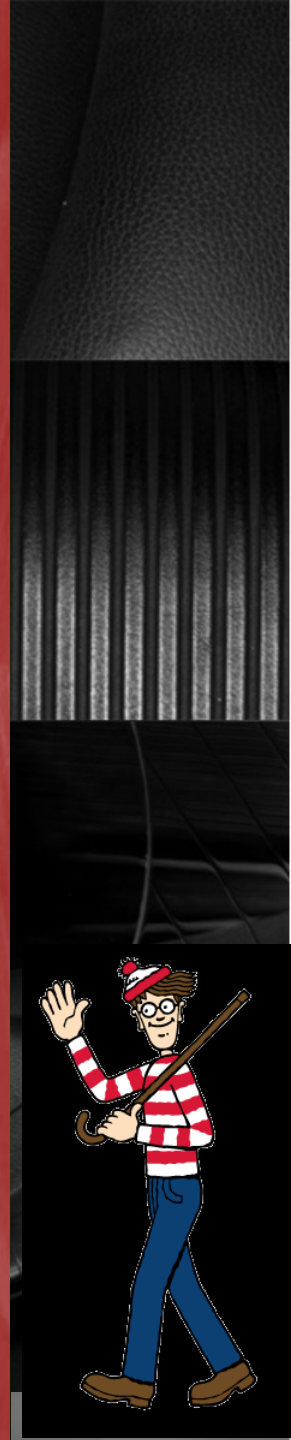
Nucleosome A?

MMTV and HMTV

La-Sigma RET 2014



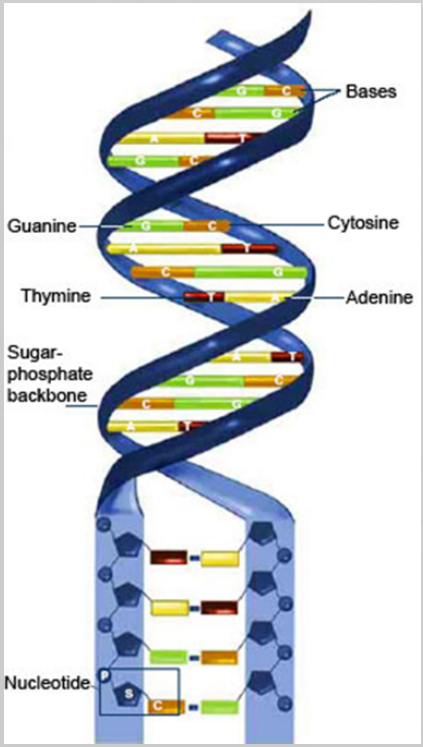
Length of DNA

- DNA has 3 billion base pairs or 3 x 10^9 bp
- The length of each base pair is roughly

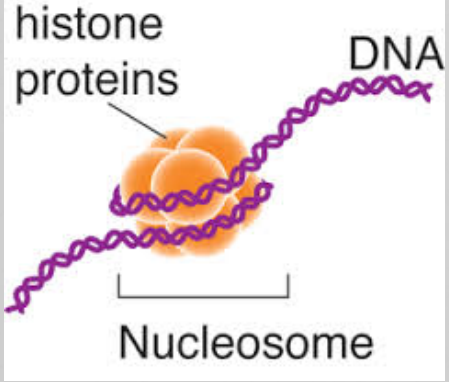
  $1/3$ of a nanometer or $1/3$ x 10^{-9} m/bp
- Combine the two and you have:

  (3 x 10^9) ($1/3$ x 10^{-9}) ≈ 1 meter in length of 1 copy of DNA

  ≈2 meters in length of entire DNA because you have 2 copies
- 2 meters is way bigger than the cell nucleosome so the DNA has to be folded and packaged. Proteins called histones do this by wrapping 147bp of DNA at a time into a giant molecular complex of proteins and DNA called nucleosomes.

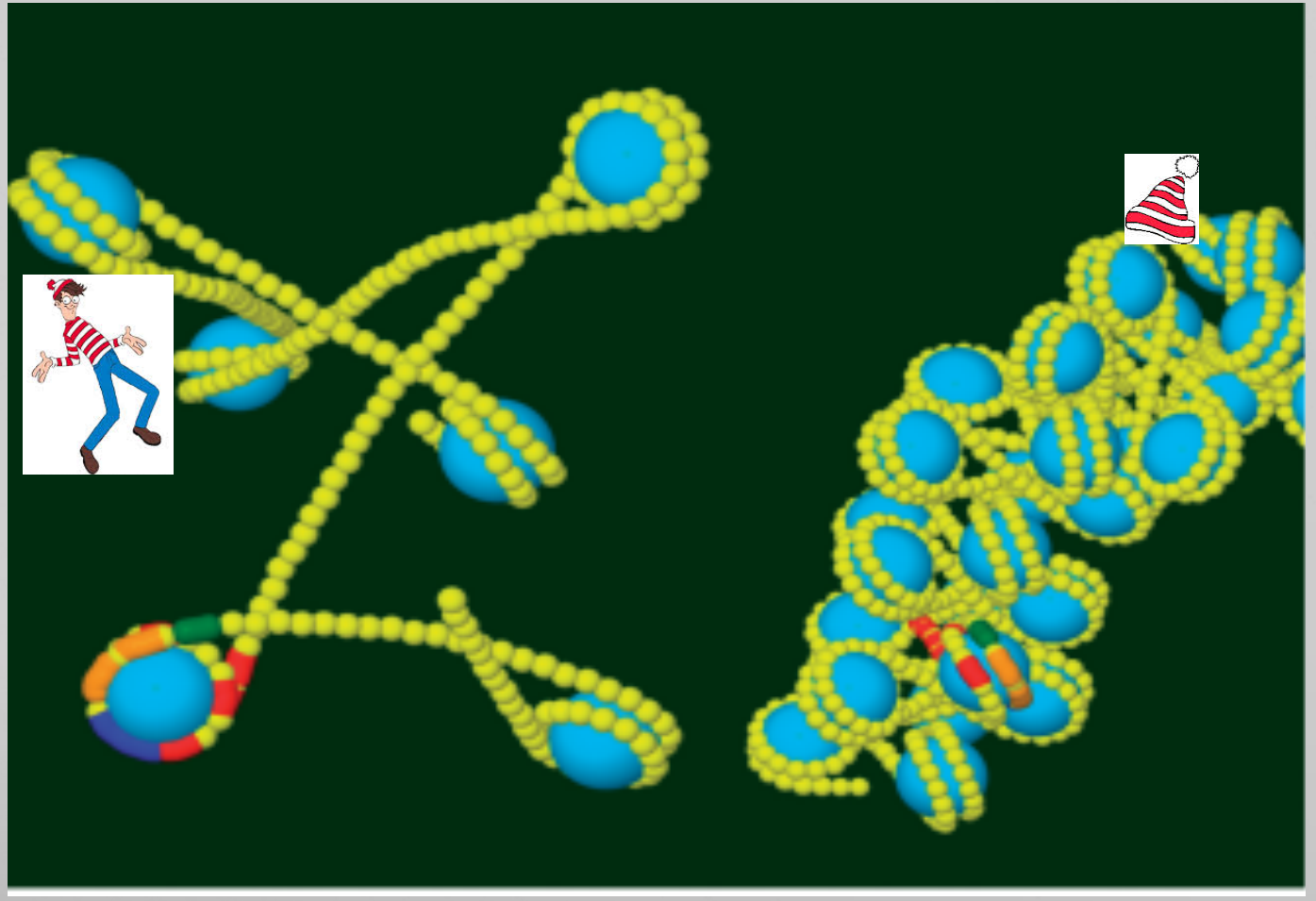


DNA basics



- The genomes of higher organisms exist not just as long strands of DNA in the familiar Watson-Crick double helix, but rather they are associated with proteins, called histones, that fold and package the DNA such that it fits into the cell nucleus
- Out of that we are going to look at a 147 base pair sequence because there are roughly 147 base pairs wrapped around a histone core
- As a case study we will look at 6 nucleosomes (histone cores) in the Mouse Mammary Tumor Virus (MMTV)
- More specifically We will study the 1st nucleosome; nucleosome A

6 nucleosomes in the MMTV



Nucleosome A….

- Looking for it:
  - There are 4^{147} OR about 10^{88} possible sequences of a nucleosome
  - (That's 1 with 88 zeroes behind it)
  - Searching for Nucleosome A is like
  - Like searching for Waldo

HUGE!!

- Reason to look for Nucleosome A:
  - Has popped up in other research. The MMTV is a model system for hormone regulation.
  - Dr. Bishop has personal history with it from graduate school… idea of ongoing research

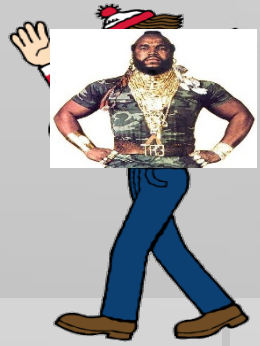
Mutations in DNA

- Point mutation or change of one amino acid in the histone core can change the way DNA interacts with the histone core.
- DNA becomes more mobile because it does not attach as securely as it would without mutations.. .this changes the entire nature of the nucleosome

Study of MMTV

- MMTV – Mouse Mammary Tumor Virus
- MMTV is a popular sequence of DNA that has been studied a lot over the years. Scientists now know how to use it for other purposes.
- Acts as a hormone regulated switch.
- In the presence of hormones, MMTV turns on gene expression. Scientists will put MMTV in front of whatever gene they are trying to express.
- Placing the hormones in a test tube with the MMTV cells …

The gene is made!!



MMTV - Mouse Mammary Tumor Virus

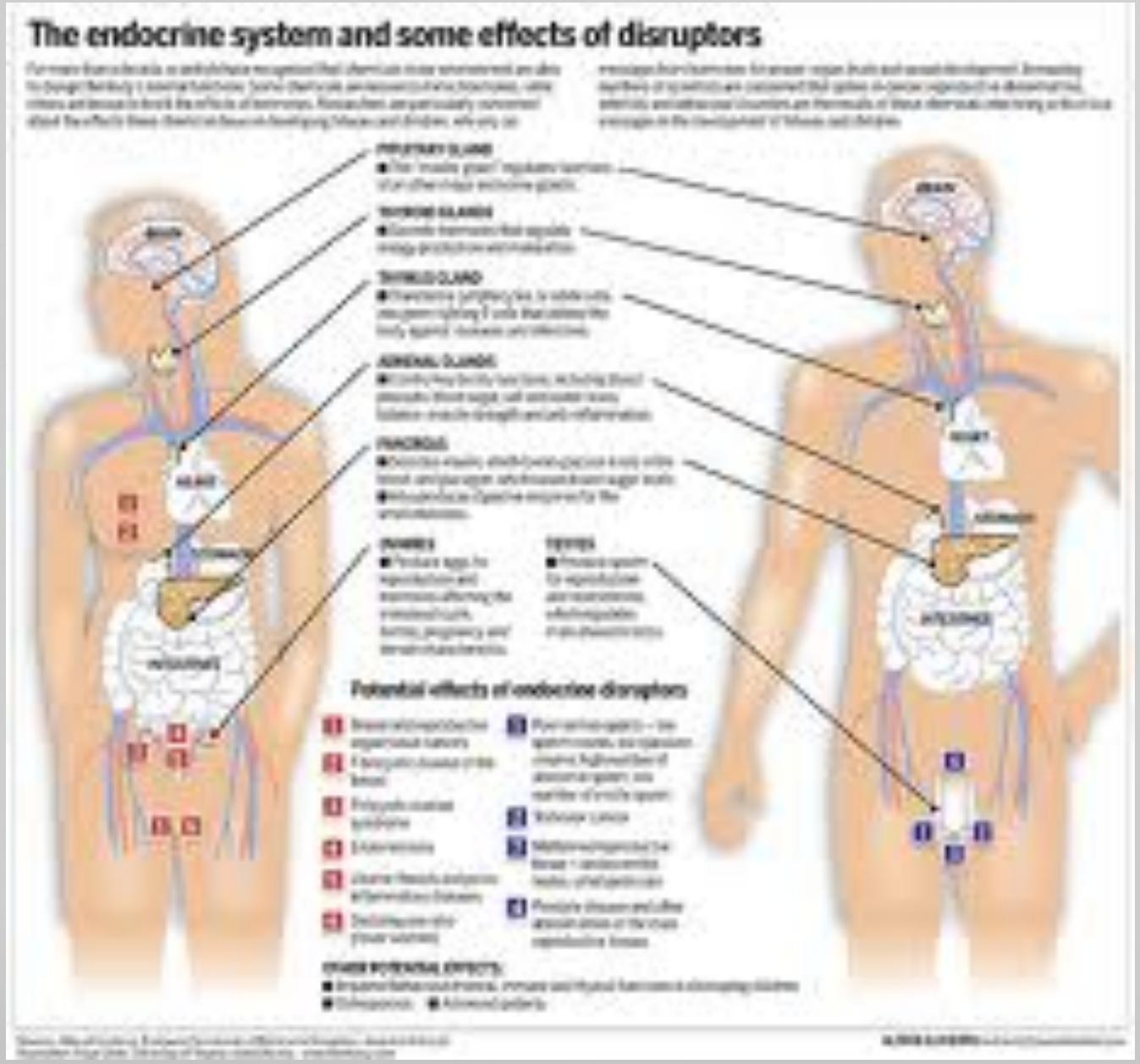
- In mice

  they pass the virus on to their young through breast milk

  tumors tend to be benign

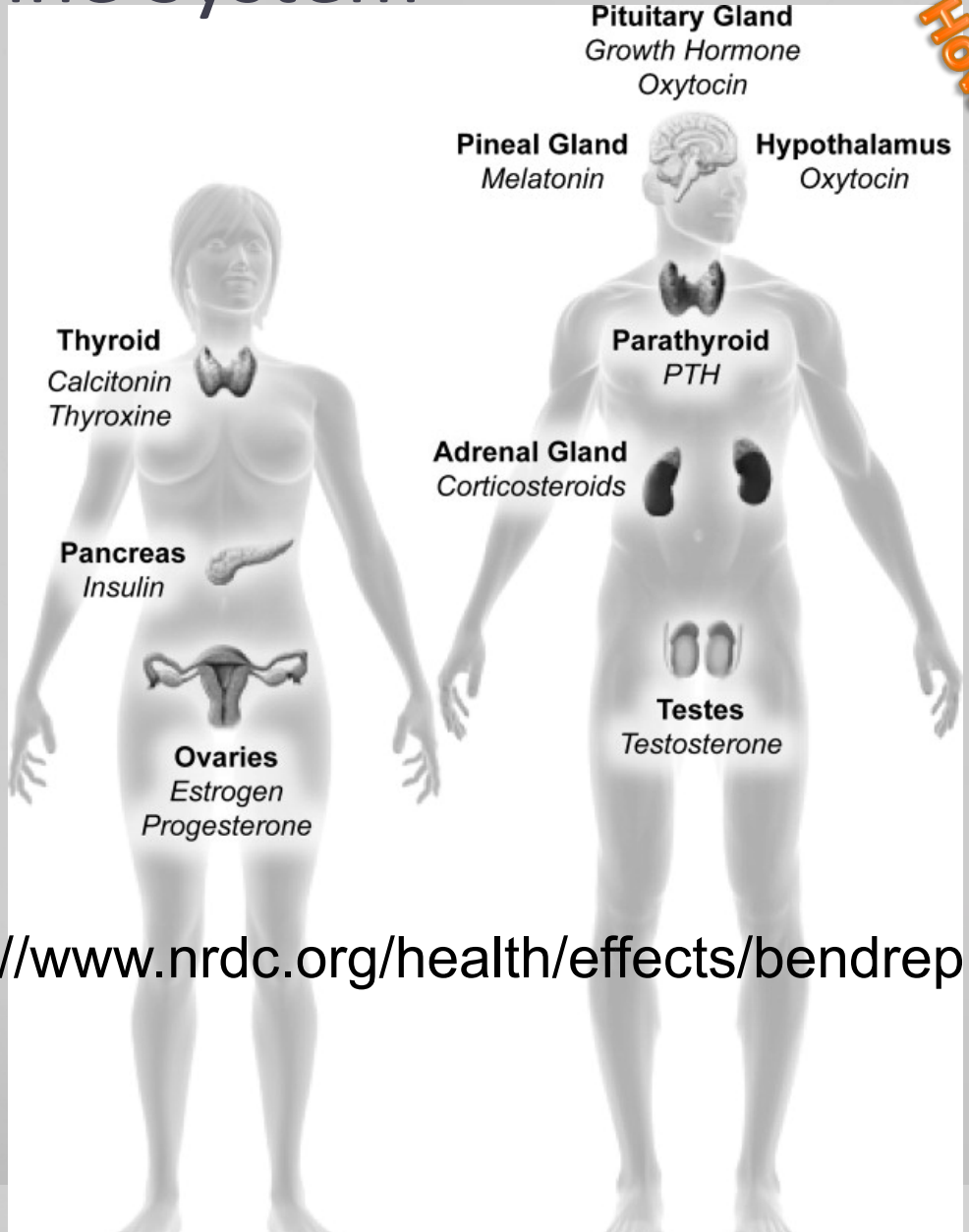
  Causes Leukemia [1]

- In humans
  - Controversial to it's role with breast cancer
  - Evidence to suggest that it plays a role in breast cancer
  - Correlation between breast cancer and leukemia – viral sequence has been found in both of these cancers
  - Have found MMTV like DNA in breast cancer [2]
  - Possible spread of the virus is transmission through our pets



http://www.nrdc.org/health/effects/bendrep.asp

The Endocrine System



How does this relate to energy??

http://www.nrdc.org/health/effects/bendrep.asp

The endocrine system: a short list

Pituitary and Hypothalamus:
Growth Hormones: cell size and number, bones
Thyroid Hormones: Temperature and metabolism
Oxytocin: contractions.
Prolactin milk production
Antidiuretic: water balance and blood pressure
Gonadotropins: FSH & Luteinizing Hormone controls gonads, menstruation

Adrenal
Epinephrine & norepinephrine: flight and fight
Mineraloccorticoids: electrolyte balance
Glucocorticoids: immune response and inflammation

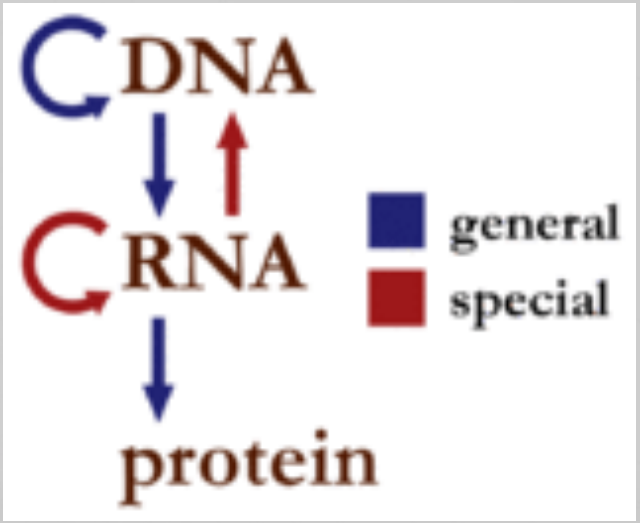
Thydroid:
Metabolism, growth & development, sexual matur**ity**

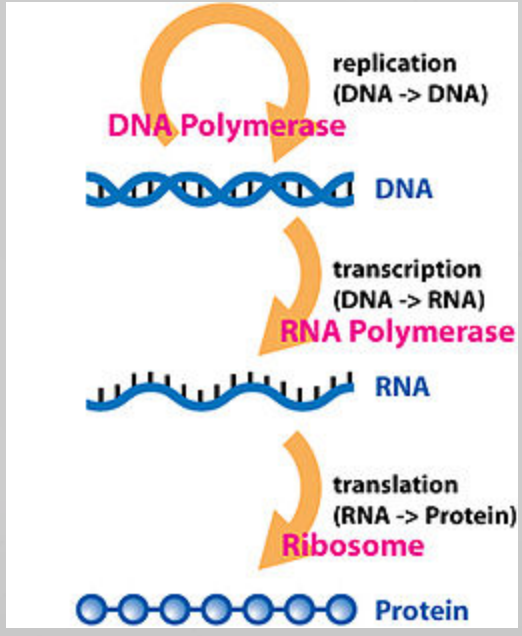
Pancreas
Insulin and glucagon: blood glucose levels

Gonads:
Testosterone, Estrogen & Progesterone: secondary sexual characteristics

Activity Time!!

- We will write your name using reverse transcriptase to create a knitted bracelet representing DNA base pairs





How to video

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