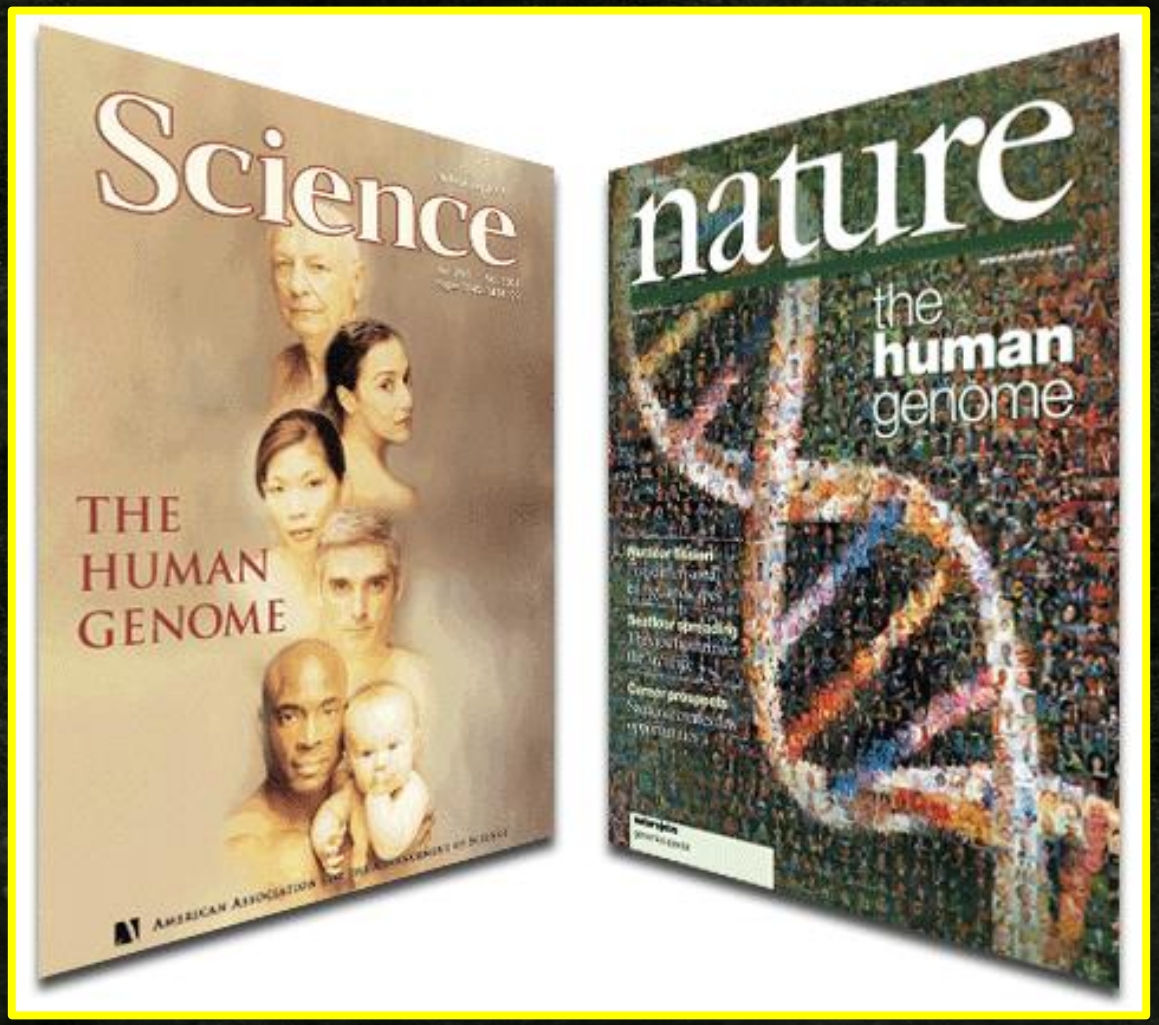
EPIGENETICS -

above Genetics

Milena Georgieva

THE HUMAN GENOME PROJECT



http://www.sciencemag.org/
http://www.nature.com/

THE HUMAN GENOME PROJECT

achievements

3.1 billion letters (A, T, C, G)

20 000 – 25 000 genes

(*roundworms have 19 000!!!!*)

2% of our genome is active

WHAT TELLS OUR GENOME

which genes to work?

how?

when?

Public resource for genes finding

Database of human genes (~ 20 000)

Database for 10 464 "**disease genes**“

GENOME COMPARATIVE ANALYSES

genetic difference between humans and chimpanzees is only

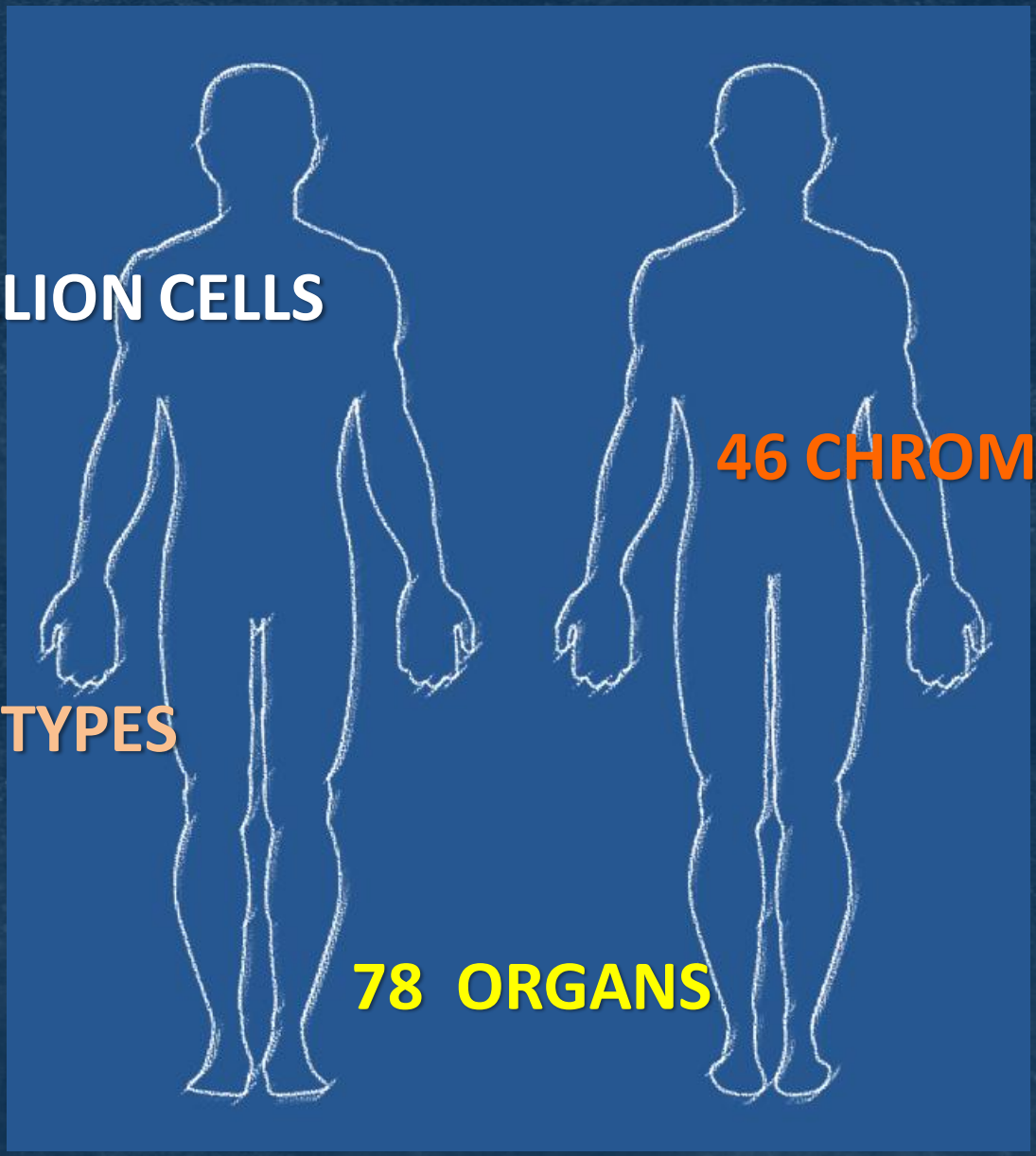
1.5 %

Georgieva M., 2013

THE MYSTERY OF IDENTICAL TWINS

Georgieva M., 2014

THE HUMAN BODY



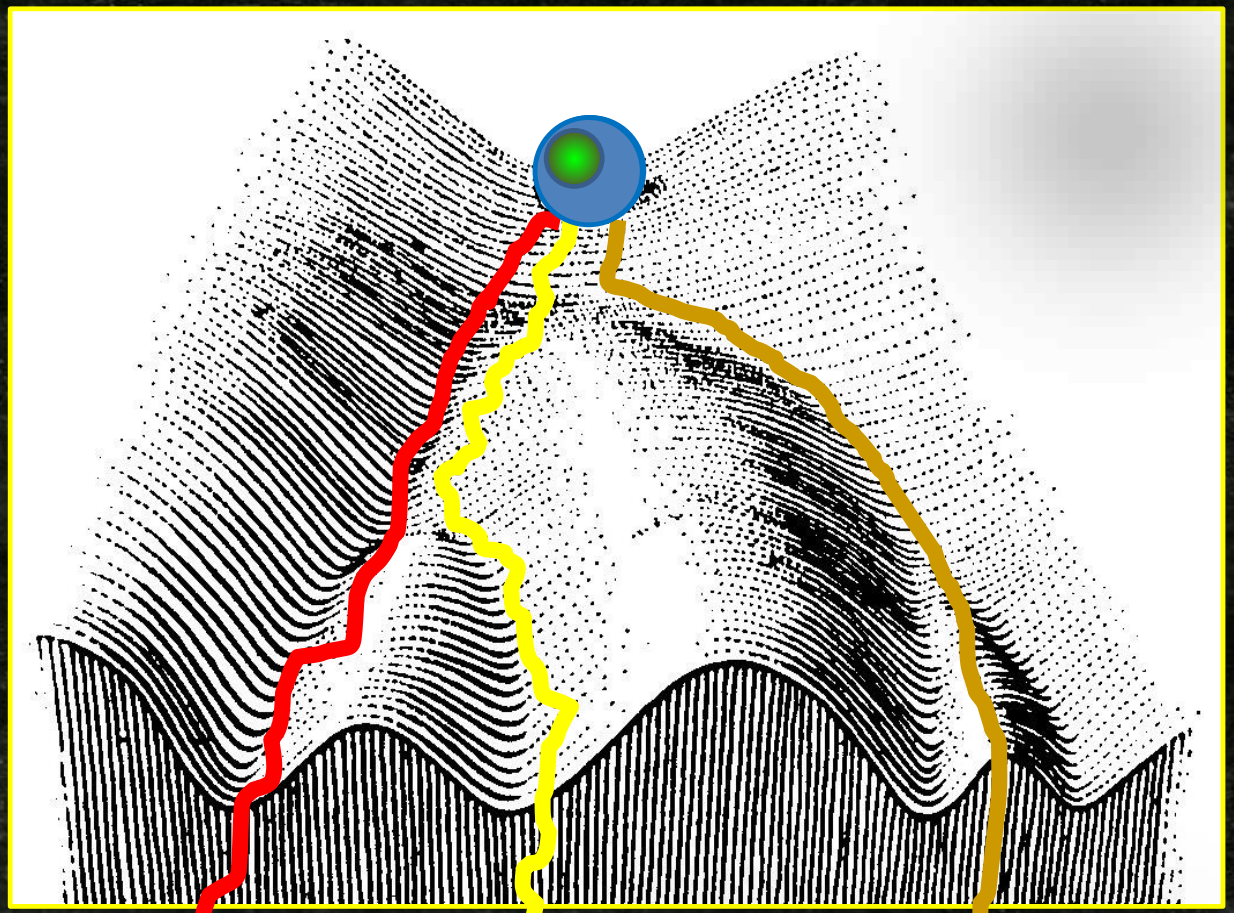
100 TRILLION CELLS

46 CHROMOSOMES

200 CELL TYPES

78 ORGANS

THE MANY FATES OF A CELL



Lung cell

Brain cell

Skin cell

Adapted from Waddington, 1953; animation Georgieva, M. (2013)

EPIGENETICS

EPIGENETICS means "*above the genetics*"

It provides information beyond DNA sequence.

Practically,

It tells identical genomes to express differently.

Image by National Geographic

THE MYSTERY OF IDENTICAL TWINS UNRAVELED

Similar epigenomes

Different epigenomes

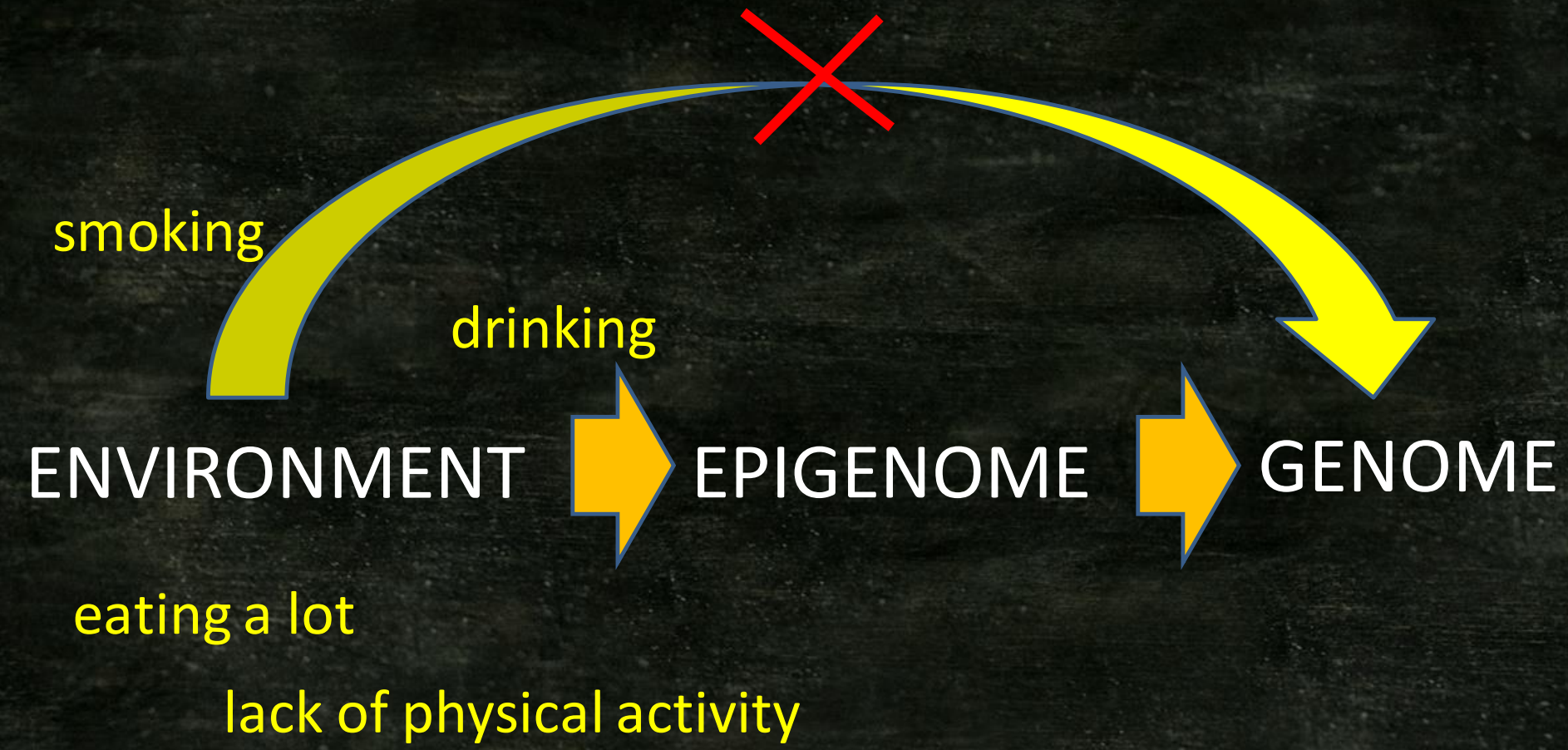
Identical genomes

Identical genomes

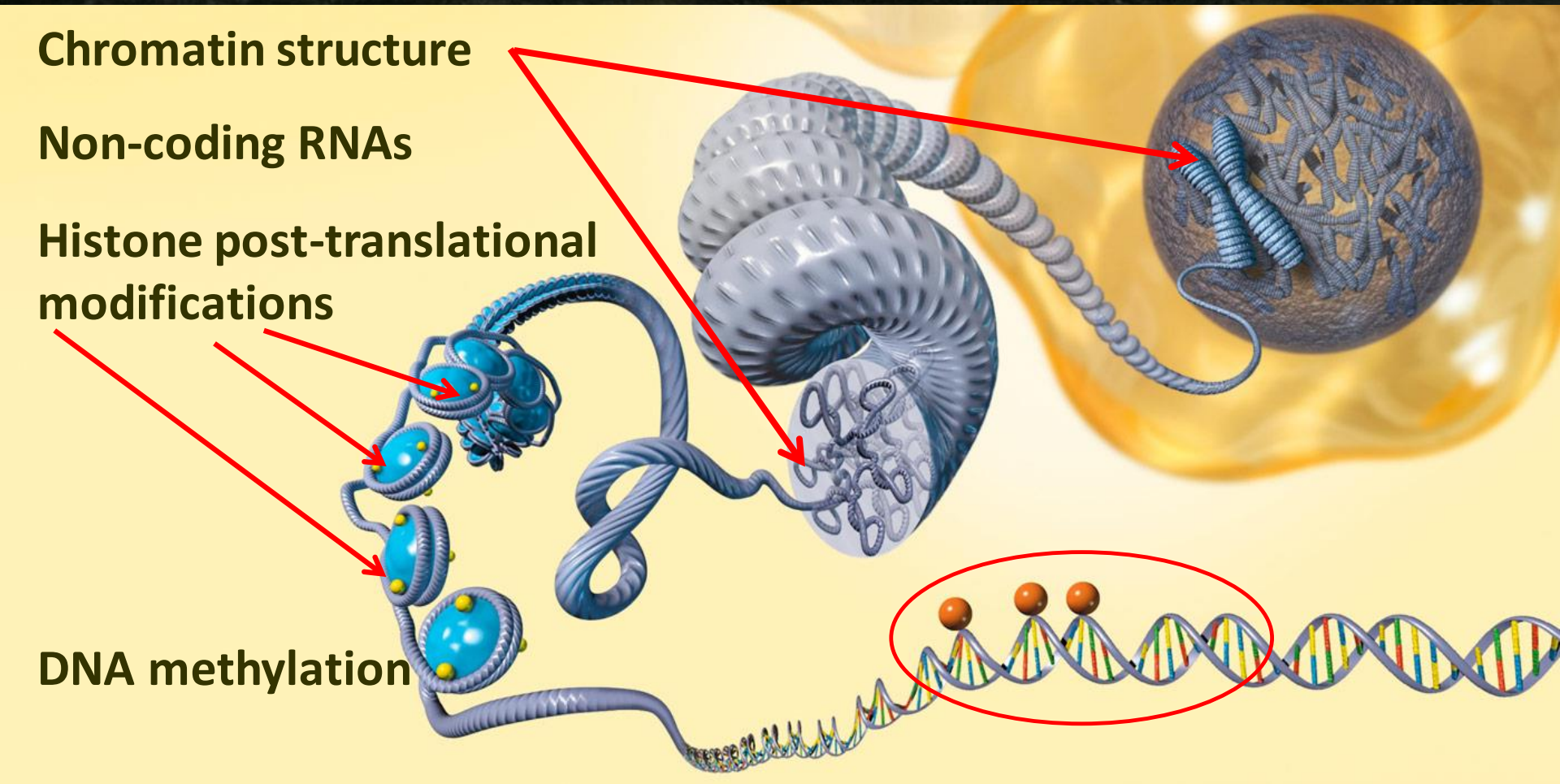
Age 5

Age 55

EPIGENETICS IN ACTION

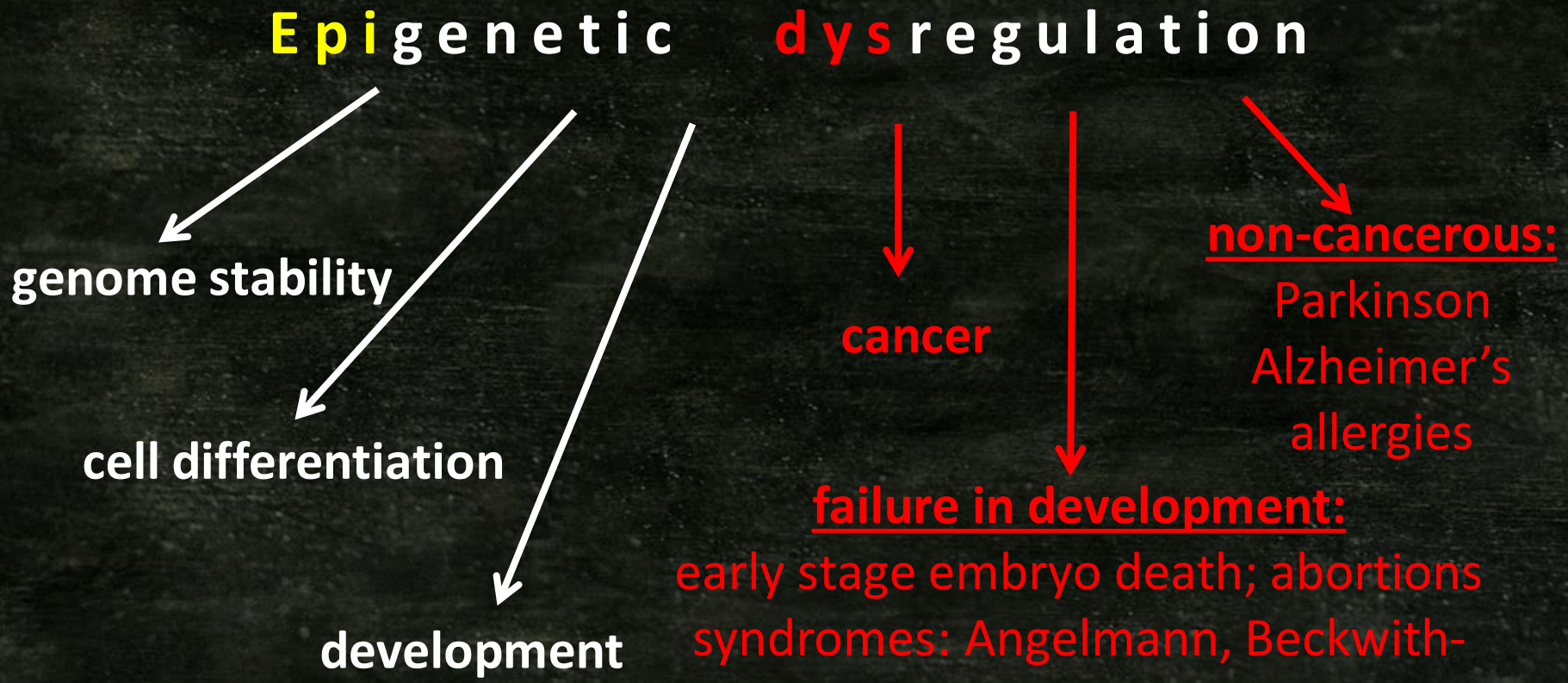


MECHANISMS OF EPIGENETICS

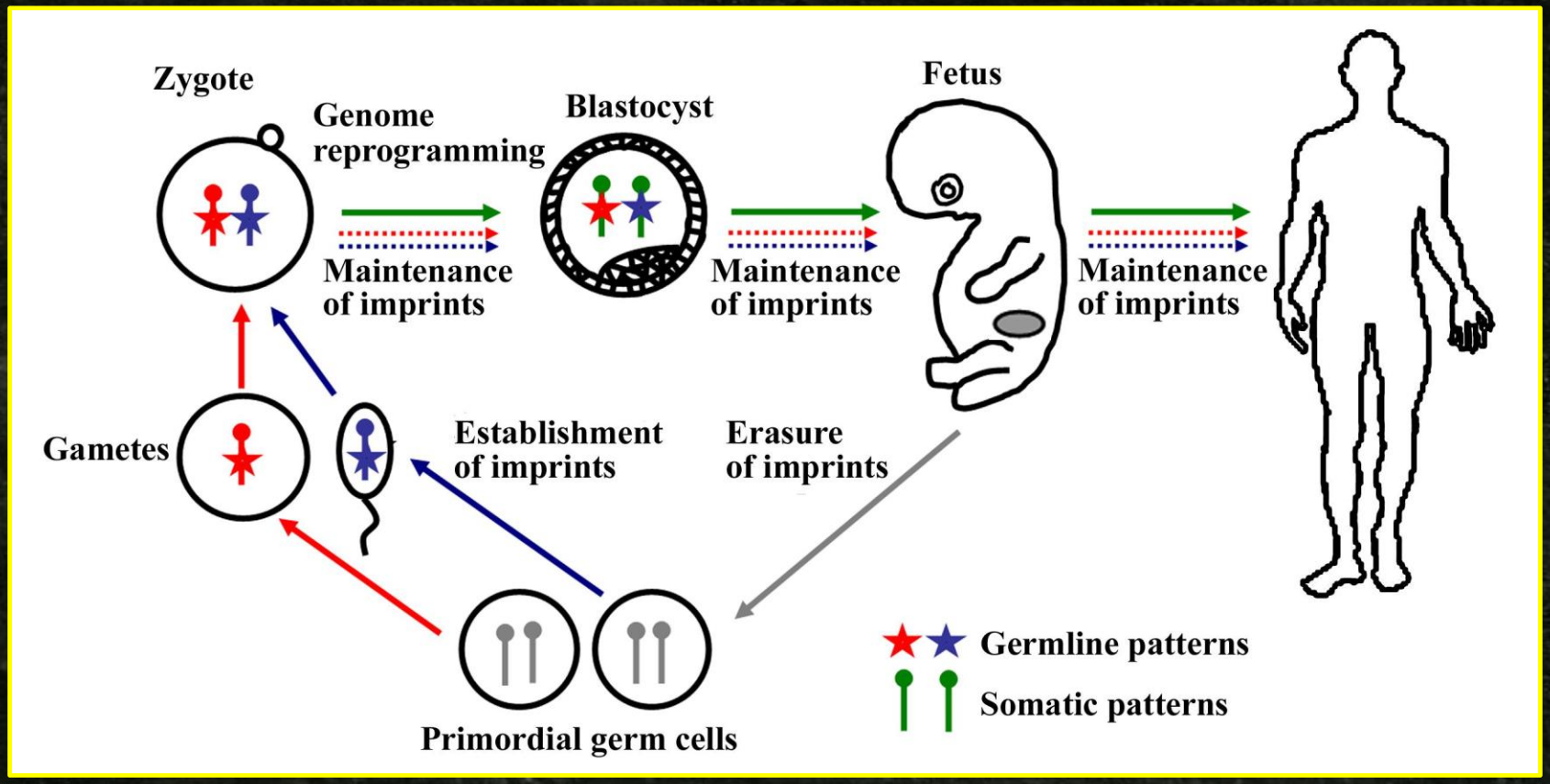


https://www.celgene.com

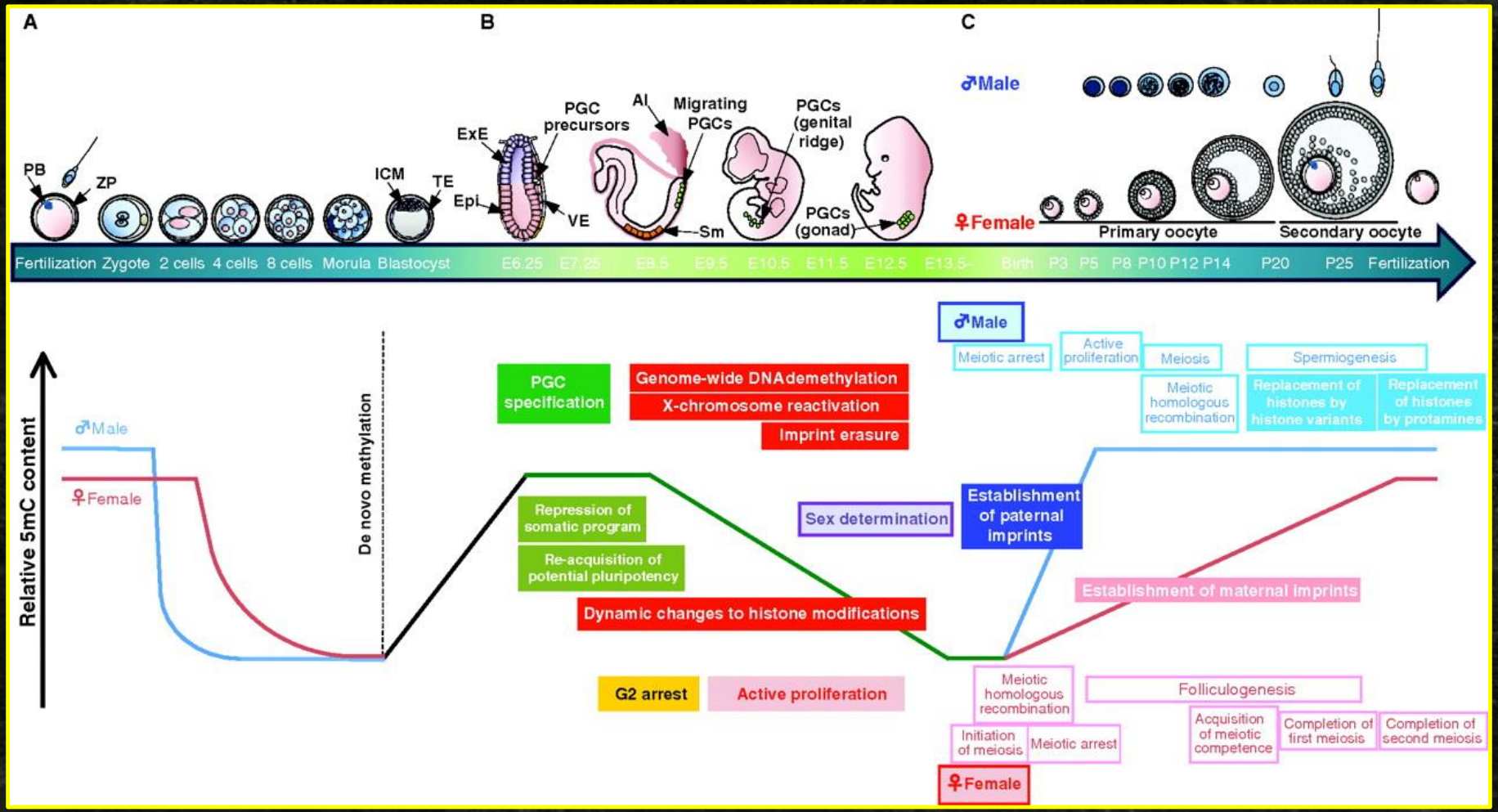
CENTRAL ROLE OF EPIGENETICS IN BIOLOGY AND MEDICINE



EPIGENETIC GENOME REPROGRAMMING



http://www.humgen.biozentrum.uni-wuerzburg.de



Saitou M et al. Development 2012;139:15-31

LIST OF EPIGENETIC DISEASES

Disease	Symptom	Aetiology
ATR-X syndrome	Intellectual disabilities, α-thalassaemia	Mutations in *ATRX* gene, hypomethylation of certain repeat and satellite sequences
Fragile X syndrome	Chromosome instability, intellectual disabilities	Expansion and methylation of CGG repeat in *FMR1* 5′ UTR, promoter methylation
ICF syndrome	Chromosome instability, immunodeficiency	*DNMT3b* mutations, DNA hypomethylation
Angelman's syndrome	Intellectual disabilities	Deregulation of one or more imprinted genes at 15q11–13 (maternal)
Prader–Willi syndrome	Obesity, intellectual disabilities	Deregulation of one or more imprinted genes at 15q11–13 (paternal)
BWS	Organ overgrowth	Deregulation of one or more imprinted genes at 11p15.5 (e.g. *IGF2*)
Rett syndrome	Intellectual disabilities	*MeCP2* mutations
α-Thalassaemia (one case)	Anaemia	Methylation of α2-globin CpG island, deletion of *HBA1* and *HBQ1*
Various cancers	Microsatellite instability	*De novo* methylation of *MLH1*
	Disruption of Rb, p53 pathway, uncontrolled proliferation	*De novo* methylation of various gene promoters
	Disruption of SWI–SNF chromatin remodelling complex	Mutations in *SNF5*, *BRG1*, *BRM*
	Overexpression of IGF2, silencing of *CDKN1C*	Loss of imprinting
Leukaemia	Disturbed haematopoiesis	Chromosomal translocations involving HATs and HMTs
Rubinstein–Taybi syndrome	Intellectual disabilities	Mutation in CREB-binding protein (histone acetylation)
Coffin–Lowry syndrome	Intellectual disabilities	Mutation in *Rsk-2* (histone phosphorylation)

In a nutshell

The epigenetic mechanisms regulate our genes

The environment influences the epigenetic mechanisms

ART could change epigenetic regulation

OUR EPIGENOME

could lead to

millions of different interpretations

Treat your epigenome well ☺

It is for your grand- and great-grandchildren

Prof. George Miloshev's Lab

Bulgarian Academy of Sciences