your genes work***. Unlike genetic changes, epigenetic changes are reversible and do not change your DNA sequence, but they can change how your body reads a DNA sequence.

**NO MORE
EXCUSES**
Don't blame it on genes

Workshop Outline

Epigenetics...chemical modifications of your genome

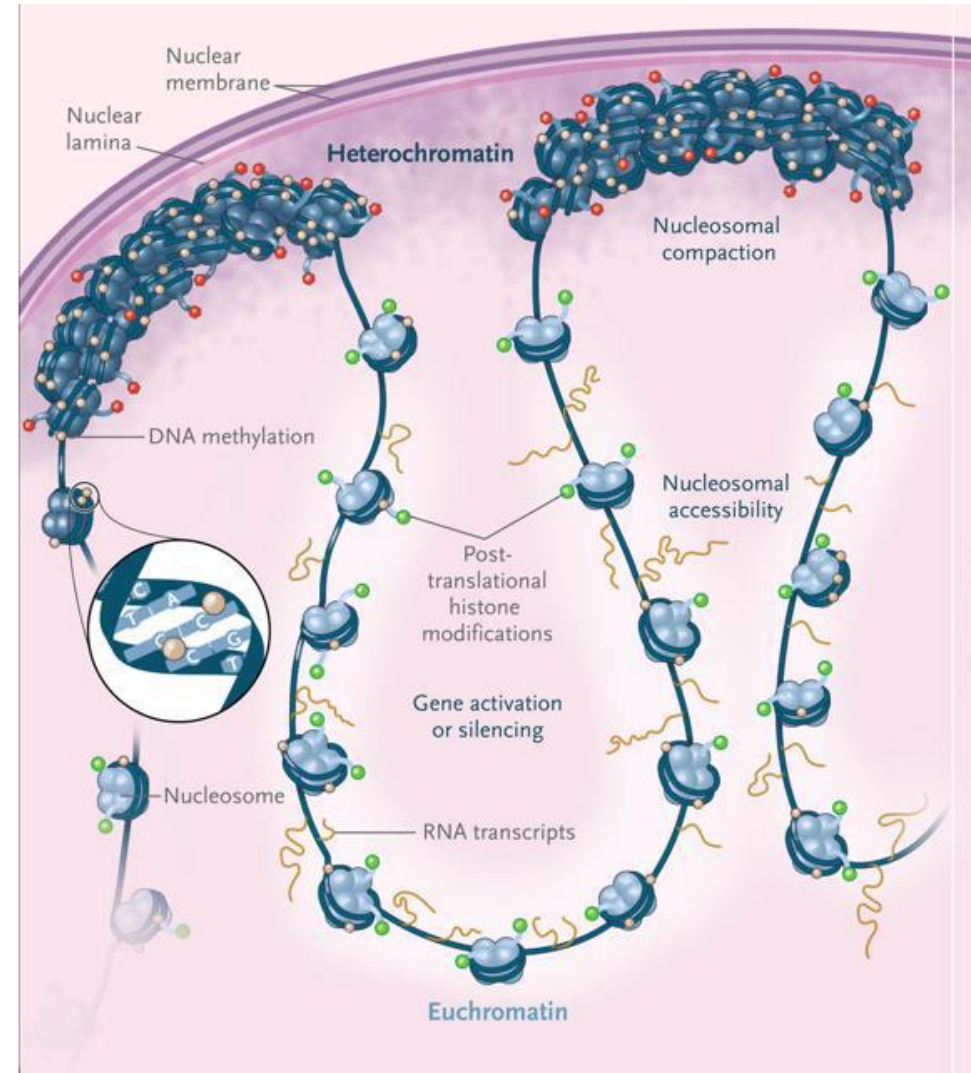
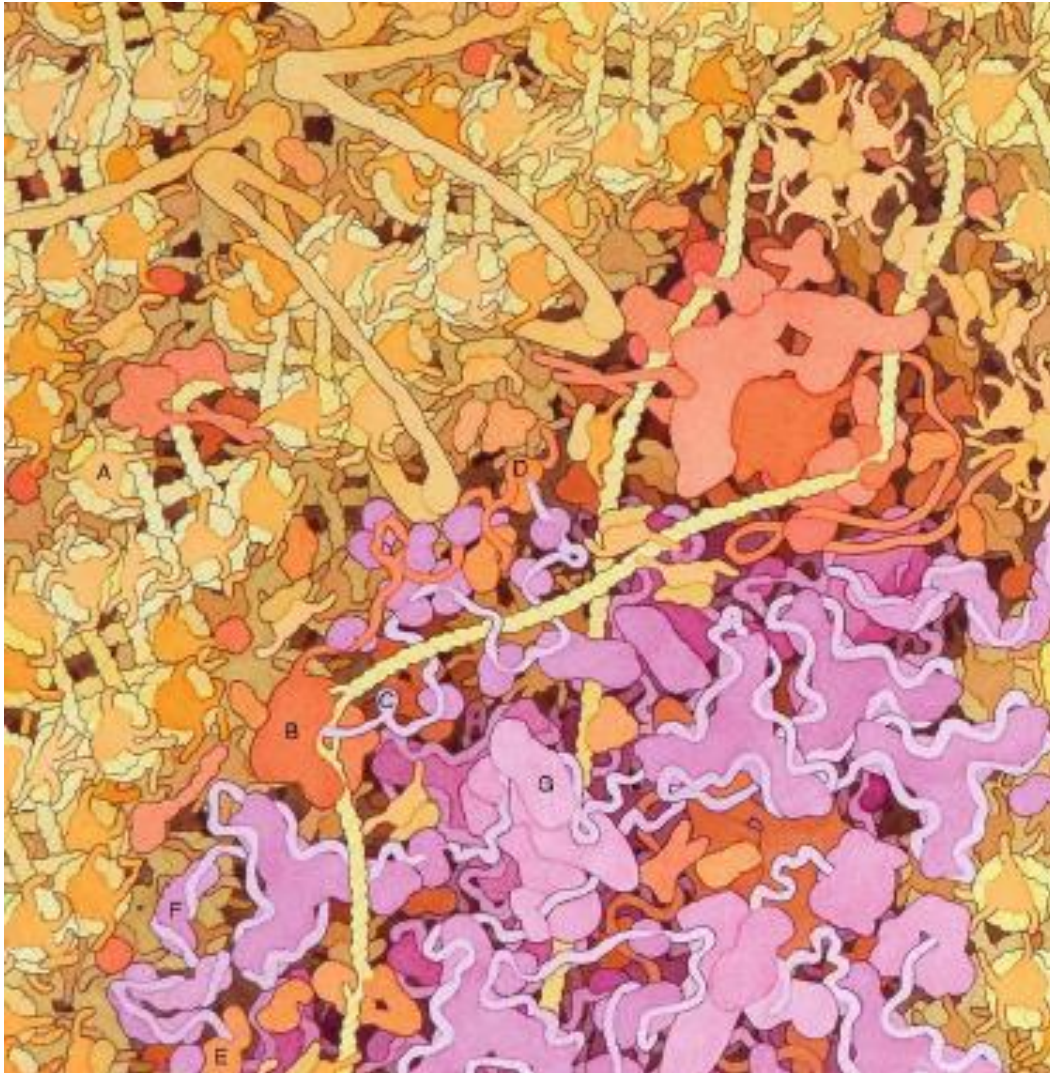
Writers / Erasers / Readers

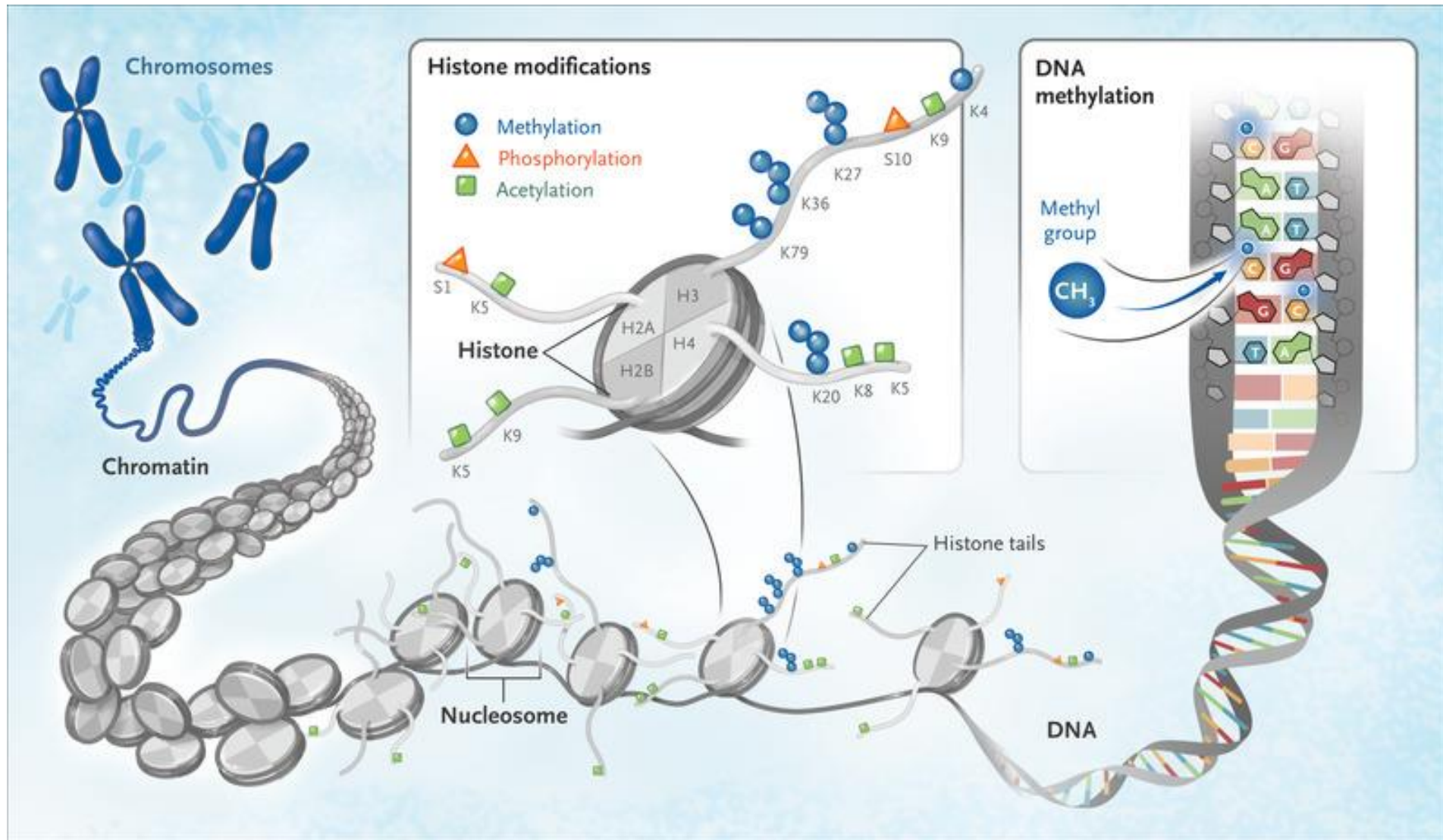
1. Histone modifications

2. DNA modifications

... methylation of CpG

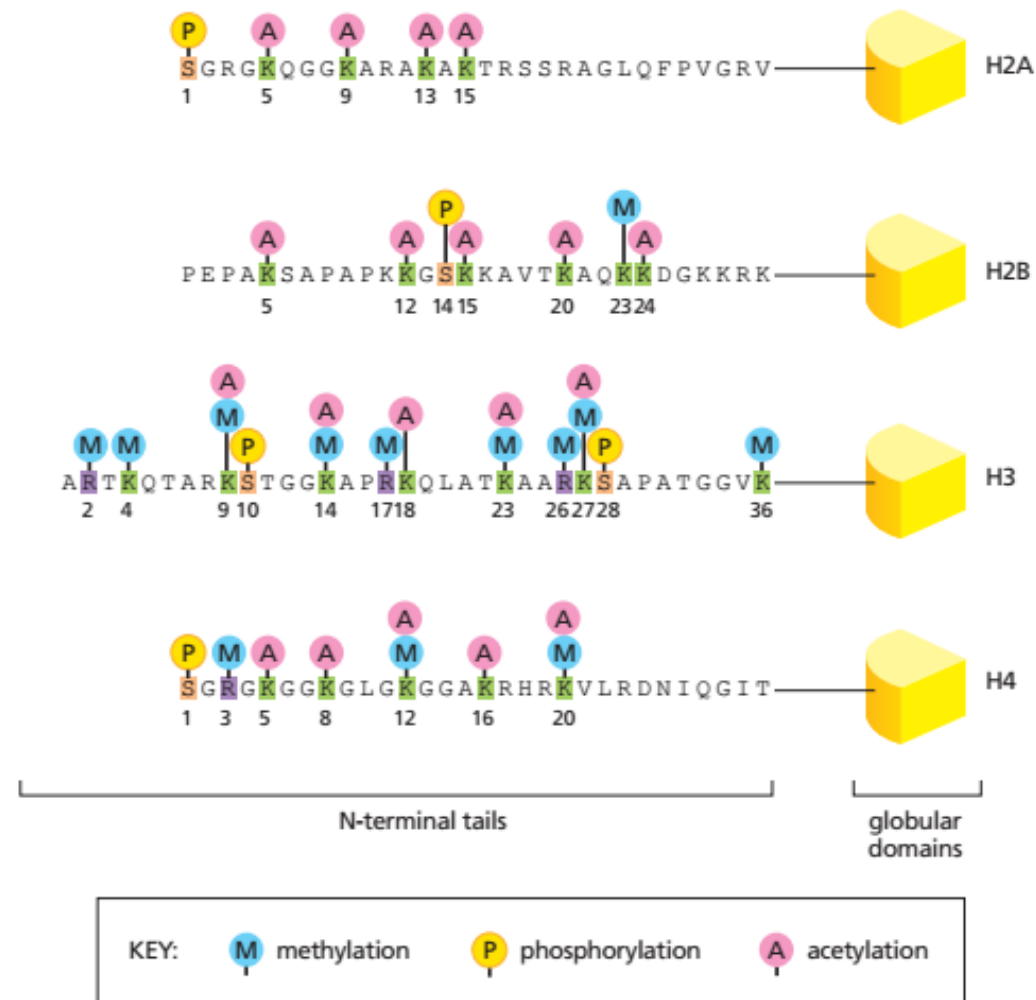
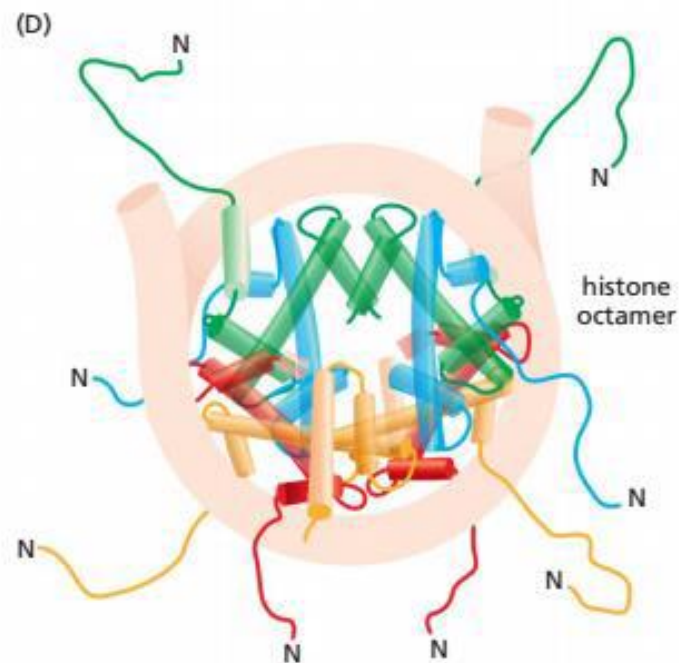
... a 3-D structure/function story





Post-translational modification of histones

Post-translational modifications of histones...



CAUTION...*rabbit holes ahead!*

Modeling chromatin....



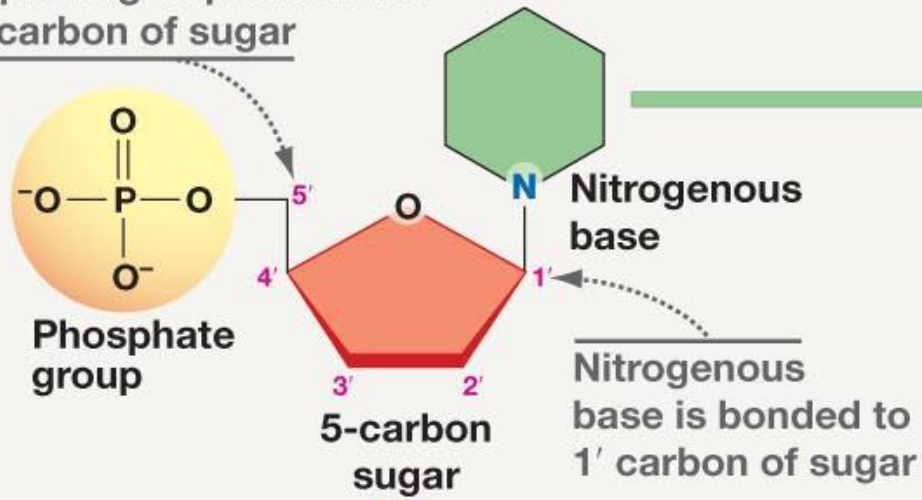
Post-transcriptional modification of DNA

Methylation of CpG to C^{Me}pG

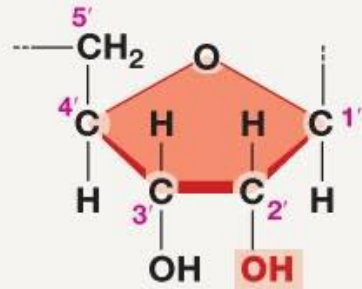


(a) Nucleotide

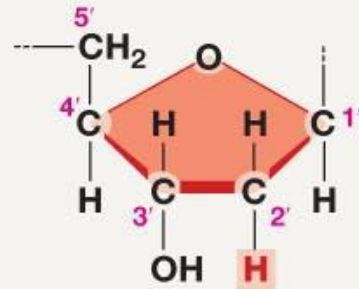
Phosphate group is bonded to 5' carbon of sugar



(b) Sugars

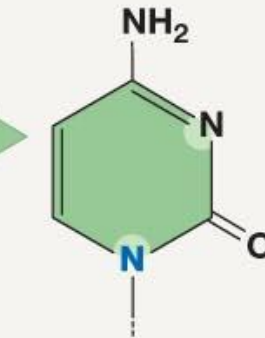


Ribose in RNA

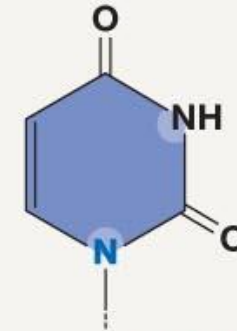


Deoxyribose in DNA

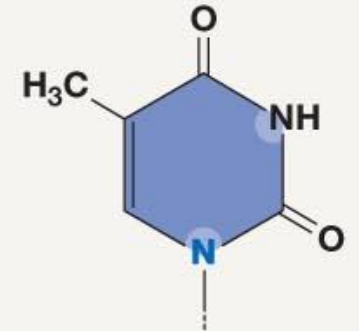
(c) Nitrogenous bases



Cytosine (C)

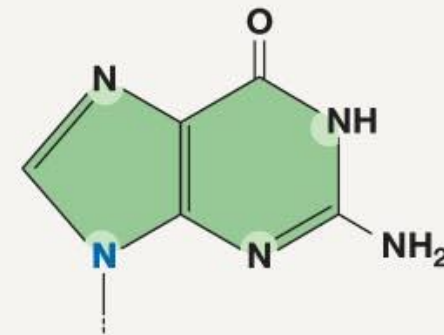


Uracil (U) in RNA

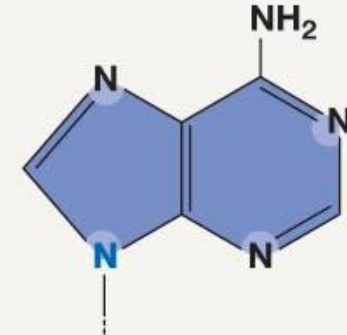


Thymine (T) in DNA

Pyrimidines



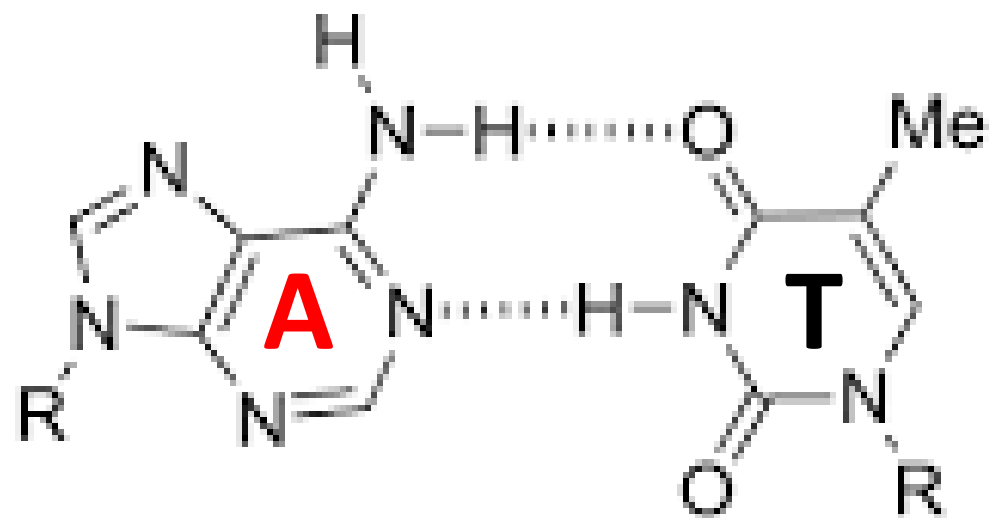
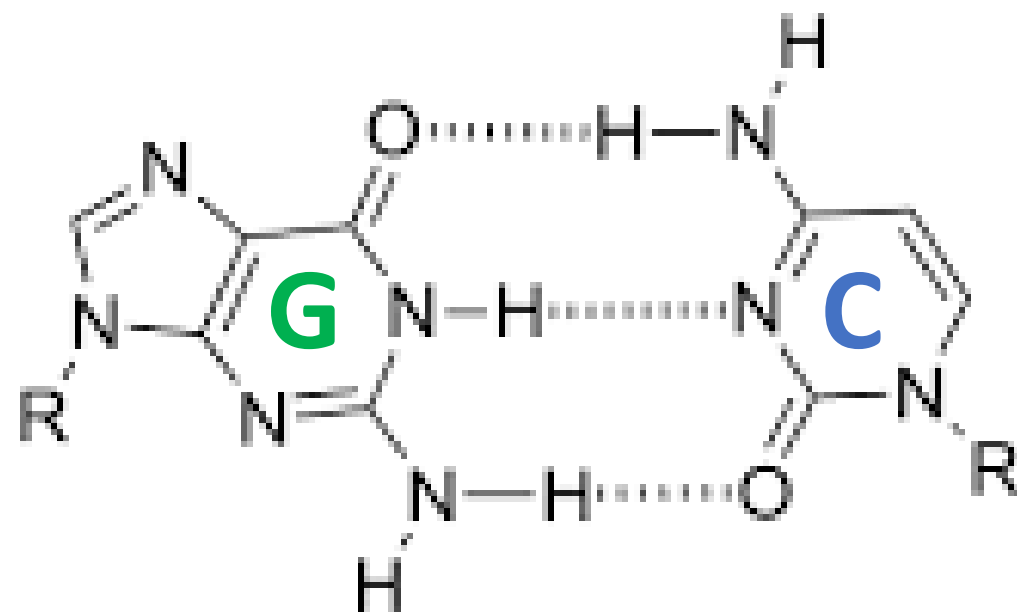
Guanine (G)

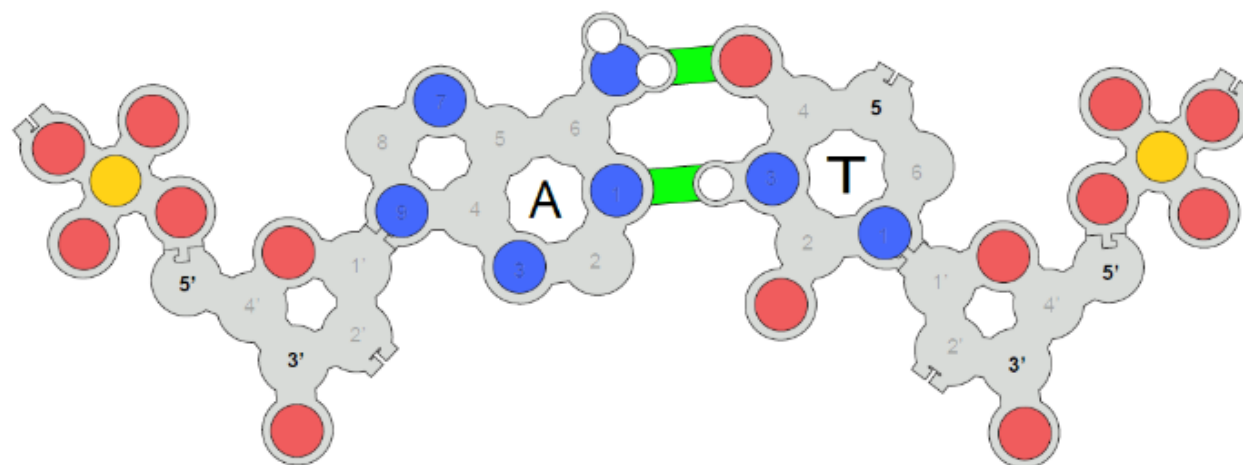
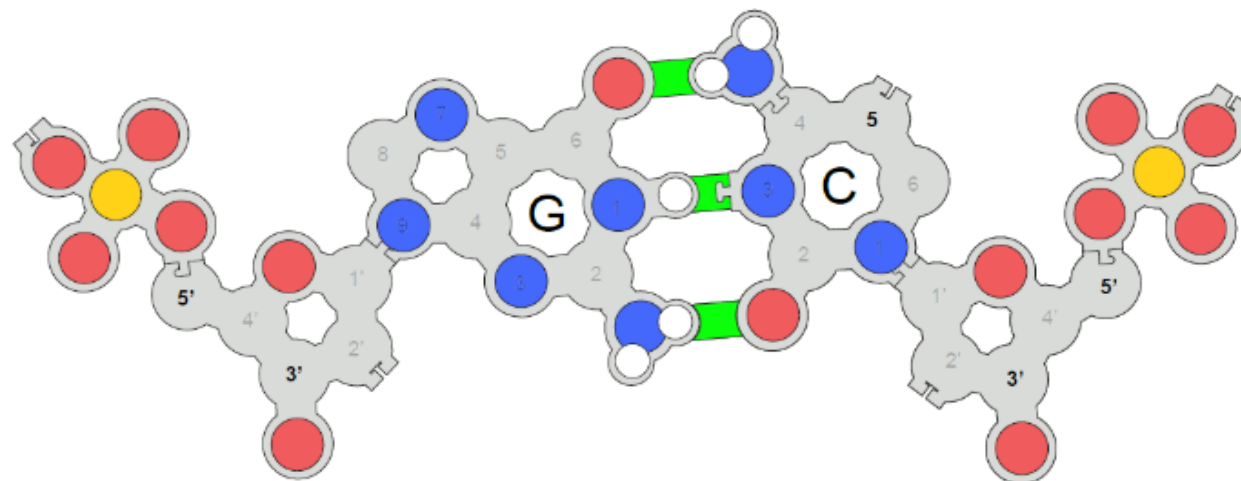


Adenine (A)

Purines are larger than pyrimidines

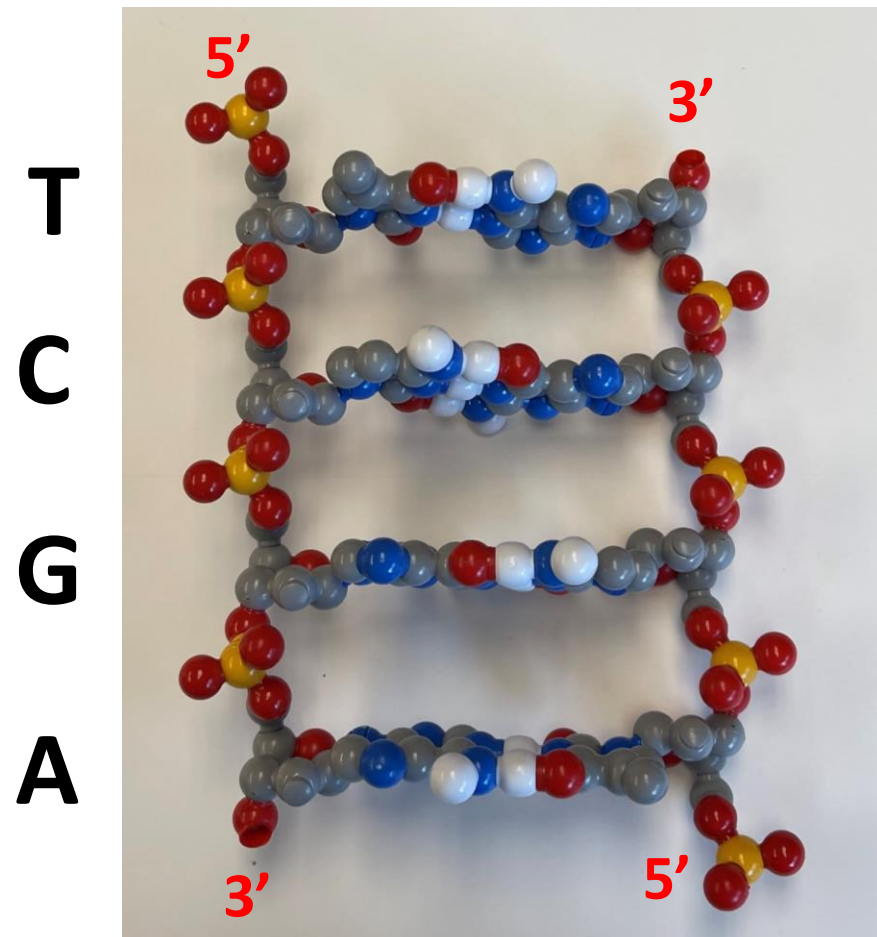
Purines

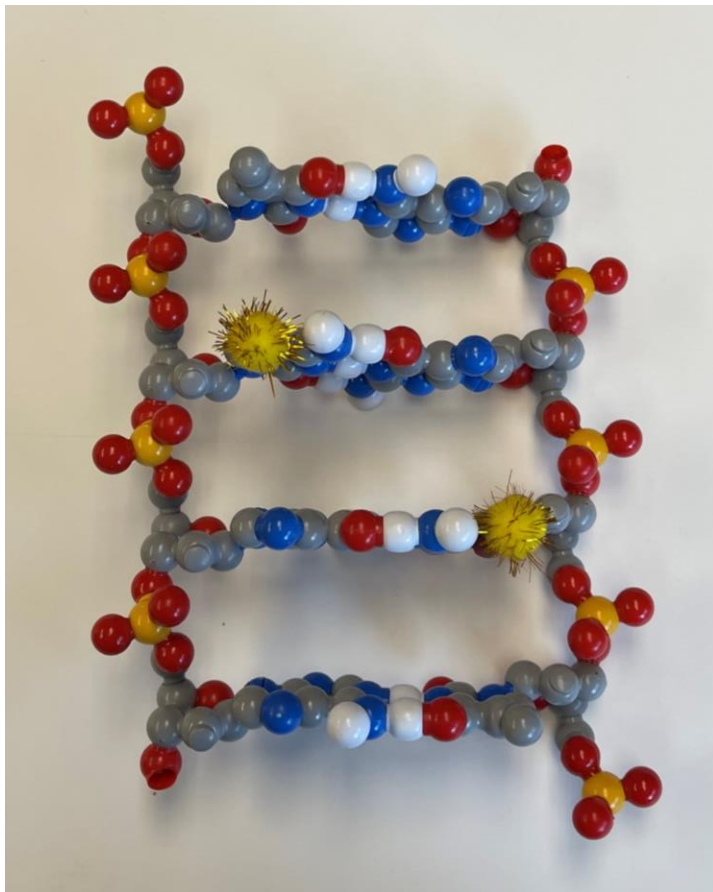




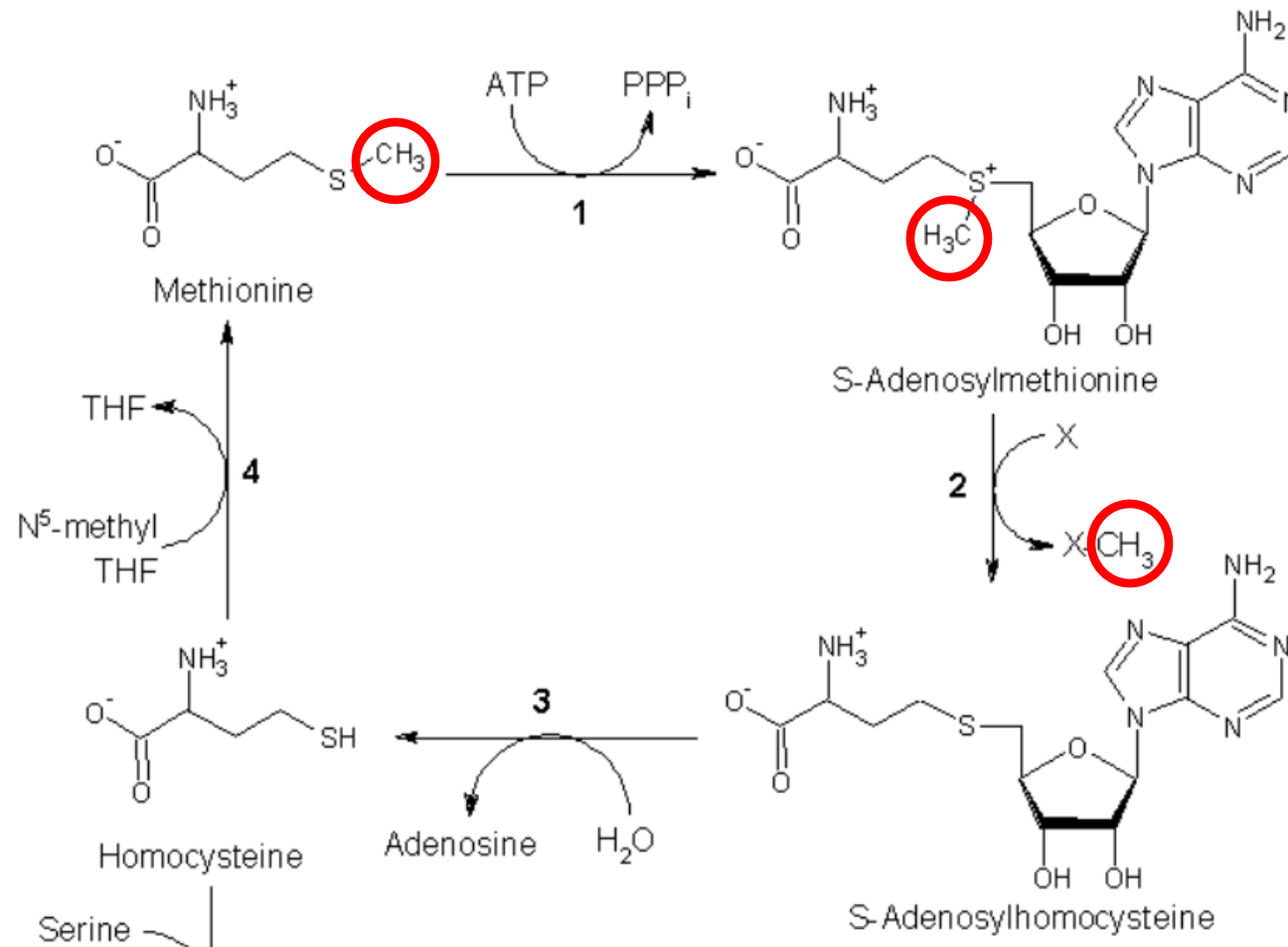
Looking for CpG's....







Methionine... *is a methyl-group donor*



FOOD

- Folate
- EGCG from green tea
- Selenium

PHYSICAL ACTIVITY

TOBACCO SMOKE

INTRAUTERINE LIFE

- Maternal diet
- Tobacco smoke

ALCOHOL

- High intake

POLLUTANTS

- Arsenic
- Chromate
- PM
- Benzene
- PAHs
- POPs

AGING

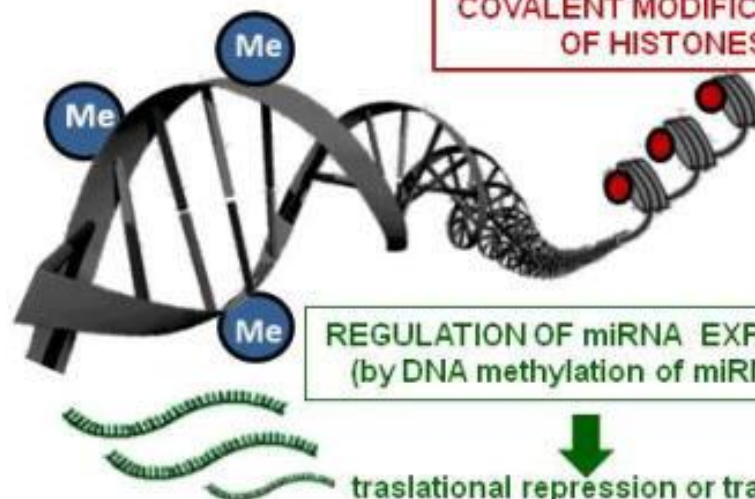
STRESS CONDITIONS

SHIFTWORK

silencing expression

↑ ↑
HYPER HYPO
gene expression
regulation

DNA METHYLATION



relaxed/compact chromatin
structure associated with
differential transcriptional activity

COVALENT MODIFICATIONS
OF HISTONES

REGULATION OF miRNA EXPRESSION
(by DNA methylation of miRNAs loci)

↓
traslational repression or transcript
degradation

FOOD

- Polyphenols from vegetables
- Selenium

PHYSICAL ACTIVITY

PHYSICAL ACTIVITY
CIGARETTE SMOKE
INTRAUTERINE LIFE

- Tobacco smoke

Fragile X Syndrome *a genetic/epigenetic disorder??*

X linked triplet repeat (**CGG**) expansion disorder

Fragile X patients do not express FMR1 and have cognitive/autism spectrum disabilities

All human genomes have CGG repeats in FMR1 5' untranslated region

Cytosines tend to become methylated at high repeat number (epigenetic modification!

Methylation of cytosines inhibits transcription of FMR1

CAUTION...*rabbit hole ahead!*



Histone / DNA cross-talk?

Yes...

What's CRISPR got to do with it??

Shin H, Choi WL, Lim JY, Huh JH (March 2022).
"Epigenome editing: targeted manipulation of
epigenetic modifications in plants". *Genes &
Genomics*. **44** (3): 307–315. [doi:10.1007/s13258-021-01199-5](https://doi.org/10.1007/s13258-021-01199-5). [PMID 35000141](https://pubmed.ncbi.nlm.nih.gov/35000141/). [S2CID 245848779](https://pubs.scisearch.org/S2CID/245848779).

Coming soon,... to a workshop near you.

Tomorrow's Science Today: *preparing for the next pandemic.*

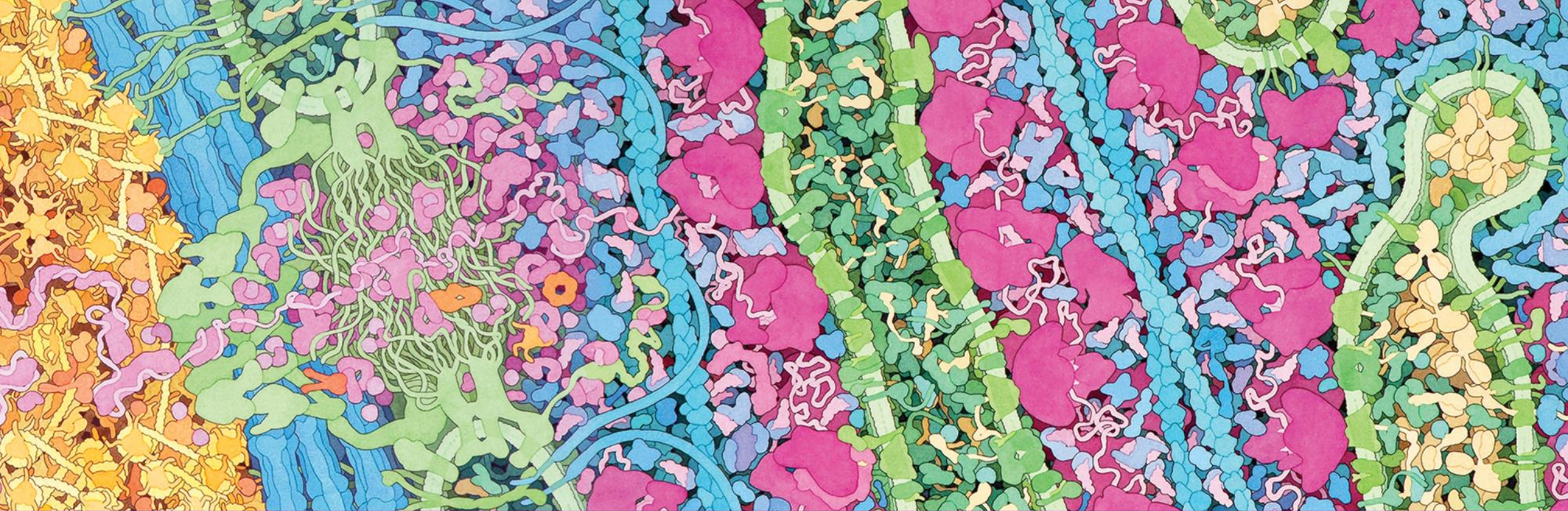
An NIH SEPA project.

- **New Instructional Materials**
 - Models, models and more models....
A Virus Collection,.. including CoV-2
Antibodies/vaccines /and your immune system
mRNA vaccines and multi-valent, ultra-potent vaccines...from synthetic biology.
 - Stories, stories and more stories....
- **A Professional Learning Experience**...beginning in the summer of 2024

But first,...enroll now in **Modeling the Molecular World, 2023**

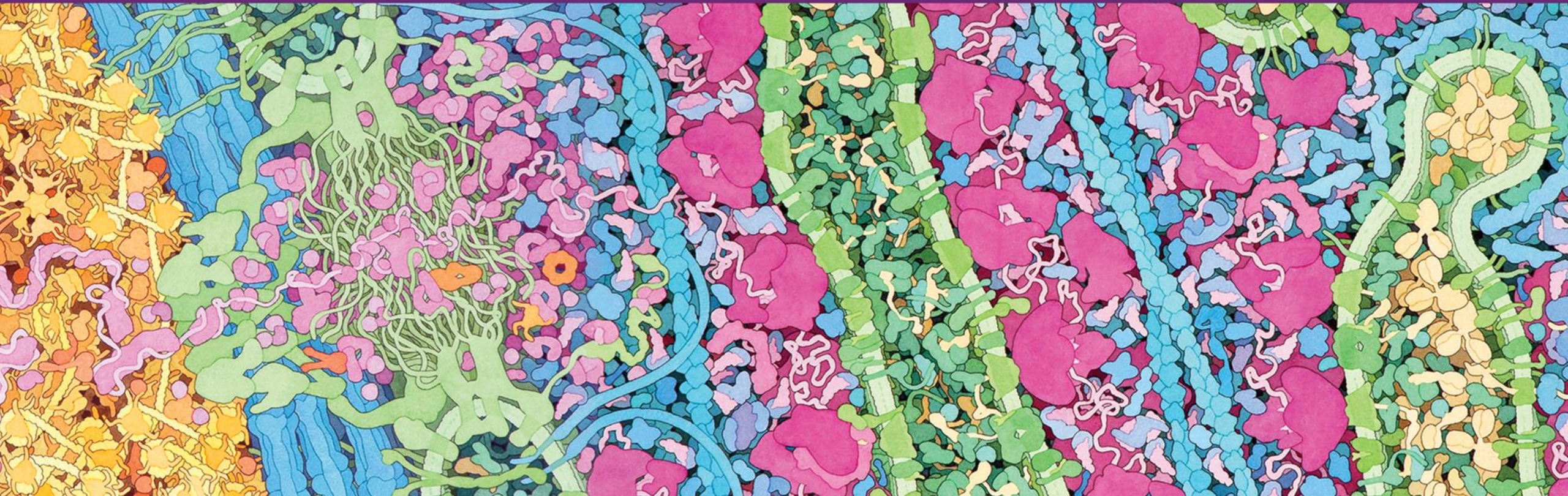
Session 1 -- June 26–30, or

Session 2 -- July 17 – 21



3d molecular
designs

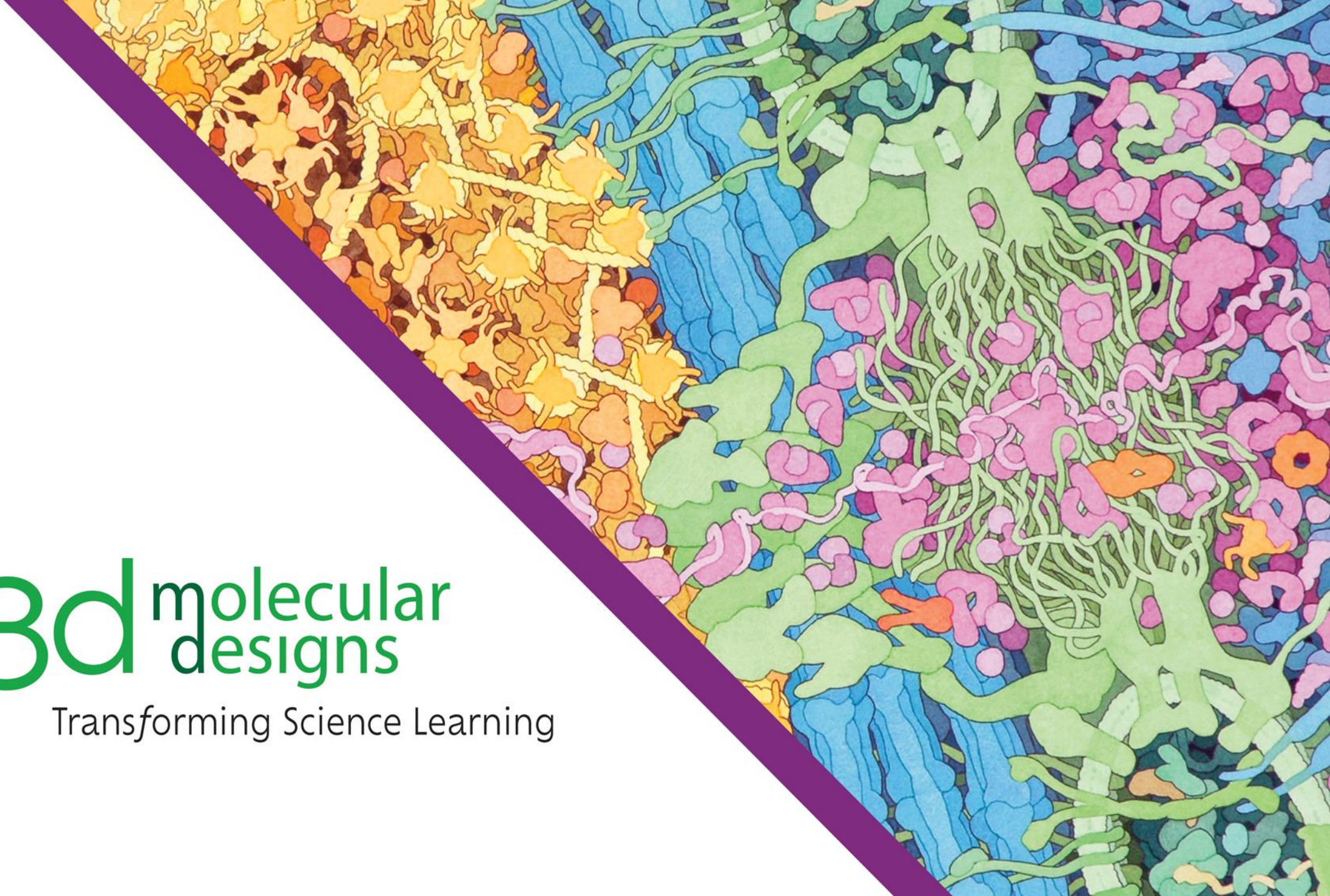
Transforming Science Learning

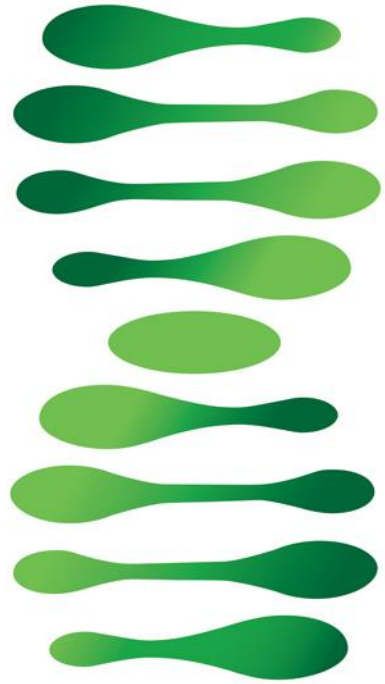




3d molecular
designs

Transforming Science Learning





Transforming Science Learning



WHY...did T replace U in DNA?

...if we had not switched...

spontaneous oxidative
deamination of C



AGUCGAAGUCAACCGAGGCUGCGCUAC
UCAGCUUUCAGUUGGCUCCGACGCGAUG



AGUCGAAGU^U_xAACCGAGGCUGCGCUAC
UCAGCUUUCAG_GUUGGCUCCGACGCGAUG

A DNA repair system can remove “U” from DNA.
But,...how can we distinguish between a
“deaminated C” and a normal U?

ANSWER: We can't.

WHY...did T replace U in DNA?

...but after we switched...

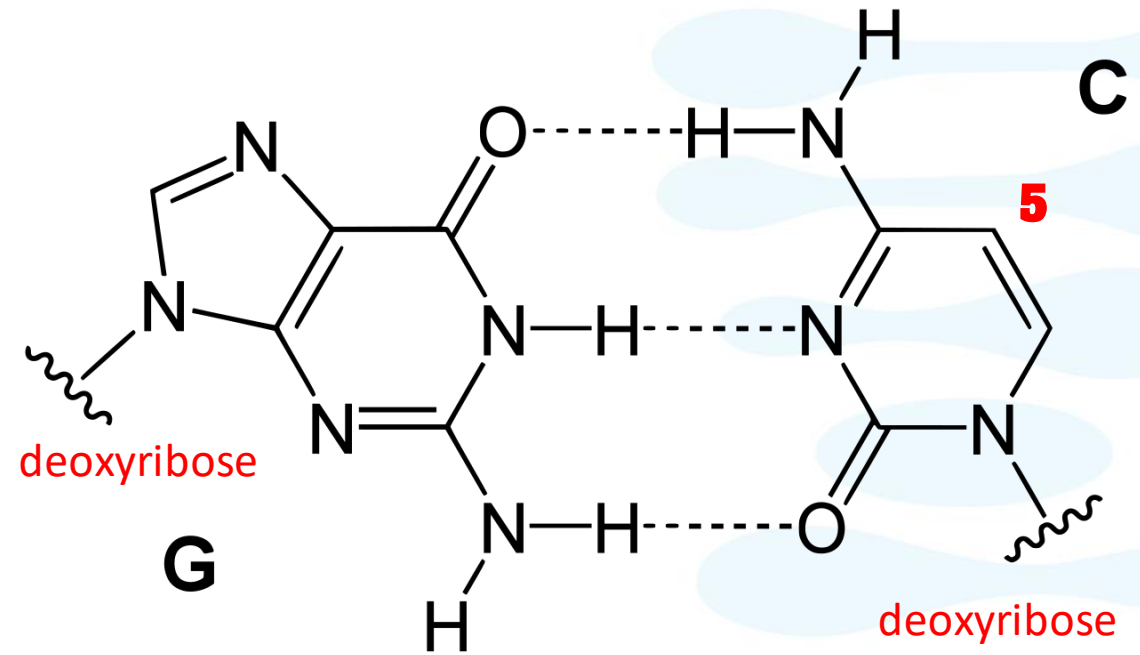
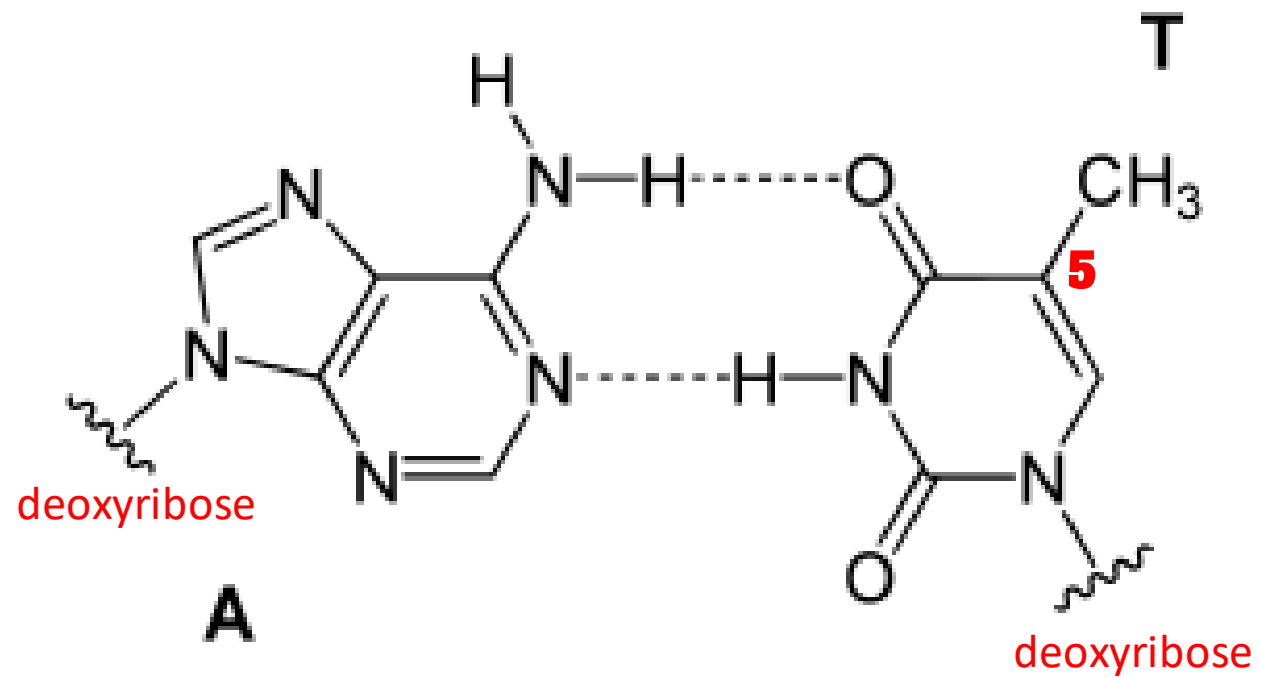
spontaneous oxidative
deamination of C

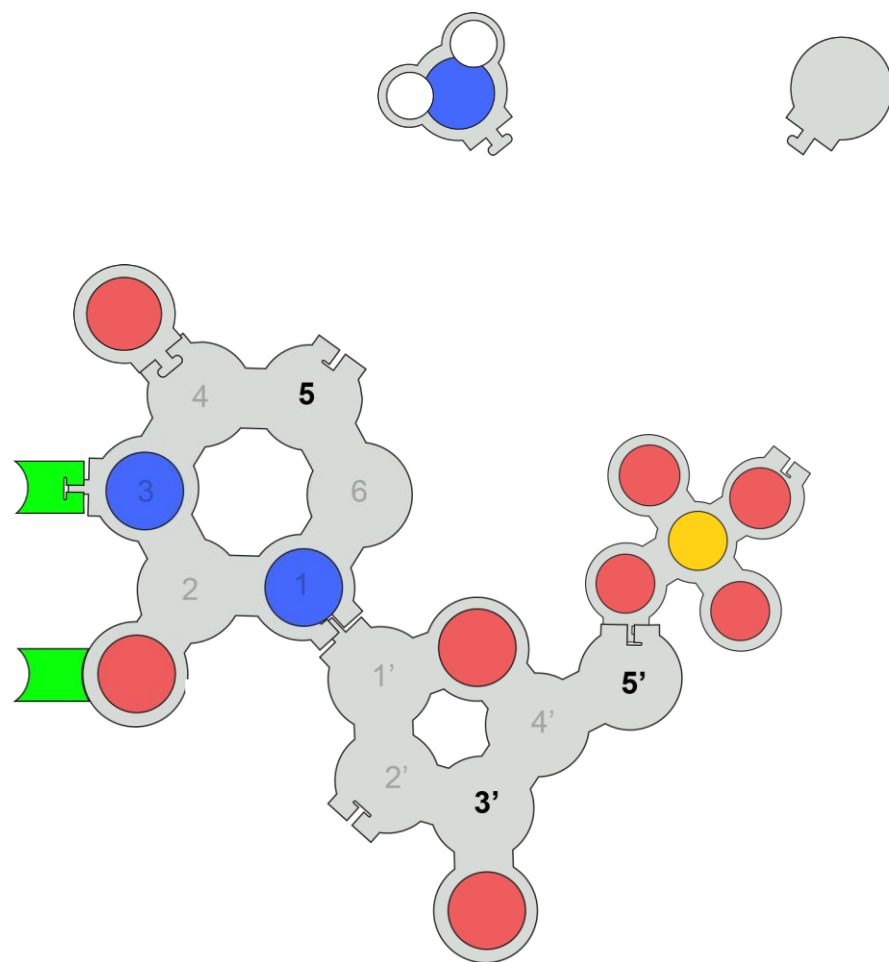
AGTCGAAGTCAACCGAGGCTGCGCTAC
TCAGCTTCA GTTGGCTCCGACGCGATG



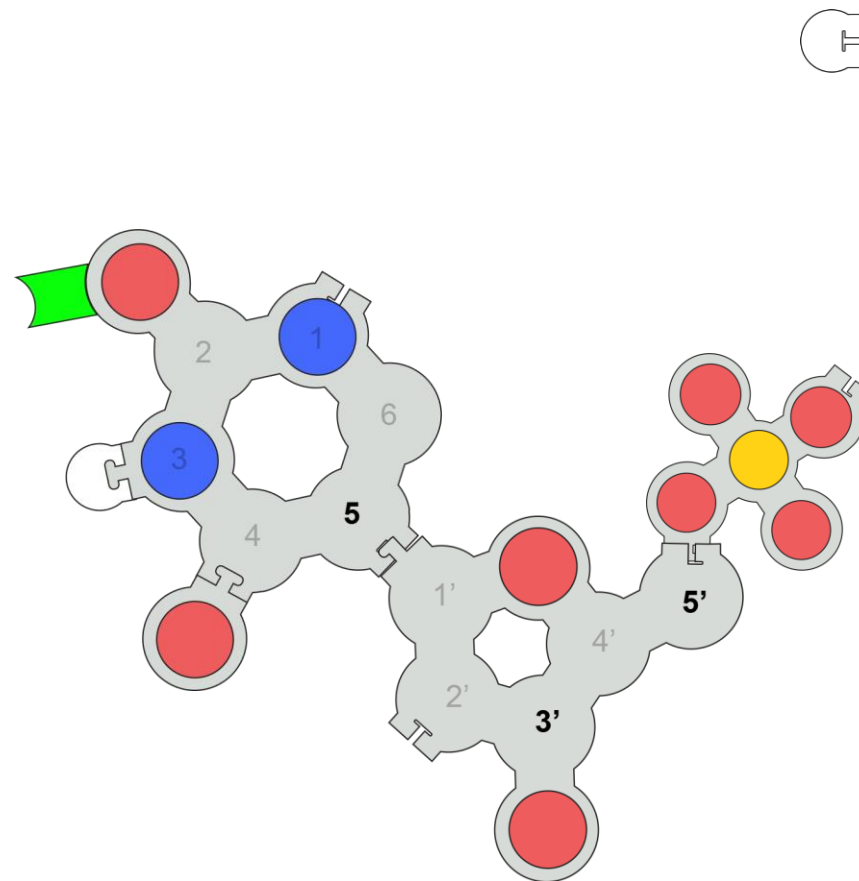
AGTCGAAGT^U_xAACCGAGGCTGCGCTAC
TCAGCTTCA_GTGTTGGCTCCGACGCGATG

Uracil glycosidase constantly scans the DNA....looking for U's.
Any U ... is a bad U...and should be repaired.

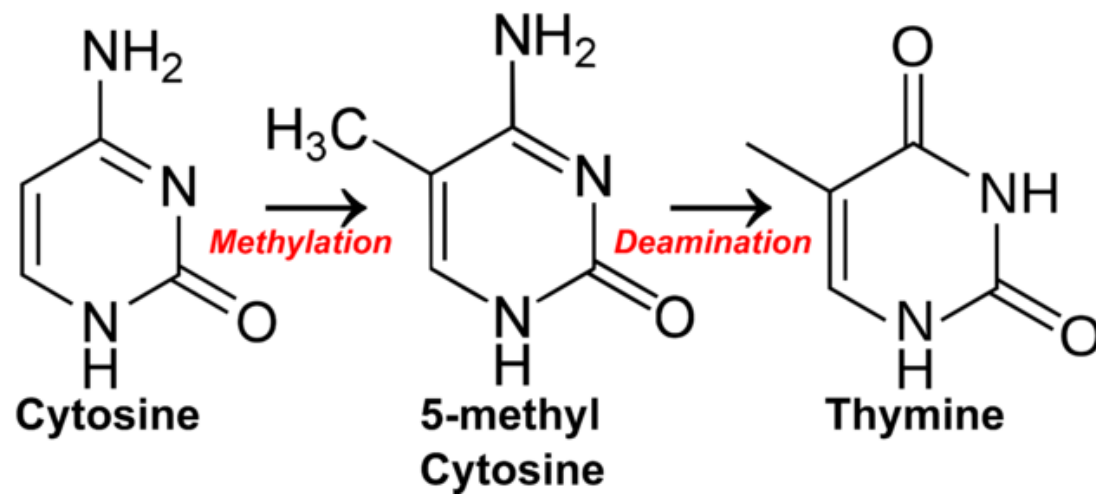


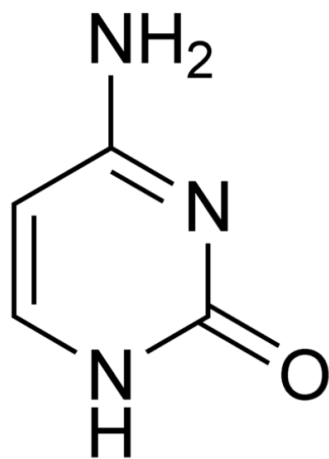


Uridine

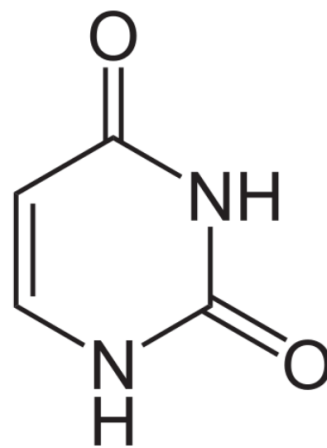


Pseudo-Uridine

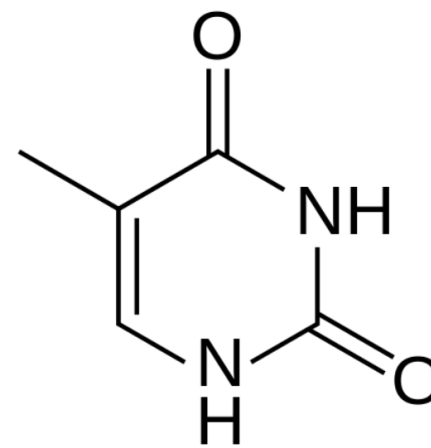




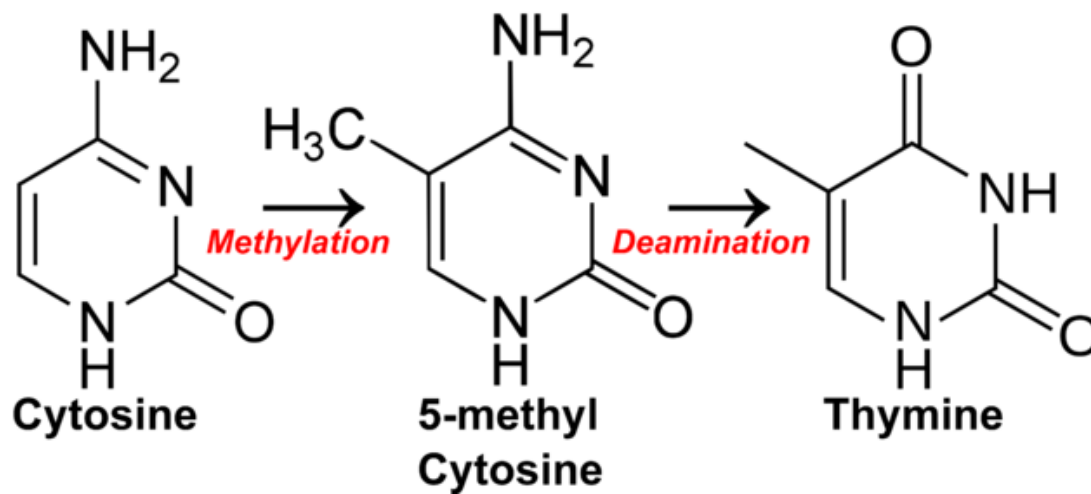
Cytosine

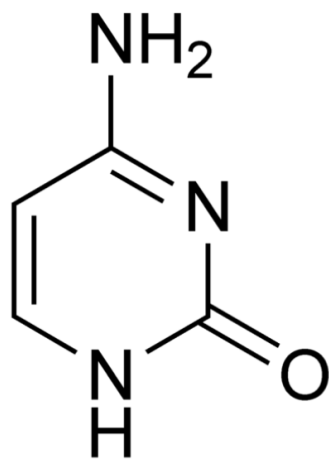


Uracil

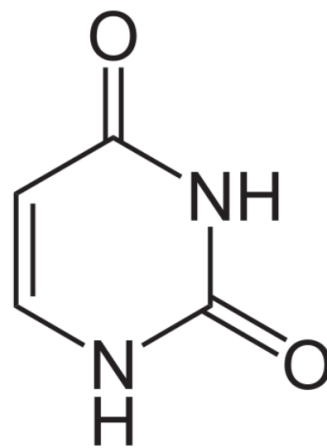


Thymine

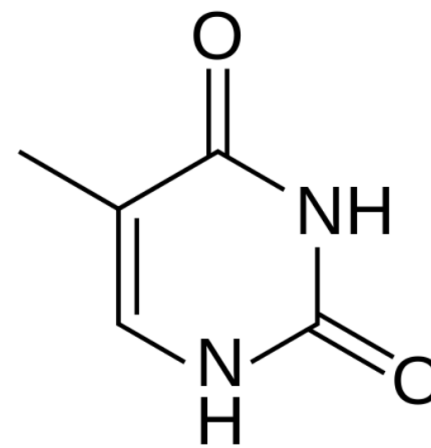




Cytosine



Uracil



Thymine

