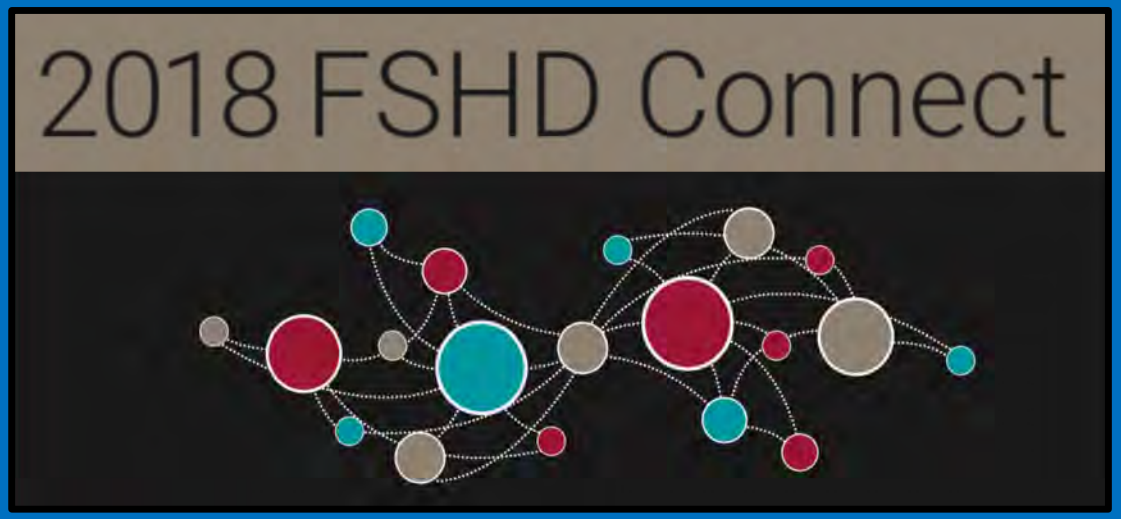

FSHD 101
DUX4: Prince Charming turned into Joker

Prof. Alexandra Belayew

University of Mons, Belgium

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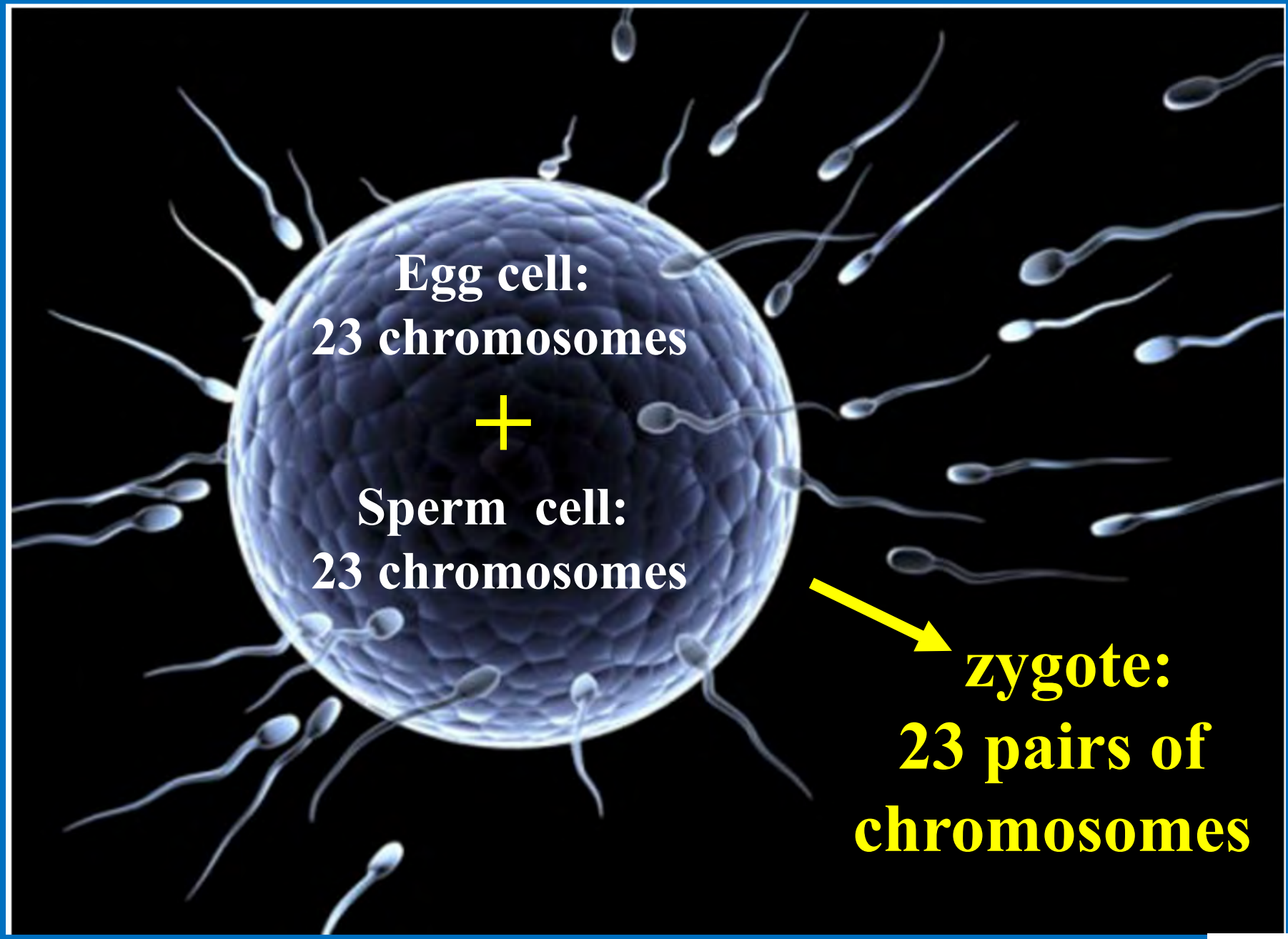
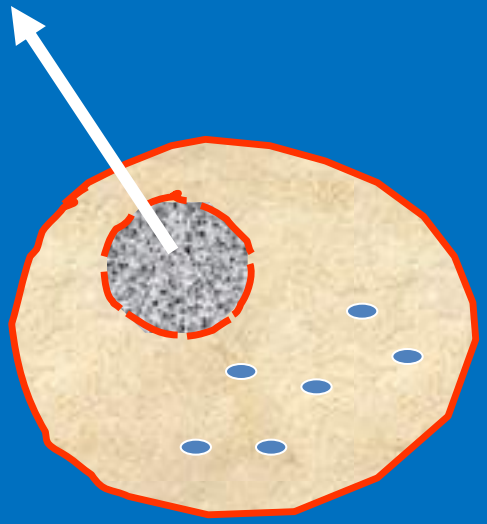


http://thelinkfwi.wixsite.com/thelink/single-post/2015/10/30/GUADELOUPE-LE-DON-DE-SPERME-ET-DOVULE-DEBARQUE

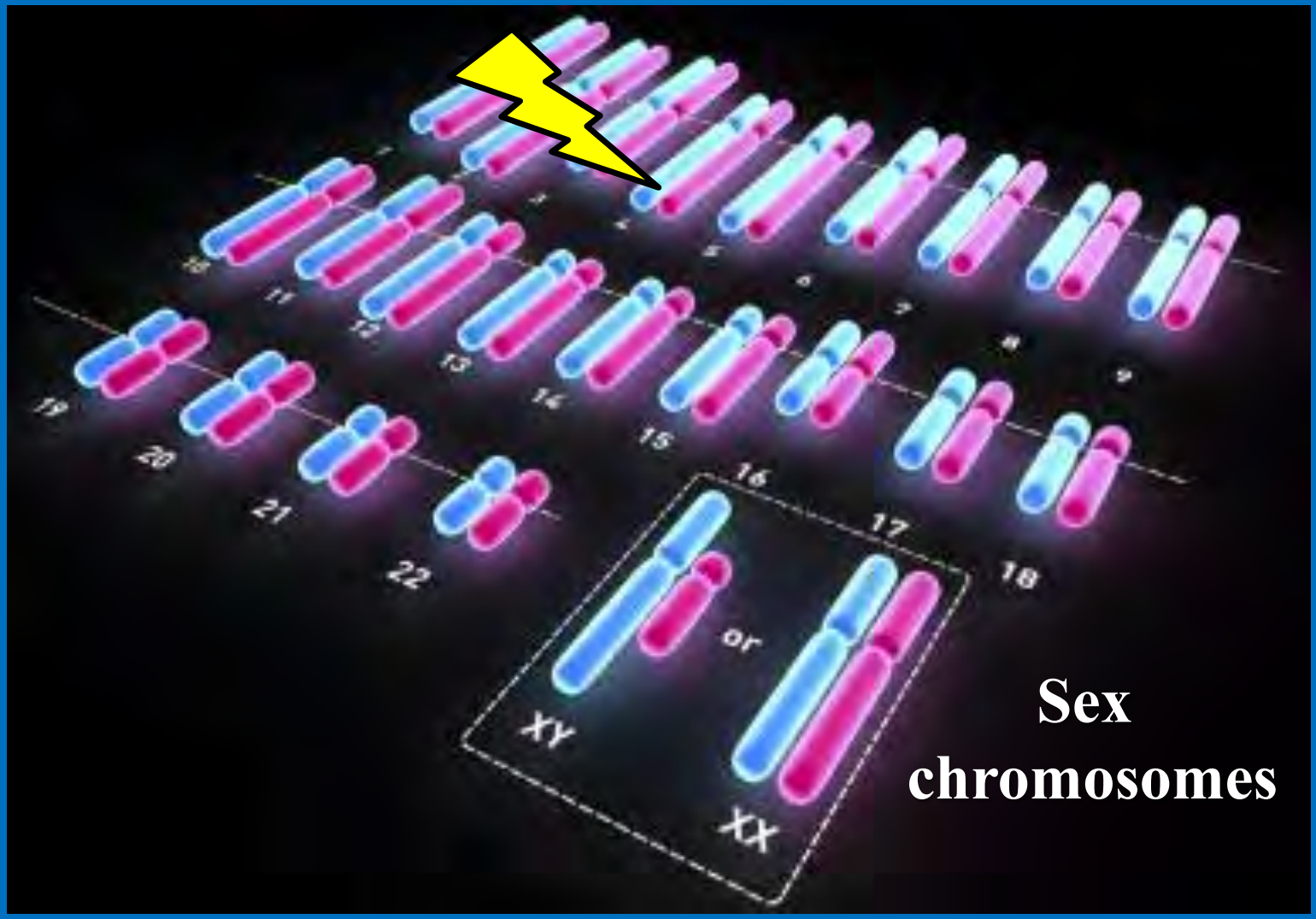
Every cell of an individual has the same genetic programm

100.000 billion cells

In the nucleus:
23 chromosome pairs

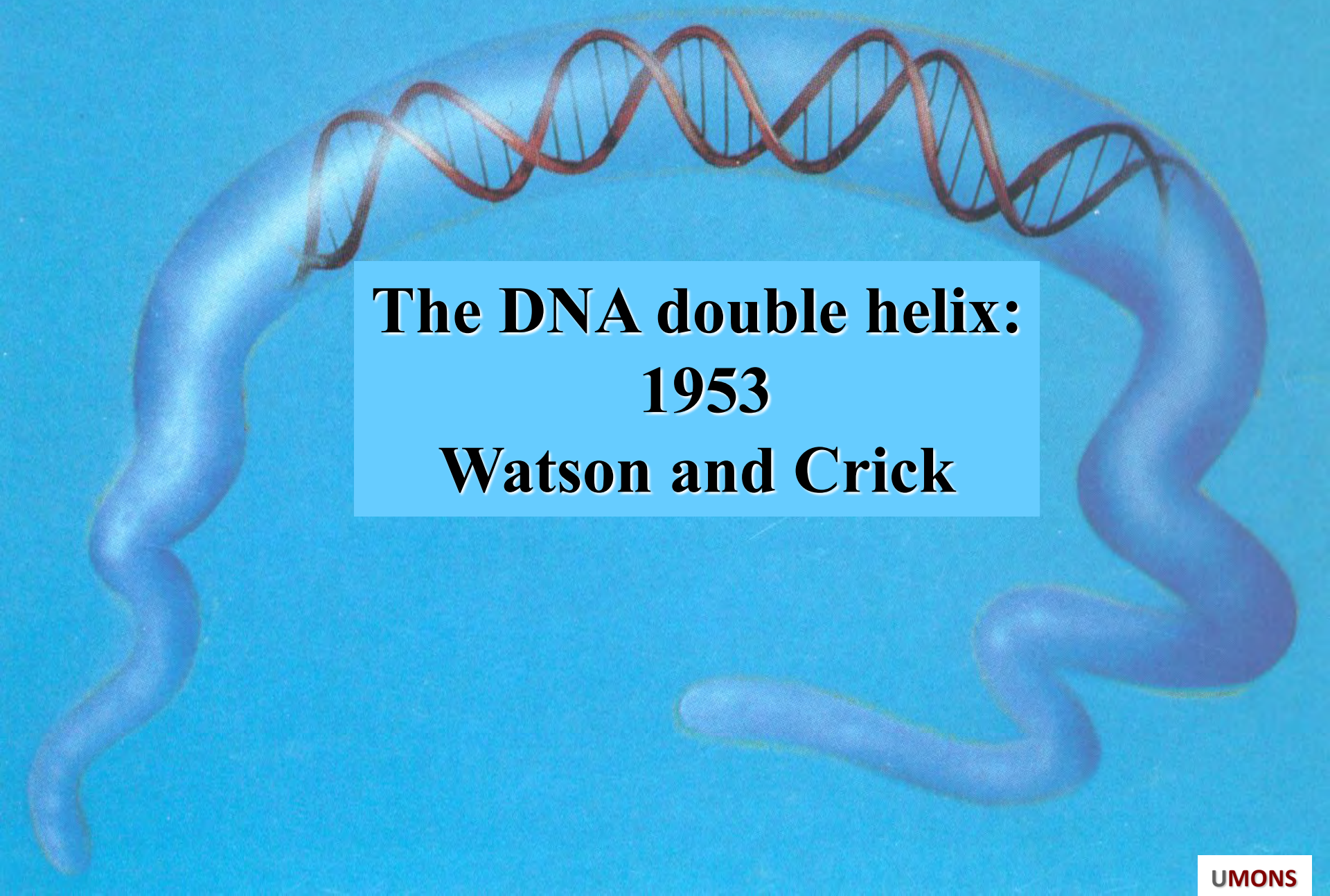


The FSHD genetic defect: one chromosome of the chromosome 4 pair



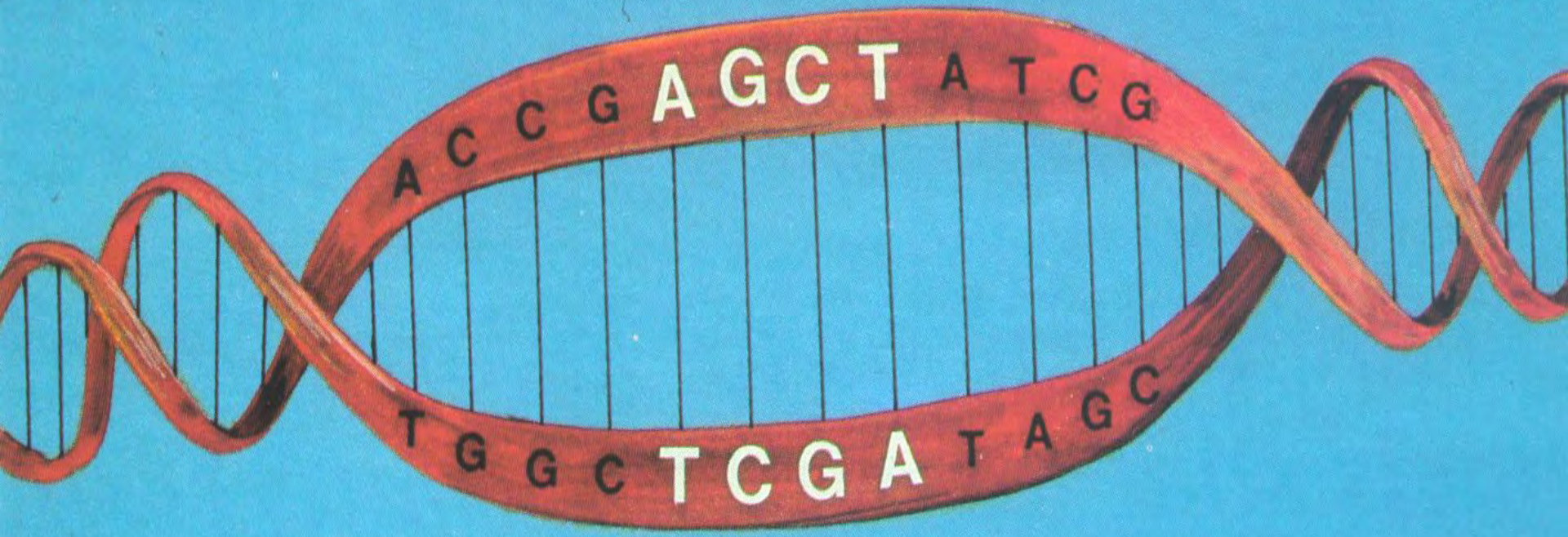
http://biology.about.com/od/basicgenetics/p/chromosgender.htm

What are chromosomes made of?



The DNA double helix:
1953
Watson and Crick

A long chain made with 4 chemicals (letters)...



… forming complementary pairs.

A gene

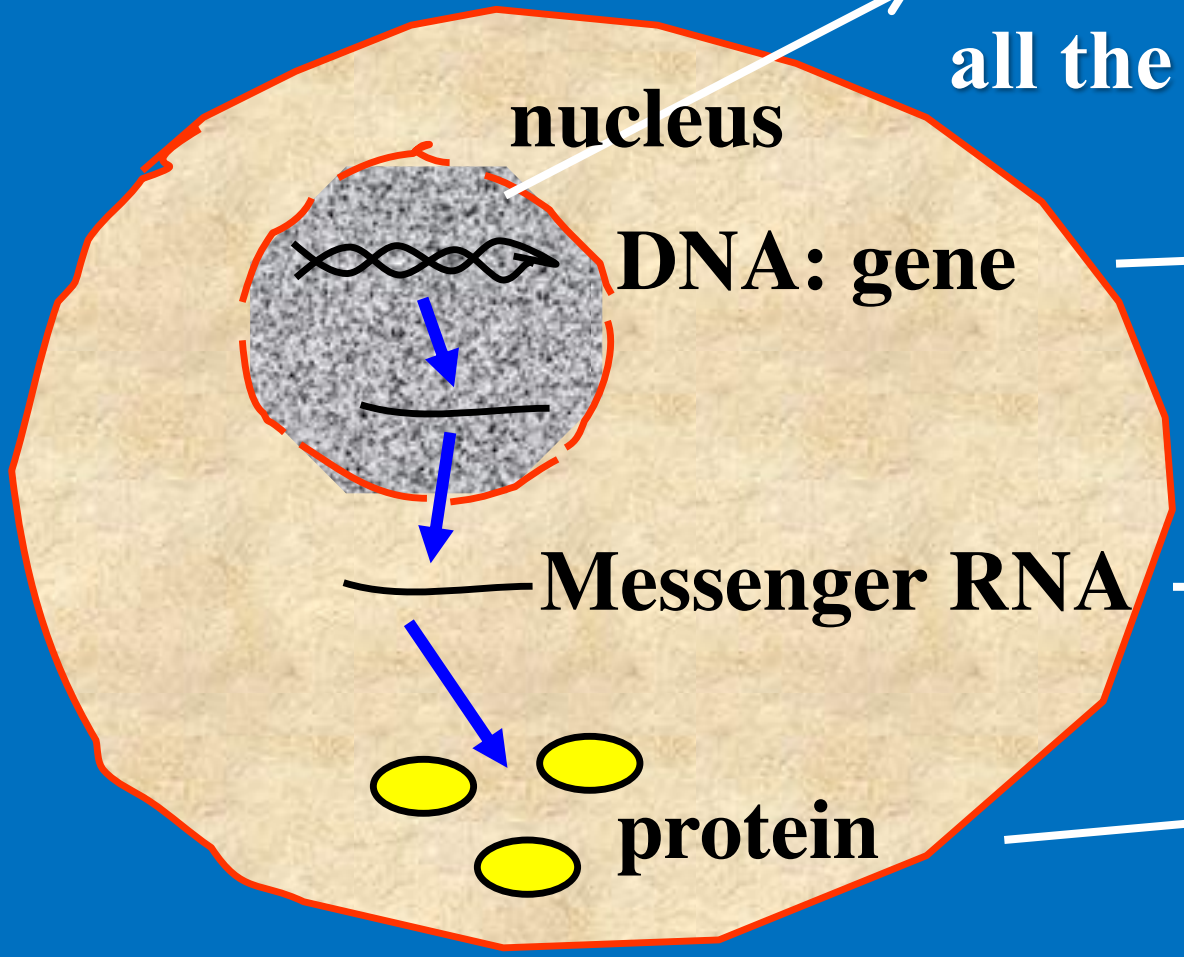
=

a DNA segment
with the recipe
to make a protein

Proteins = cookies!

http://easyday.snydle.com/20-christmas-cookies-to-try-this-holiday-season.html

Expressing a gene = baking a cookie!



Central library:
all the recipe books

= recipe

= copy

= cookie

A cookie

The bakery staff

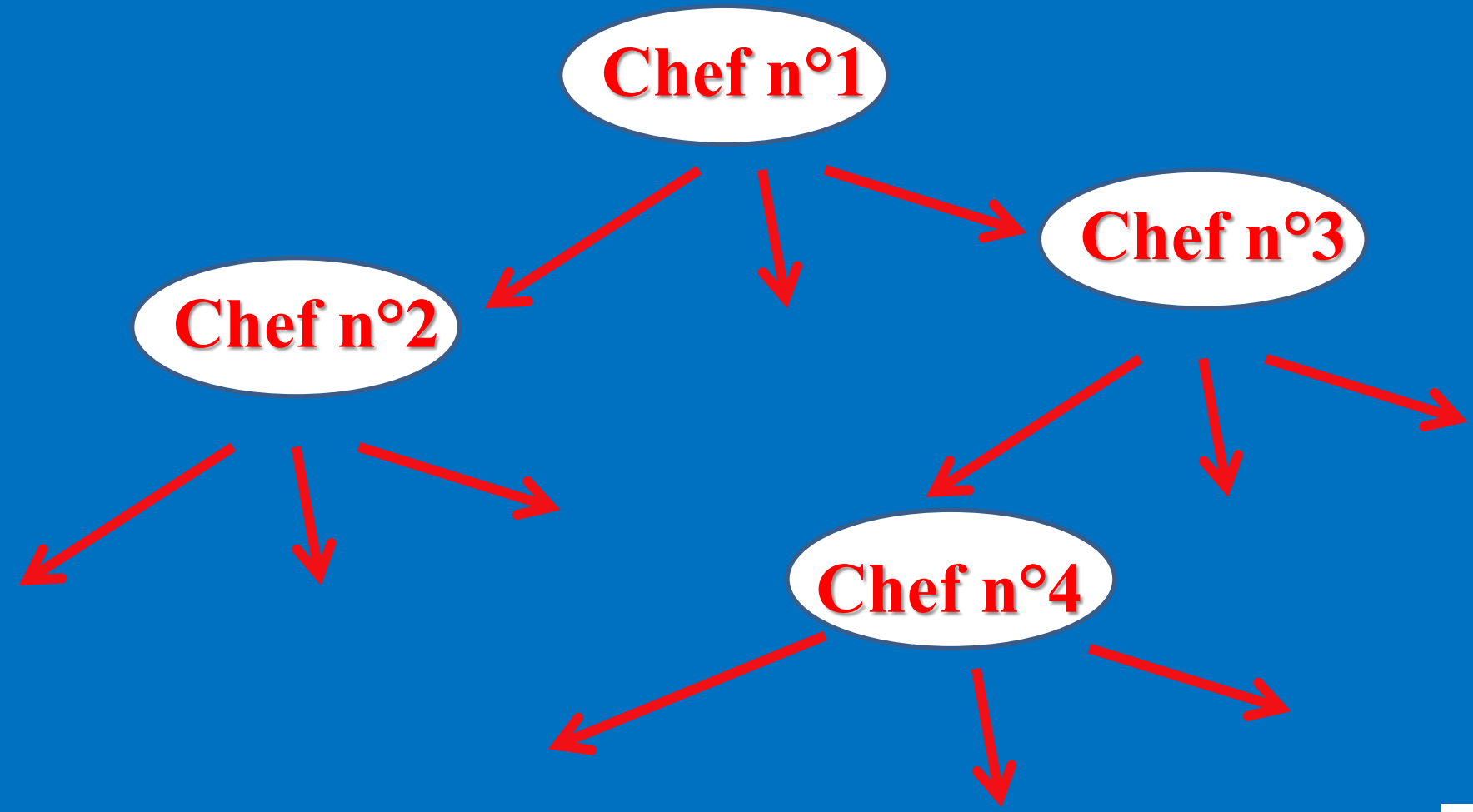
A cookie Chef!

The bakery staff

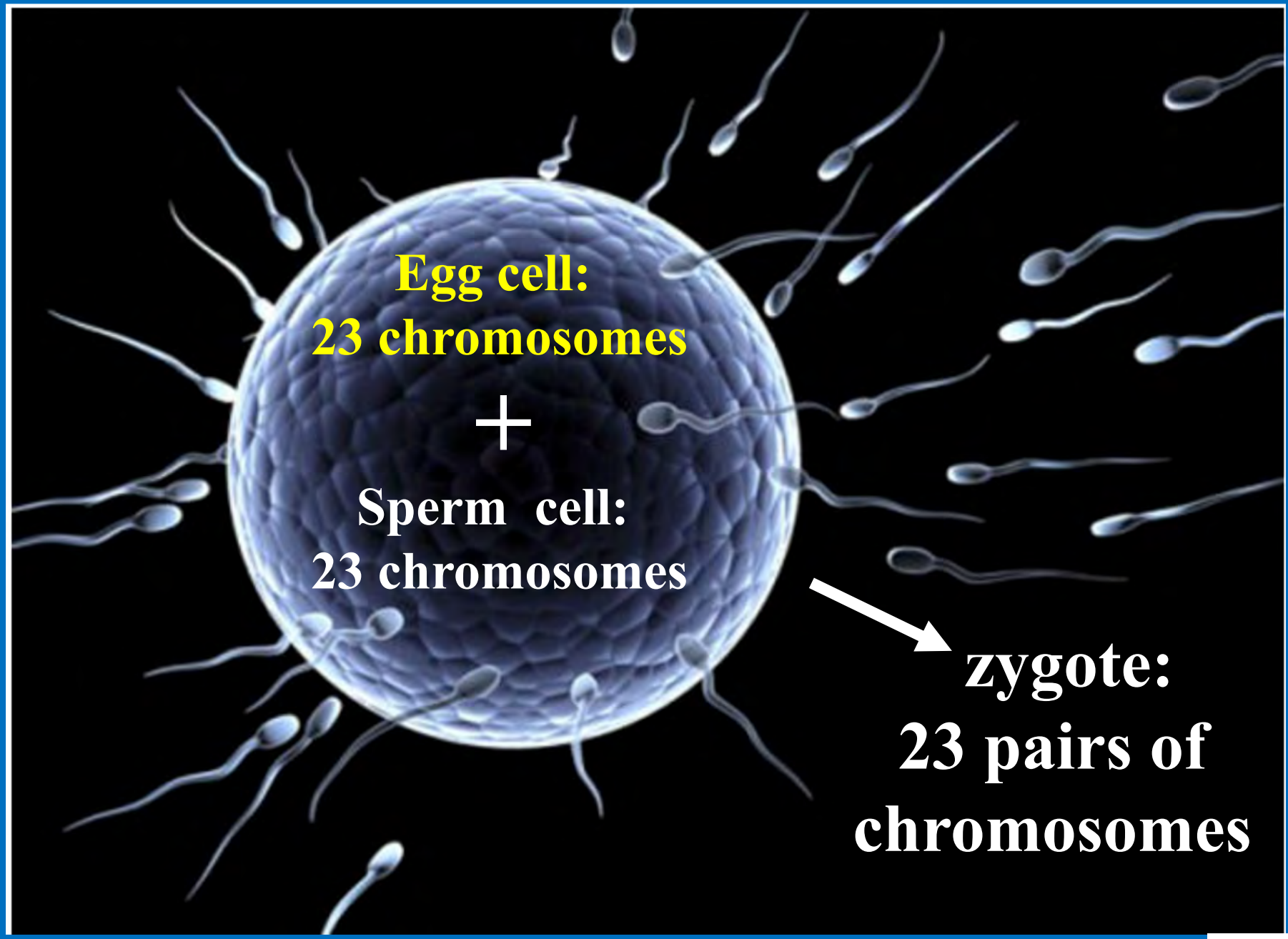
A cookie Chef!

=> decides which cookies get to be baked in the cell i.e. which genes/recipes are to be used

The bakery staff : a cascade of cookie Chefs

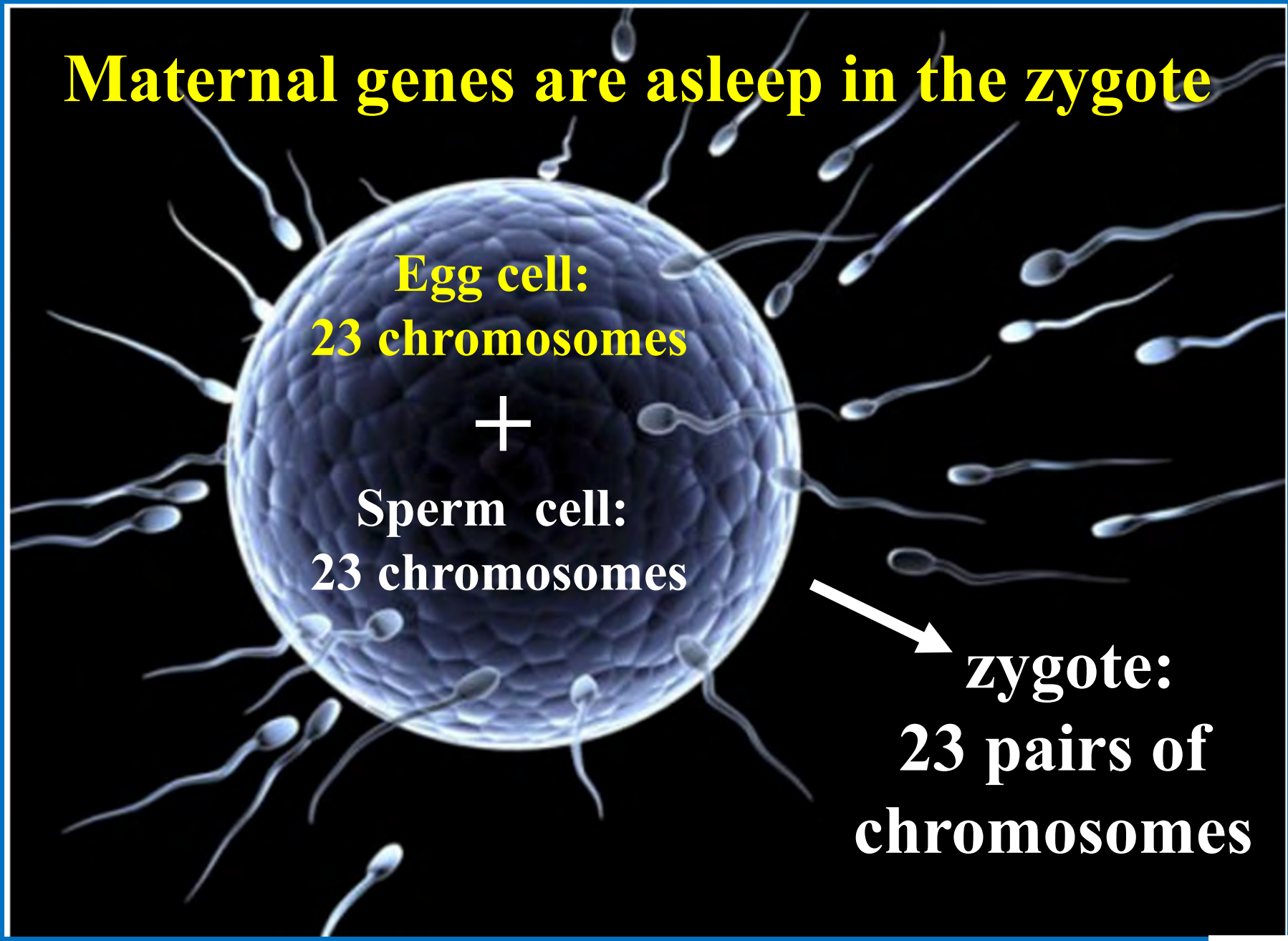


An example of a cookie Chef : Prince Charming!



http://thelinkfwi.wixsite.com/thelink/single-post/2015/10/30/GUADELOUPE-LE-DON-DE-SPERME-ET-DOVULE-DEBARQUE

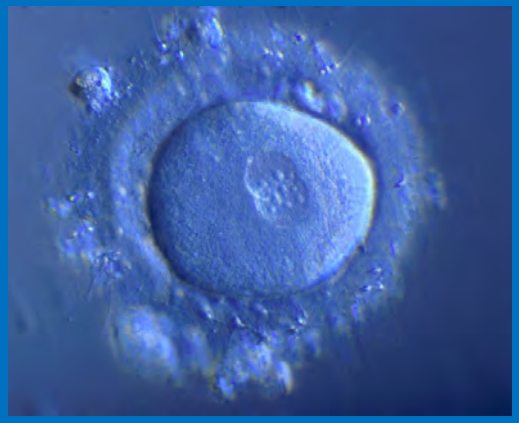
Maternal genes are asleep in the zygote



http://thelinkfwi.wixsite.com/thelink/single-post/2015/10/30/GUADELOUPE-LE-DON-DE-SPERME-ET-DOVULE-DEBARQUE

He wakes up maternal genes in the zygote to start embryo development

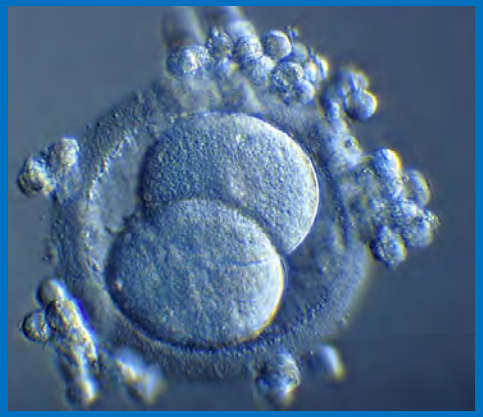
Prince Charming wakes up maternal genes



zygote

1

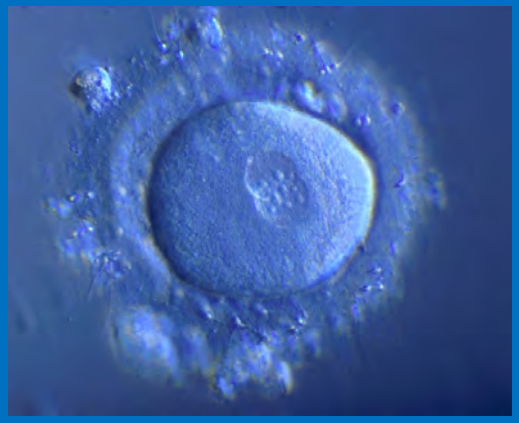
First cell division



2

http://www.gfmer.ch/Livres/FIV_atlas/FIV_ICSI.htm

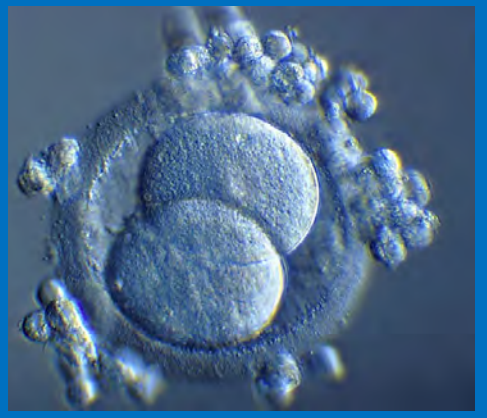
Prince Charming is DUX4: the embryo Chef



zygote

1

First cell division



2

4

8

http://www.gfmer.ch/Livres/FIV_atlas/FIV_ICSI.htm

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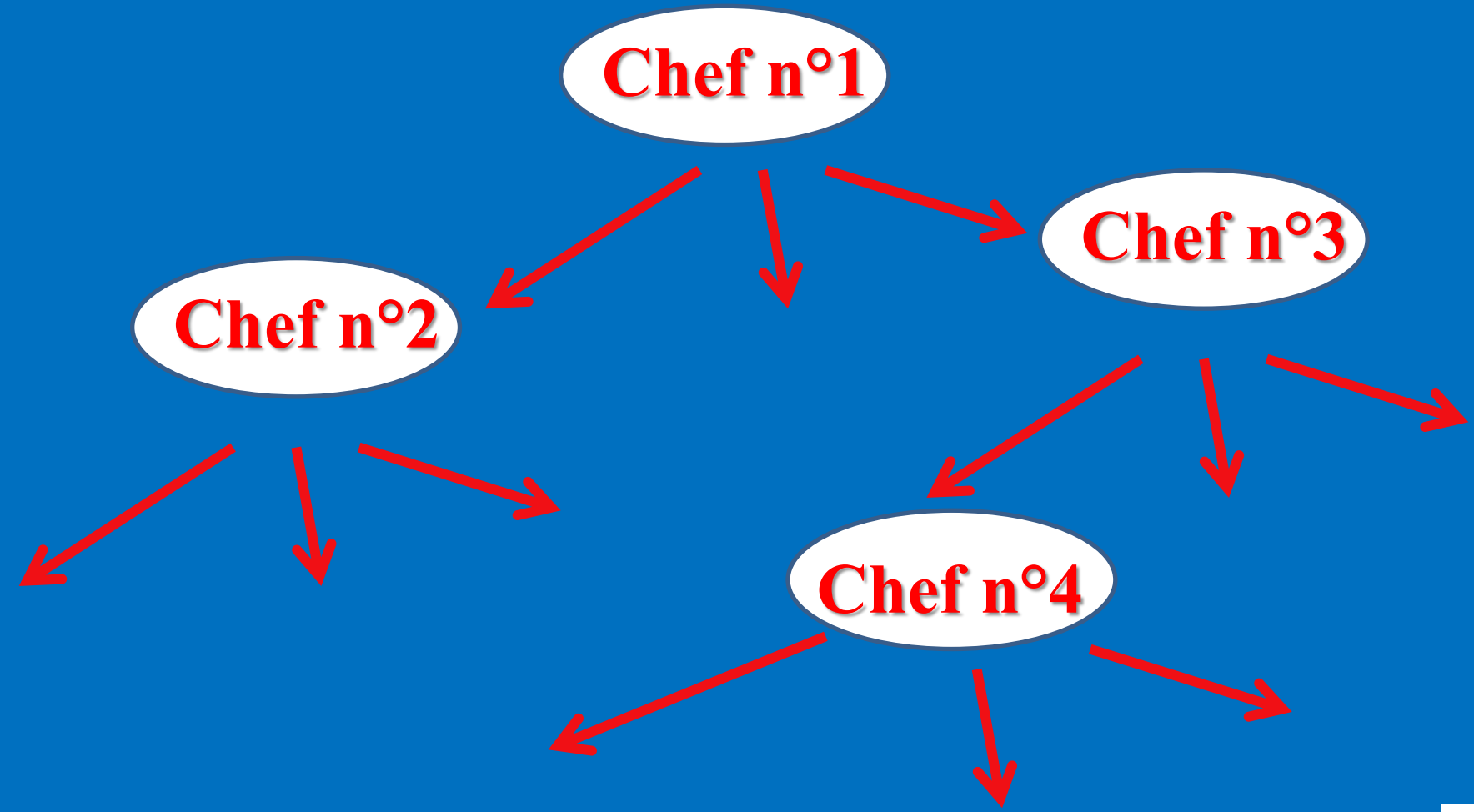
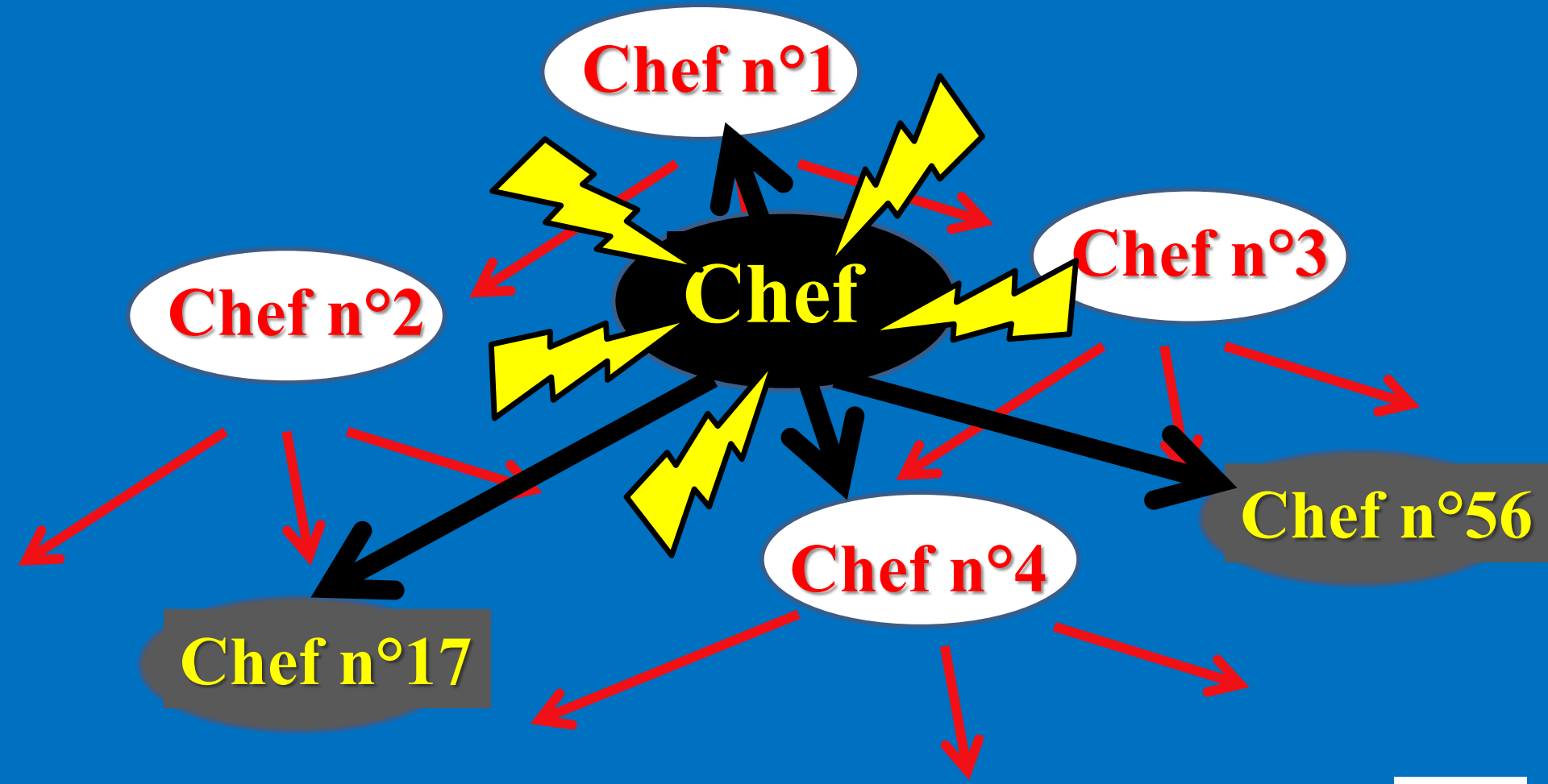
The bakery staff in the muscle



Chaos in the muscle!

Arrival of the embryo Chef



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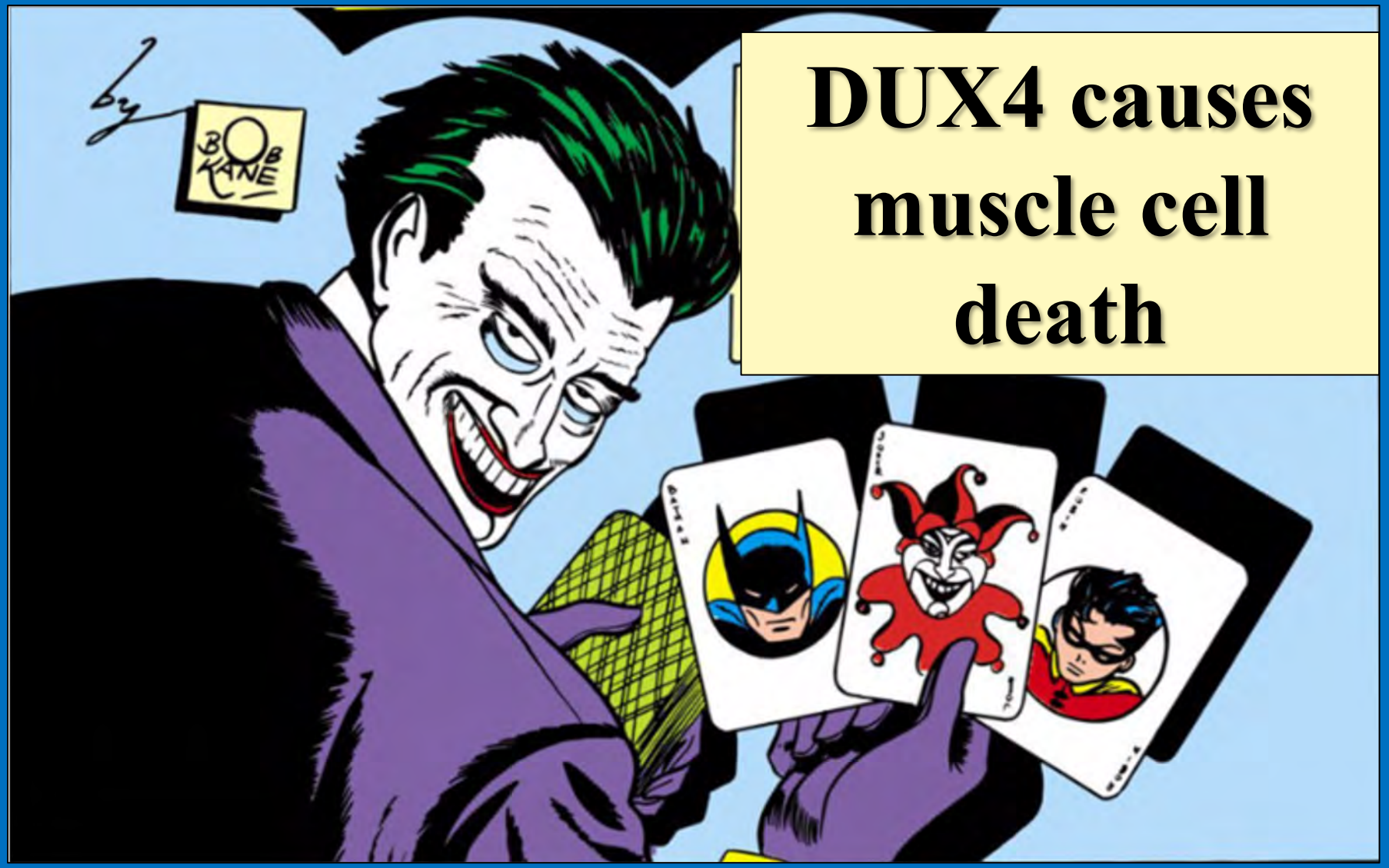
DUX4:
Prince Charming
turned into

UMONS

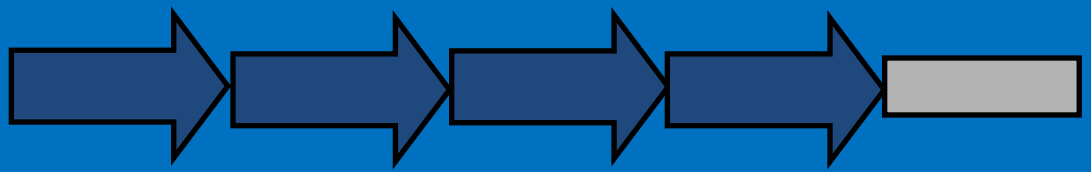


https://modernmythologies.wordpress.com/2015/03/14/retro-review-batman-1-1940-the-joker-the-joker-returns/

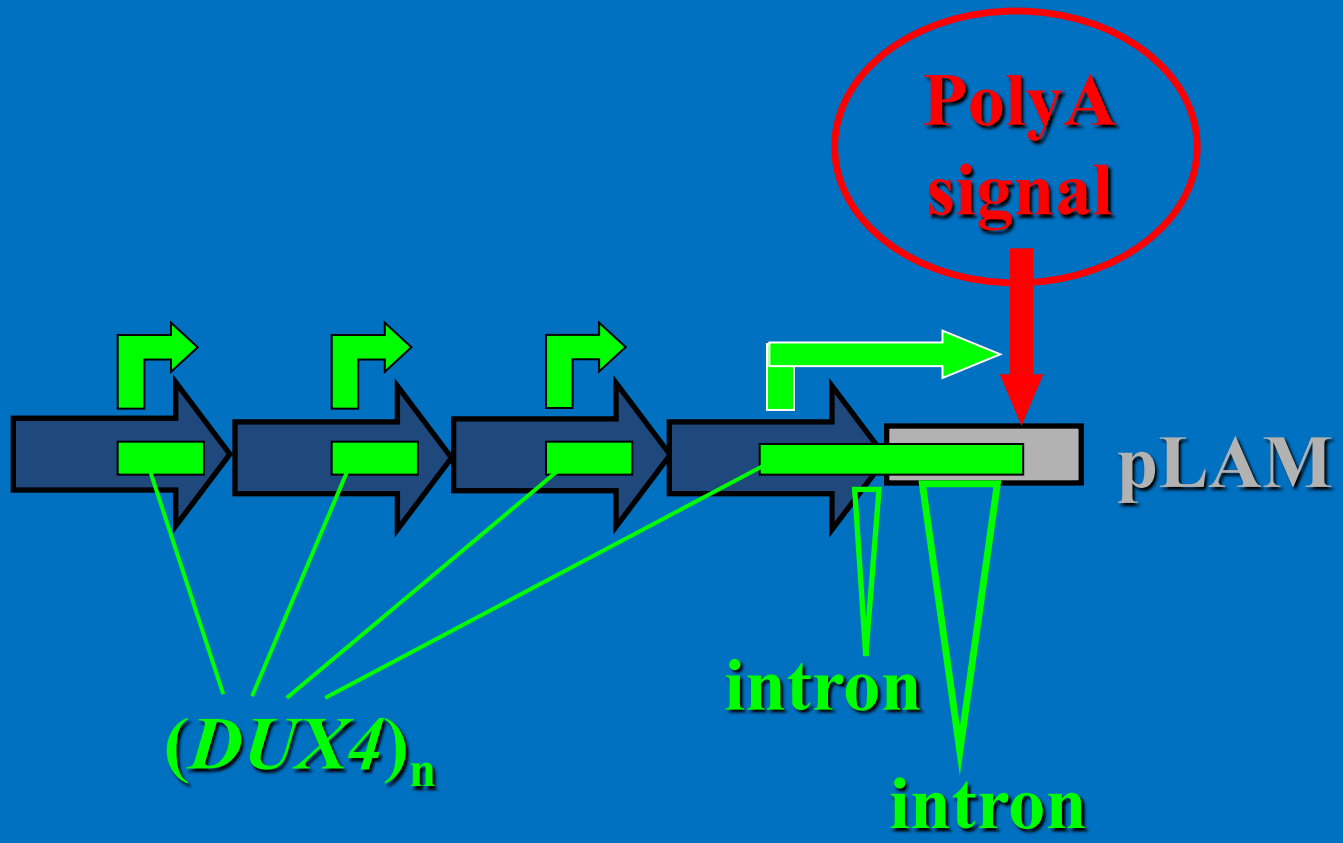
When can a muscle cell express DUX4/Joker?

1. Genetic condition: a full *DUX4* gene

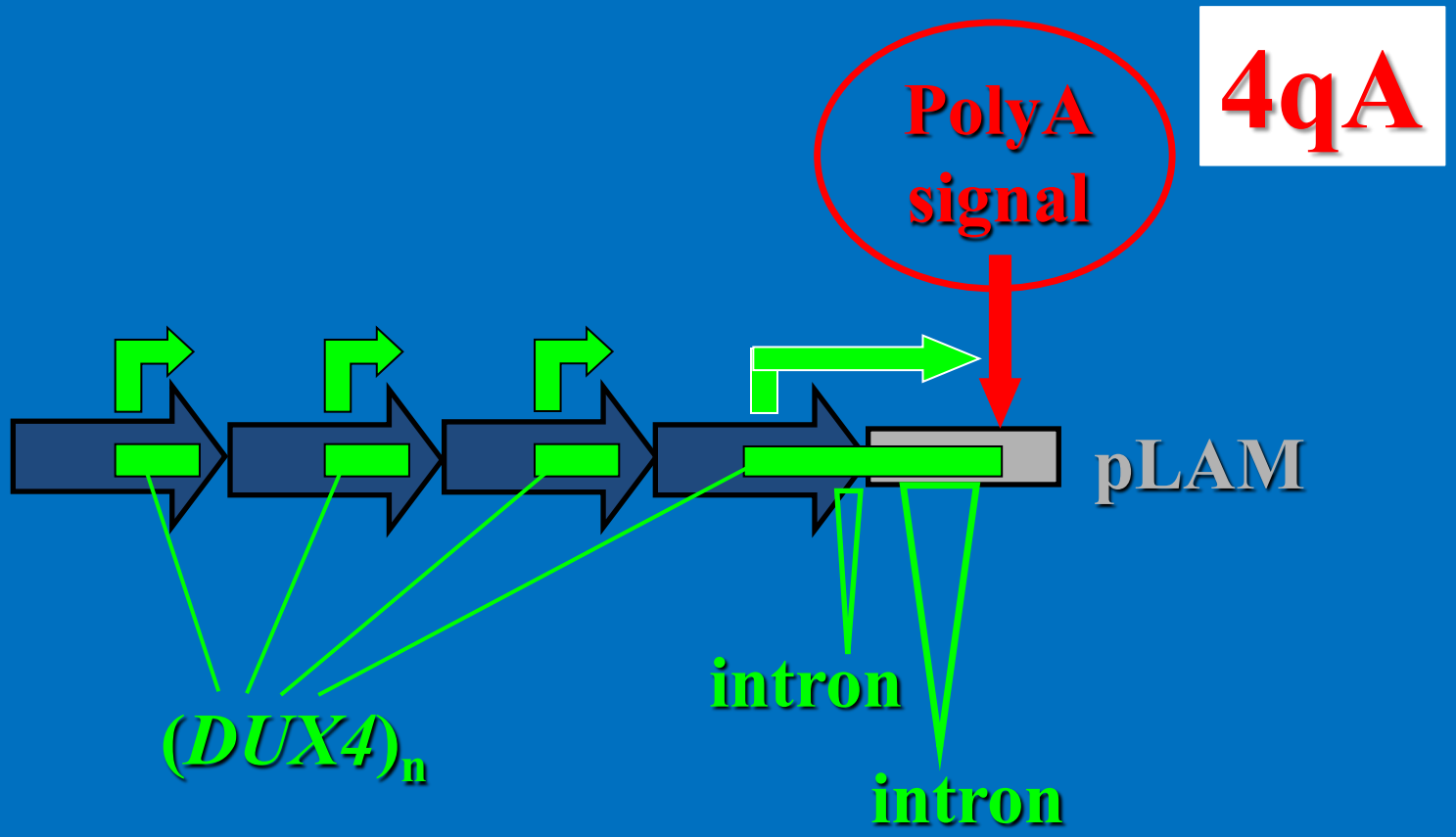
The D4Z4 repeated elements on chromosome 4



Only the last DUX4 gene has an end!



Only the last DUX4 gene has an end!



When can a muscle cell express DUX4/Joker?

1. Genetic condition:
   a full *DUX4* gene (4qA)
2. Epigenetic condition:
   an open chromatin

Epigenetic modification:
+ methyl group on DNA

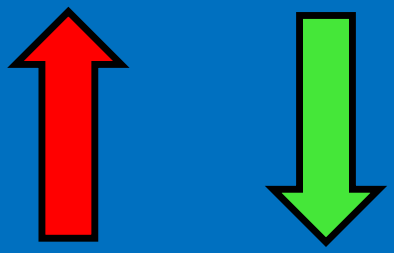
DNA hyper-methylation

=> gene "OFF"

DNA hypo-methylation => gene "ON"

DNA hyper-methylation

ATCTTCAGTCTGGCA => gene "OFF"



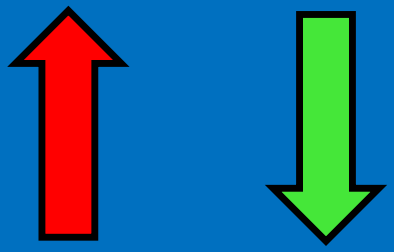
ATCTTCAGTCTGGCA

DNA hypo-methylation => gene "ON"

DNA hyper-methylation

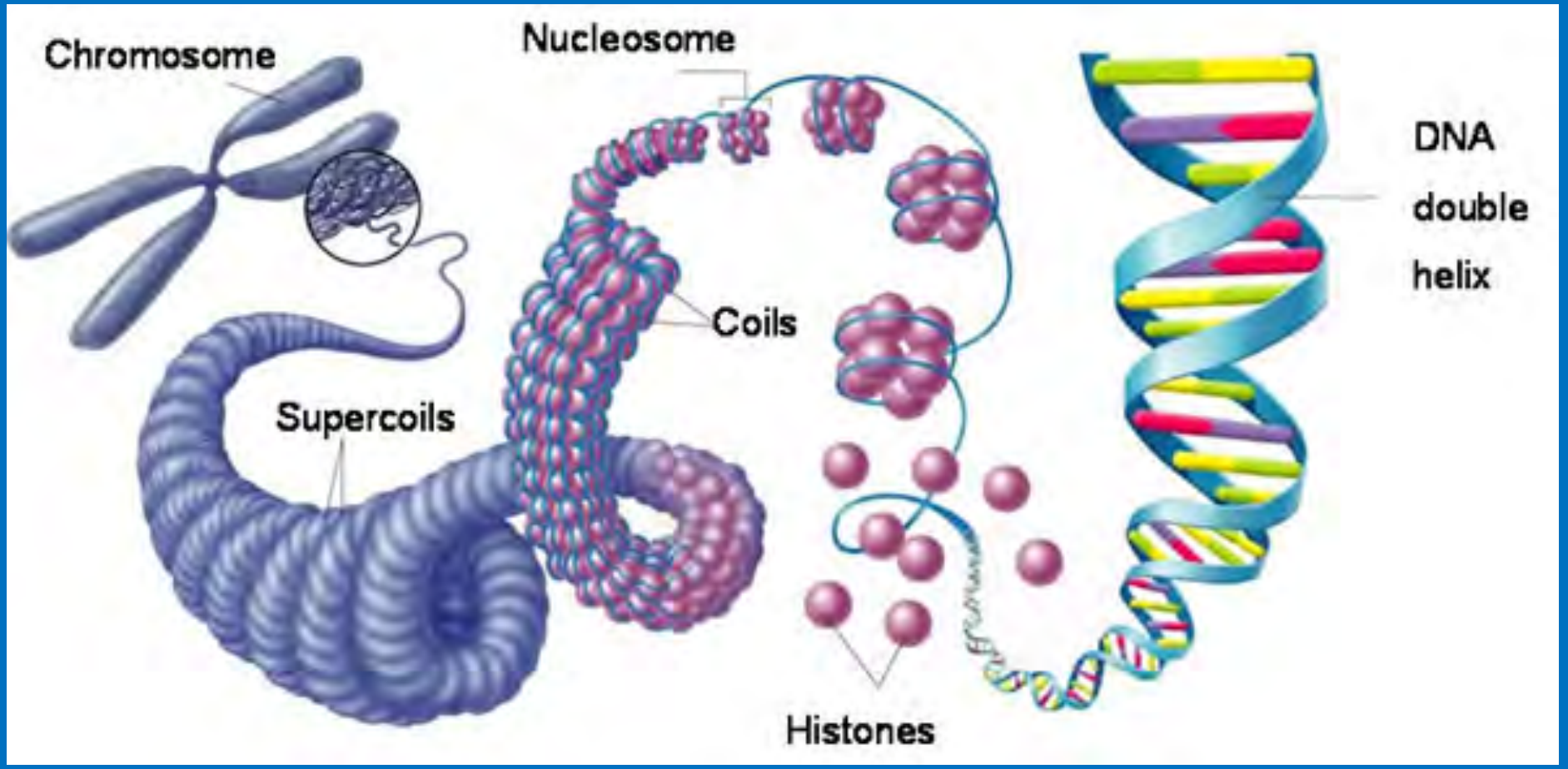
=> gene "OFF"

SMCHD1



DNA hypo-methylation => gene "ON"

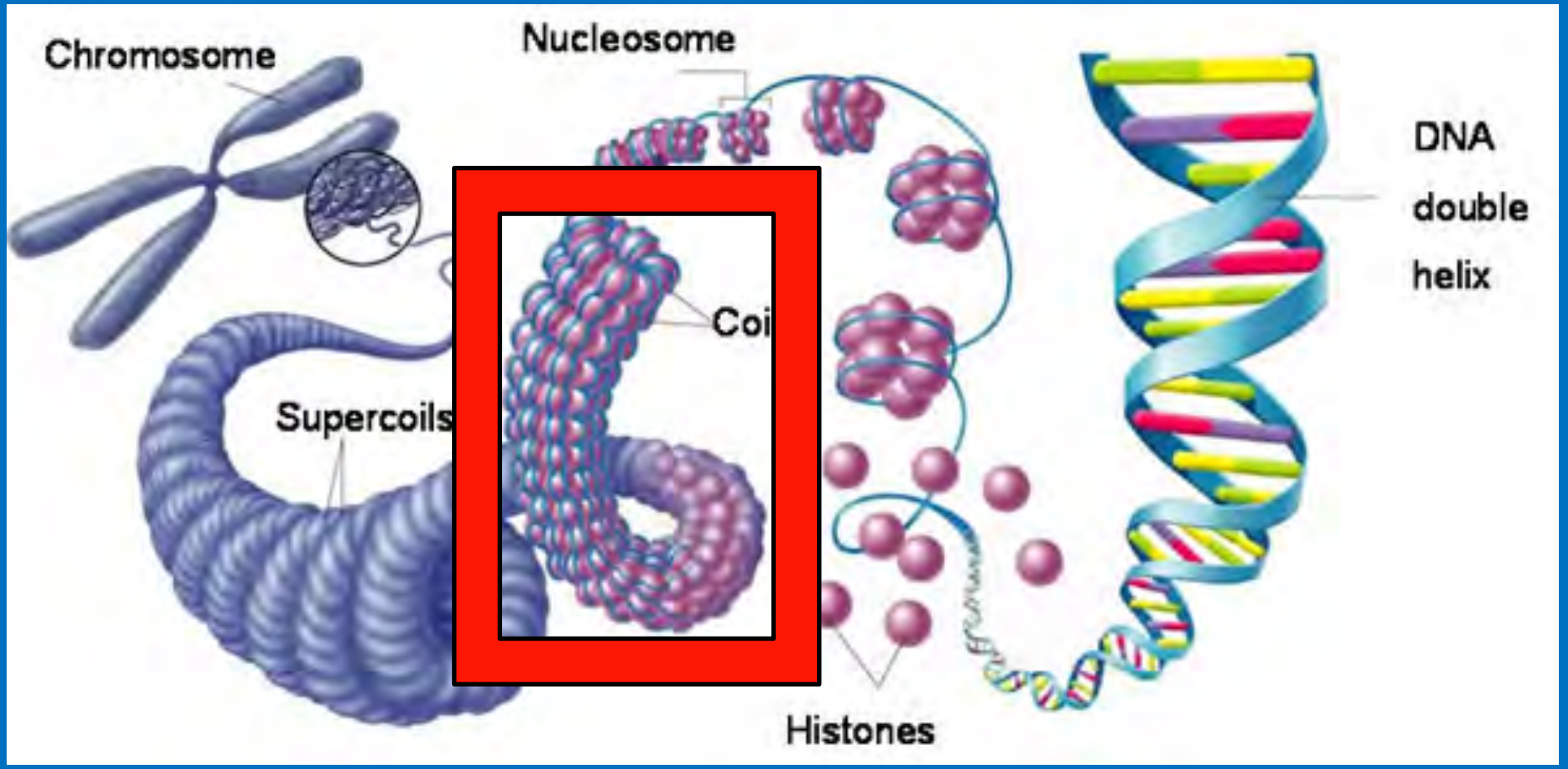
DNA is packed up with proteins = chromatin



http://www.goldiesroom.org/Multimedia/Bio_Images/14%20Mitosis%20and%20Asexual/00%20Eukaryotic%20Chromosomes.jpg

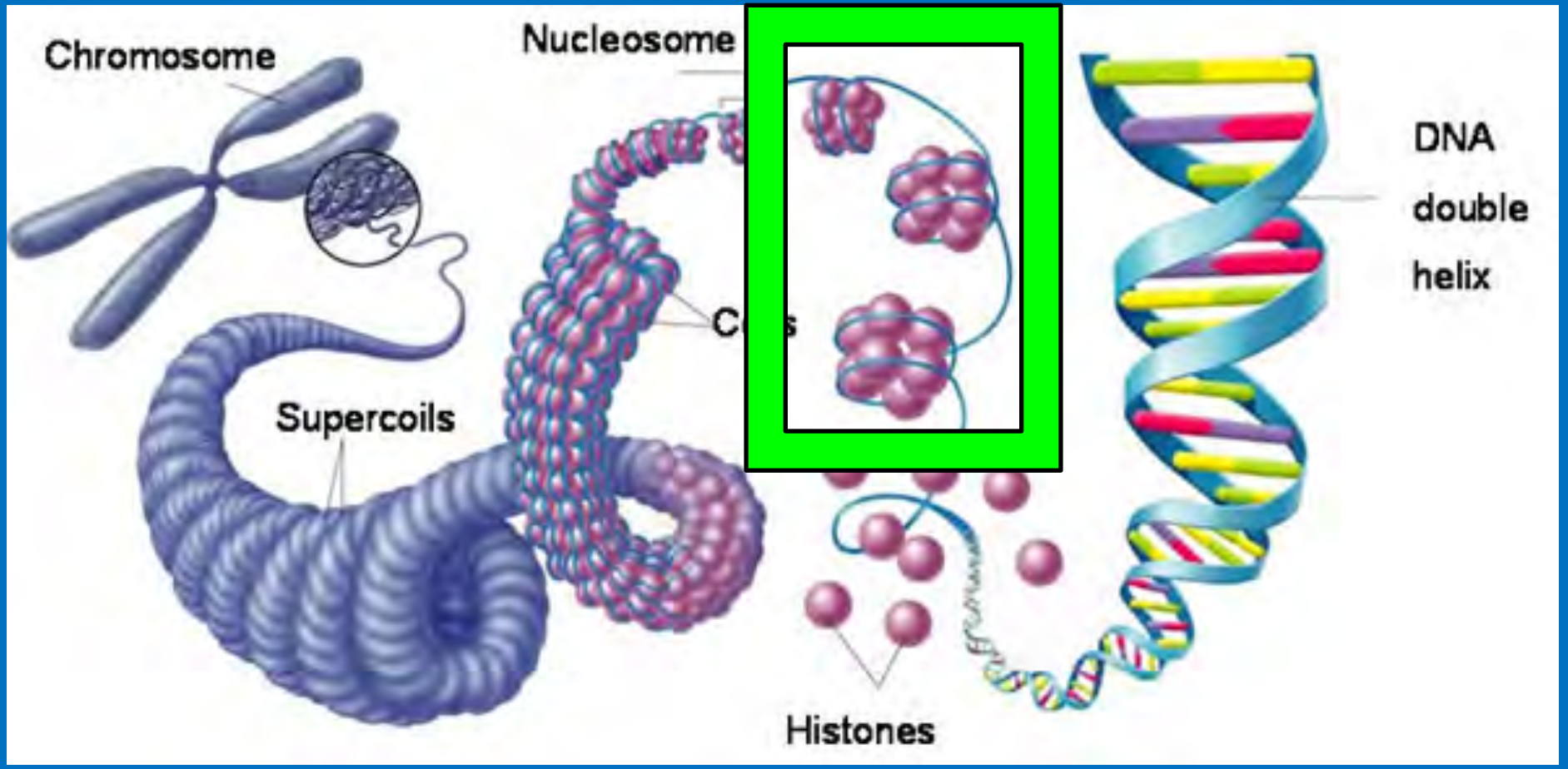
If chromatin is closed => *DUX4* gene "OFF"

(hypermethylated DNA)



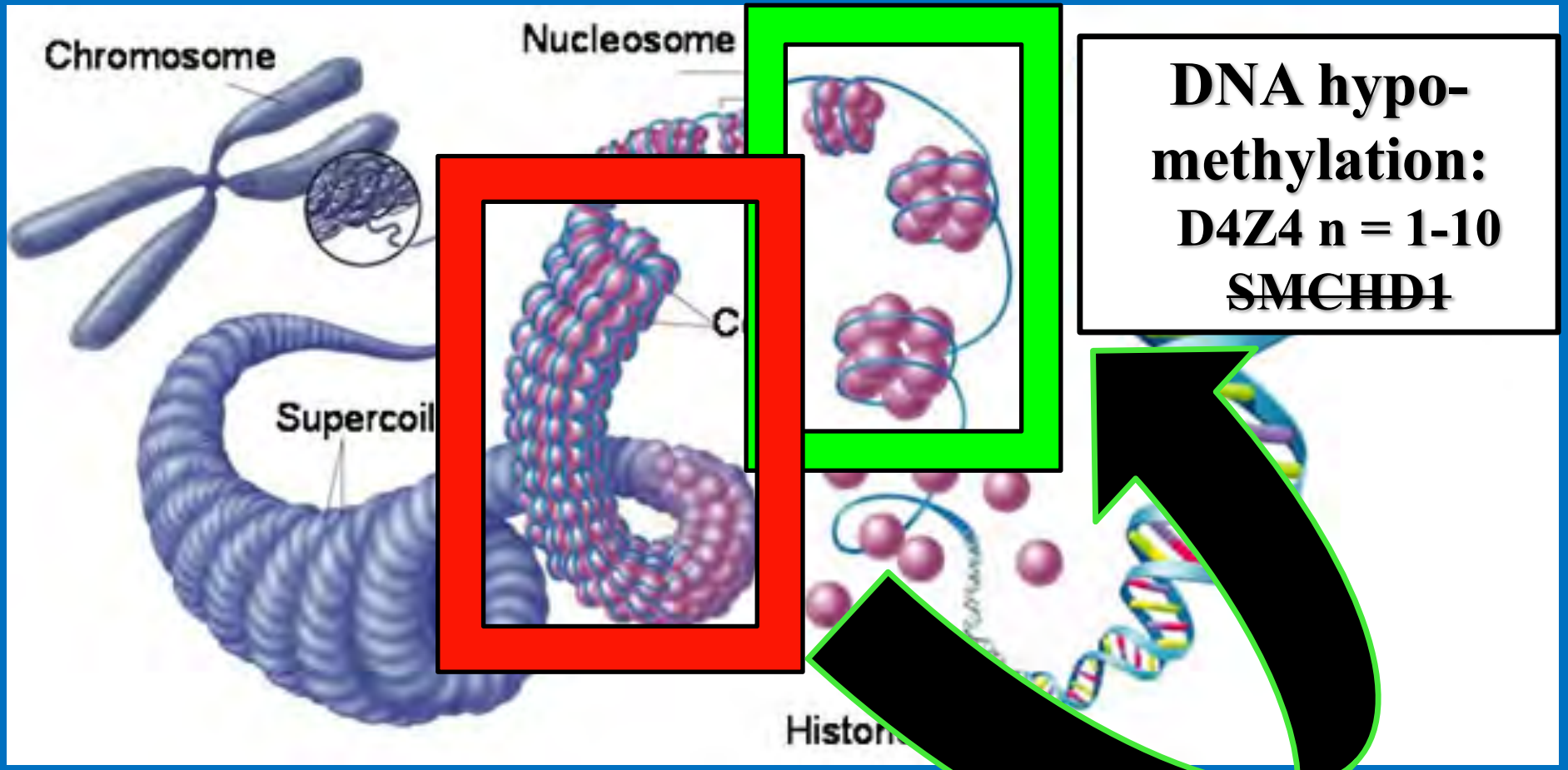
http://www.goldiesroom.org/Multimedia/Bio_Images/14%20Mitosis%20and%20Asexual/00%20Eukaryotic%20Chromosomes.jpg

If chromatin is open => *DUX4* gene "ON"
(hypomethylated DNA)



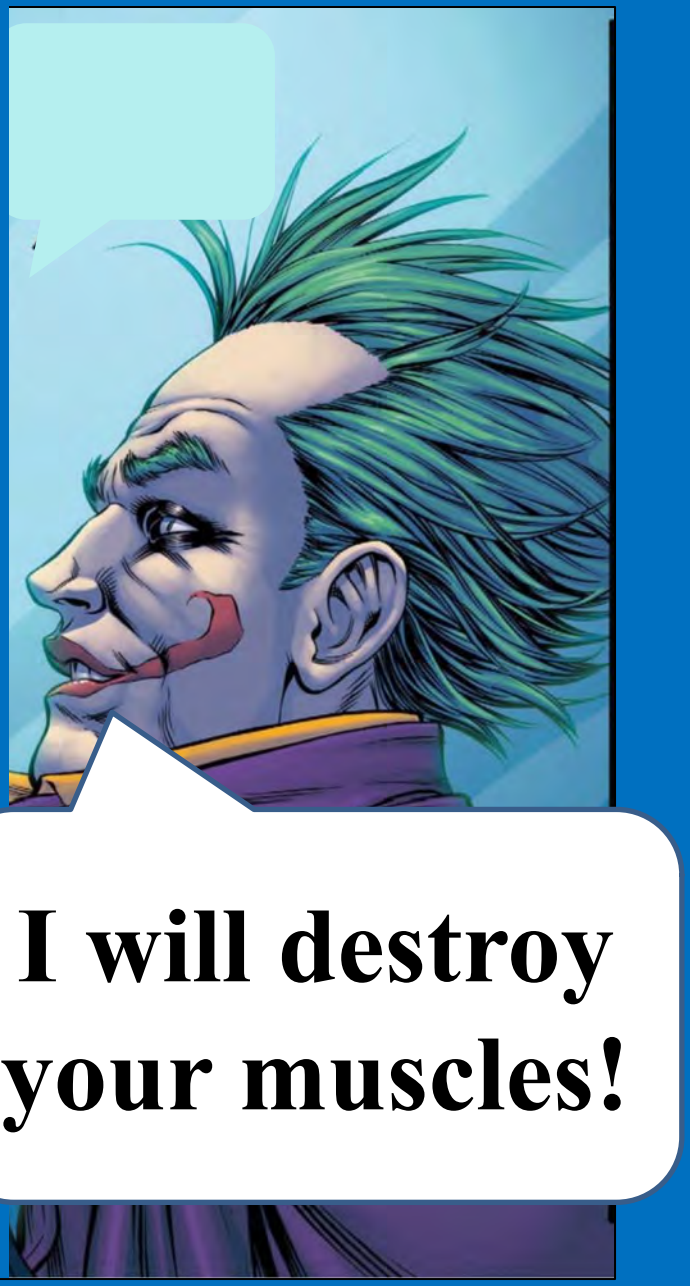
http://www.goldiesroom.org/Multimedia/Bio_Images/14%20Mitosis%20and%20Asexual/00%20Eukaryotic%20Chromosomes.jpg

Chromatin switch from close to open: => *DUX4* gene "ON"

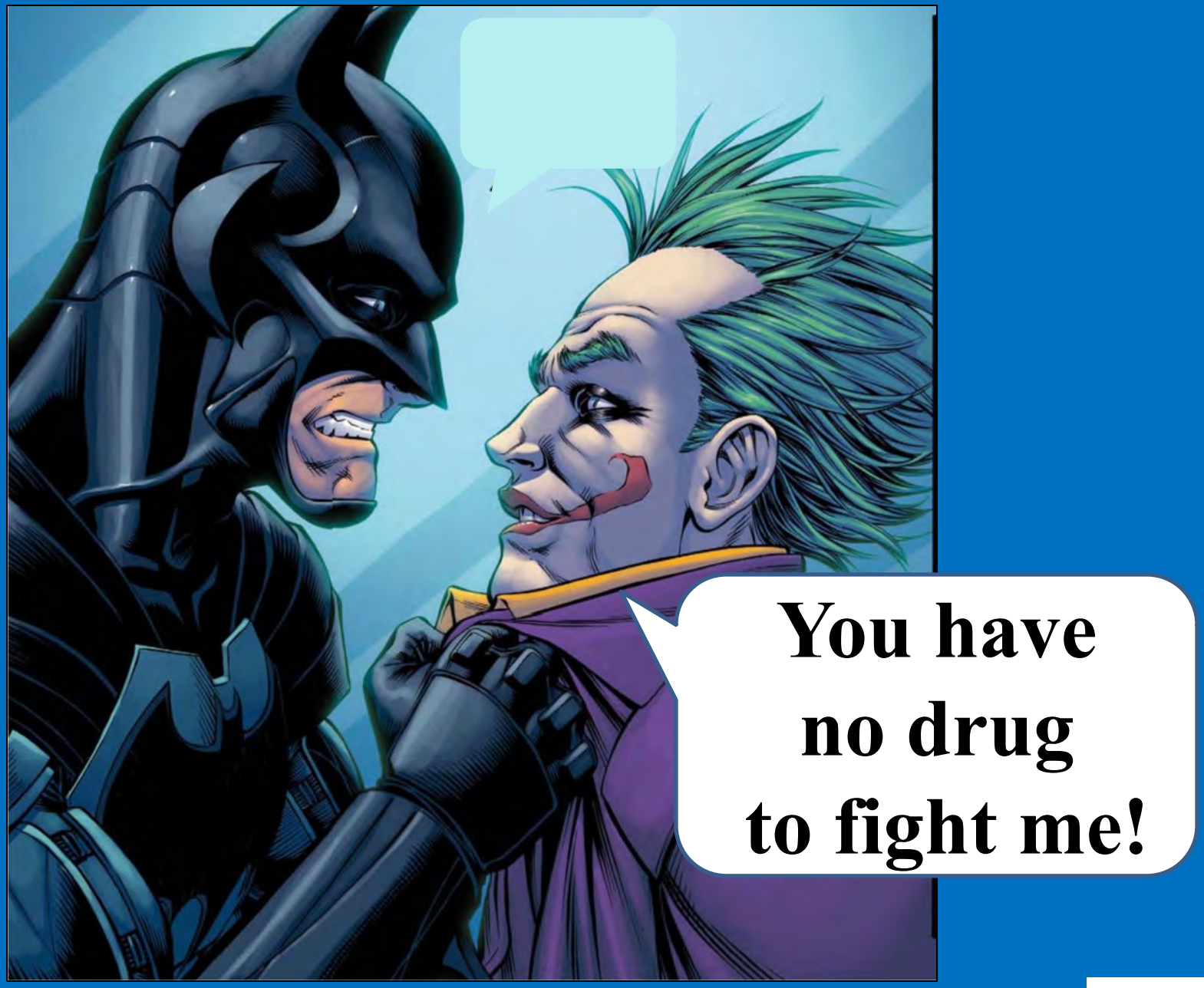


http://www.goldiesroom.org/Multimedia/Bio_Images/14%20Mitosis%20and%20Asexu osomes.jpg

Genetic + epigenetic conditions => DUX4 /Joker is expressed



https://comicnewbies.com/2013/06/15/batman-interrogates-the-joker/



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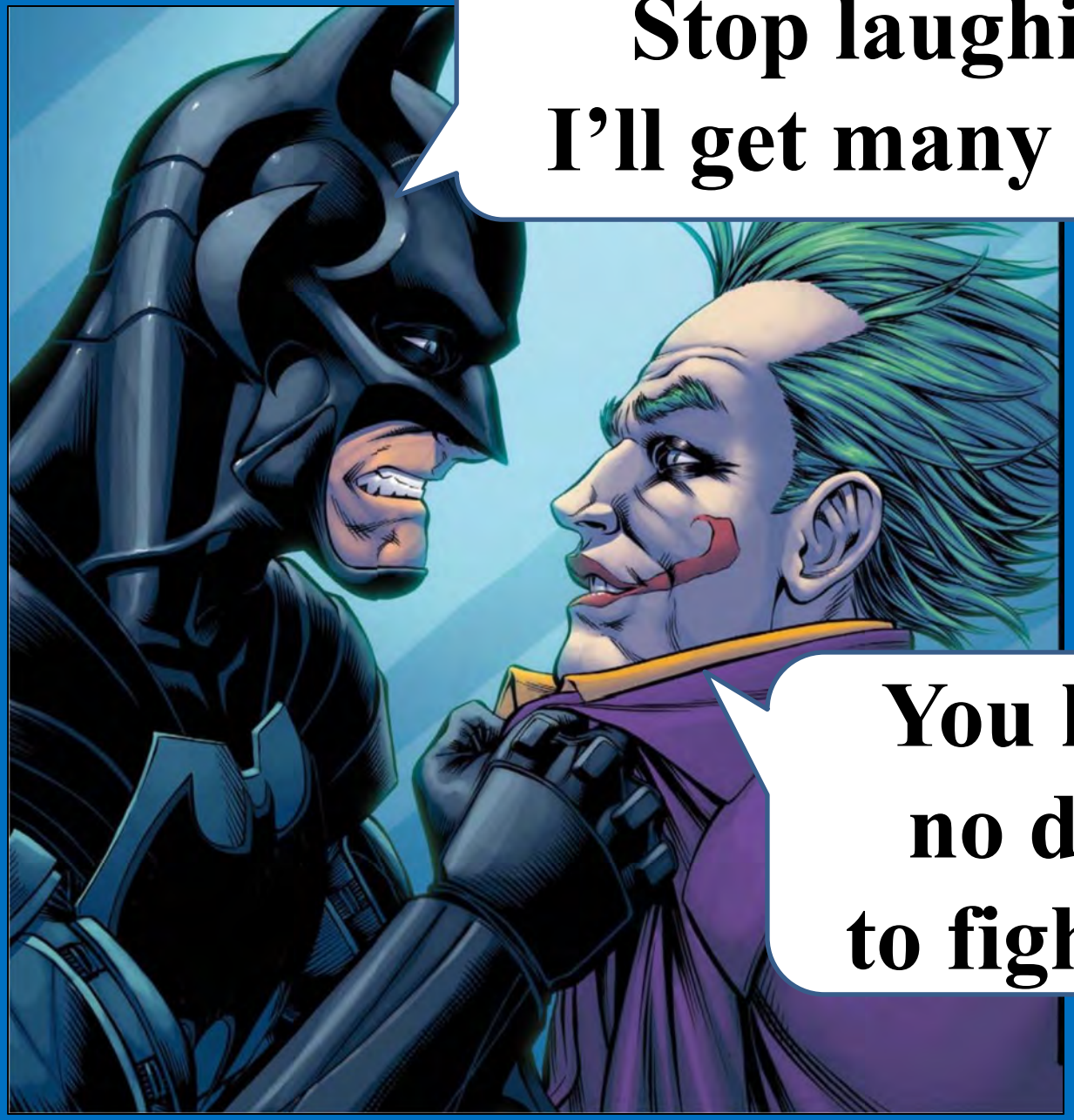

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