

source:: https://en.wikipedia.org/wiki/DNA_methylation#/media/File:DNA_methylation.jpg

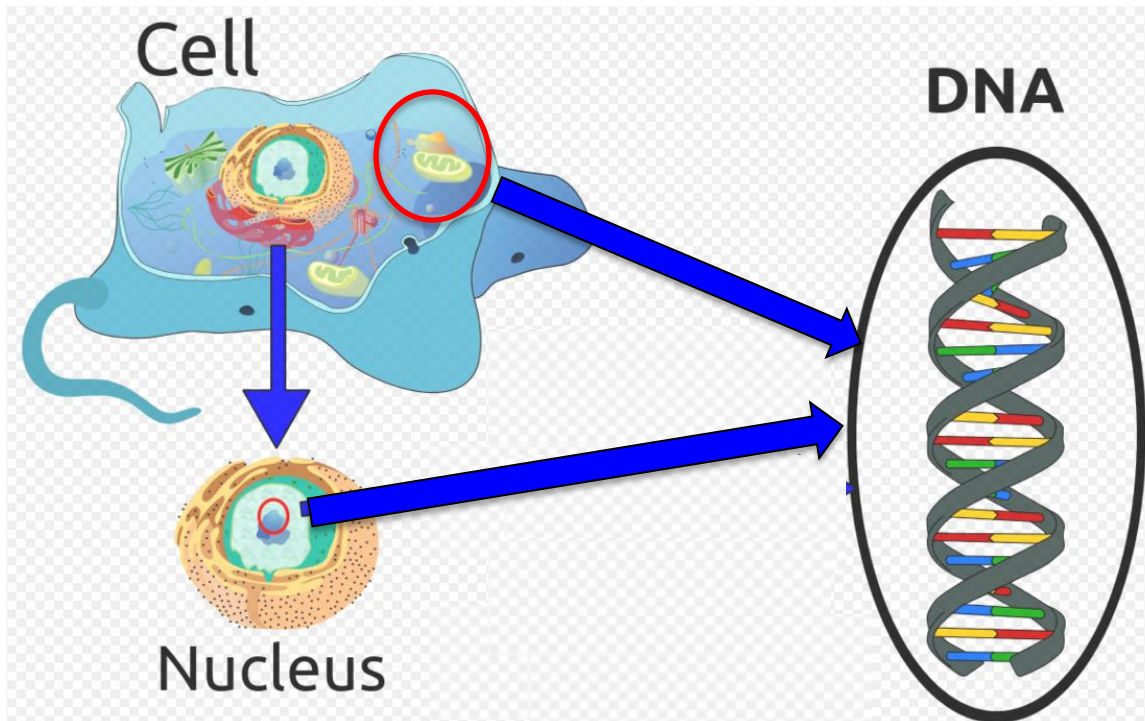
Molecular Age Estimation

European Migration Network (EMN) Conference, 02.02.2016

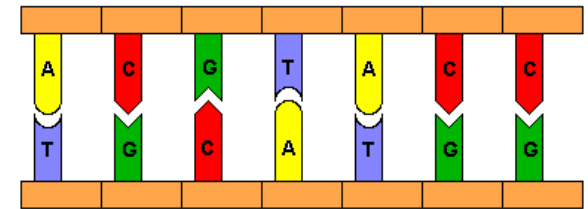


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An Intro to DNA



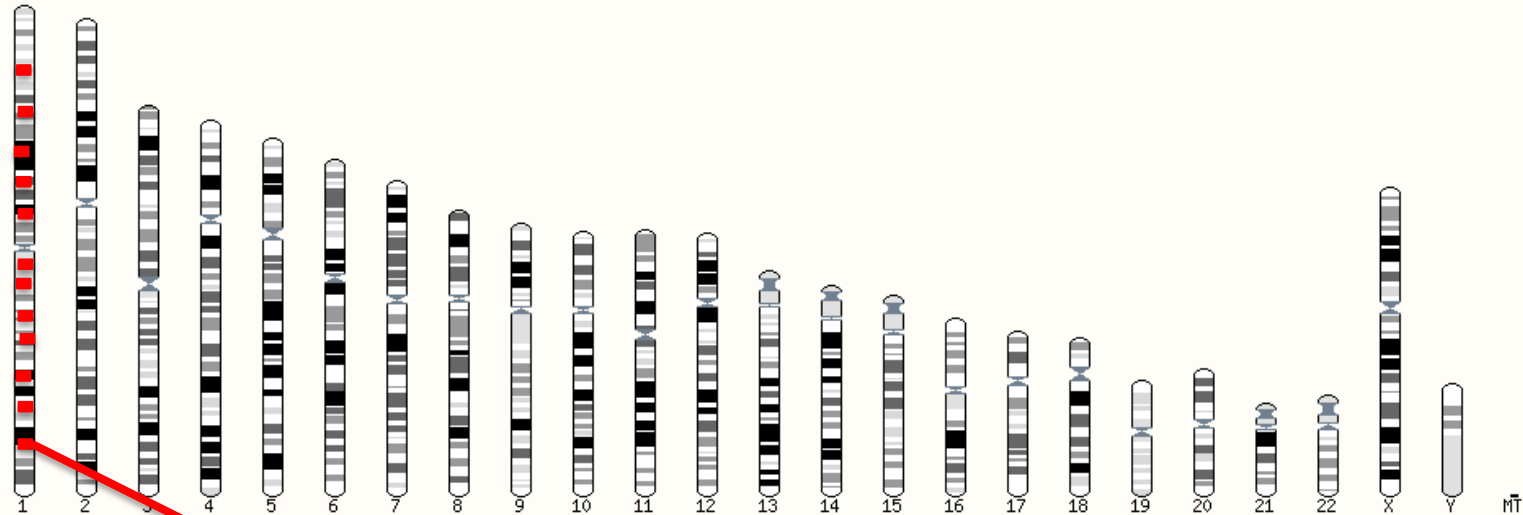
source: https://commons.wikimedia.org/wiki/File:Eukaryote_DNA-en.svg



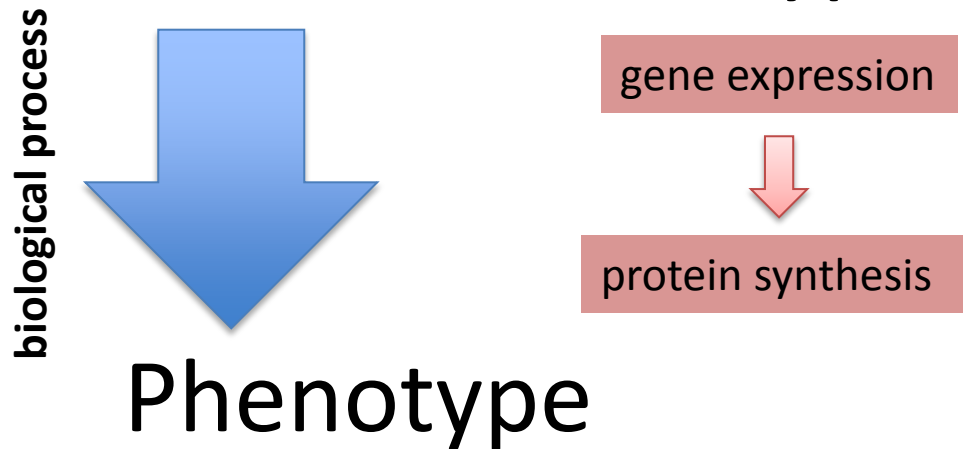
Sequencing

ACGTACC

The Human Genome



Genes = Genotype



Phenotype Prediction



- Find **genetic markers**
- Build **statistical model**
- **Predict trait**

Prediction - Easy



genotype of single DNA marker
correlates **with phenotype**

- Several genetic disorders
- Red/green colorblindness

Prediction - Hard



genotype of many DNA markers
correlates **with phenotype**

- Many diseases
- Externally Visible Characteristics (EVCs) such as eye, hair and skin colour, hair morphology, height, ...

Ageing is a Biological Process



programmed theories

Programmed Longevity
Endocrine Theory
Immunological Theory

damage or error theories

Wear and tear theory
Cross-linking theory
Rate of living theory Free radicals theory
Somatic DNA damage theory.

Biological vs Chronological Age



- Chronological age: time since birth
- Biological age: cell age, defined by ageing process

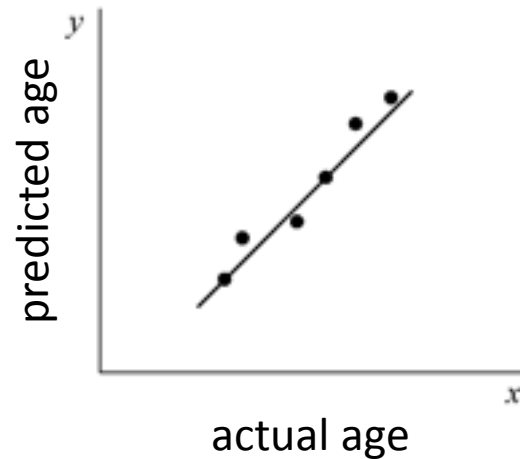
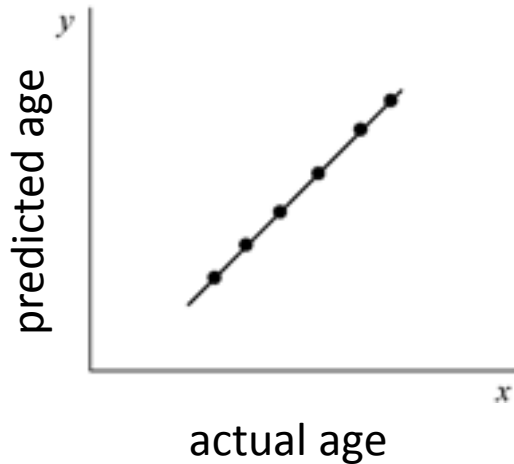
An Age Prediction Model



DNA Marker(s) that:

- correlate(s) with **chronological age**
- shows **little inter- and intraindividual variation**
- measurements are **easy to obtain**

Regression analysis



Goodness of fit R^2 :

Pearson Correlation
Coefficient

MAD = mean absolute
deviation

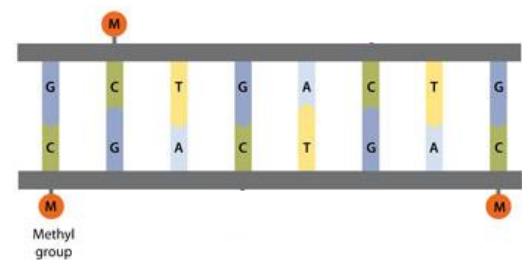
RMSE = root mean
squared standard
error of estimate

Age estimation: Epigenetics



Epigenetics: study of how factors external to the actual DNA sequence influence phenotype

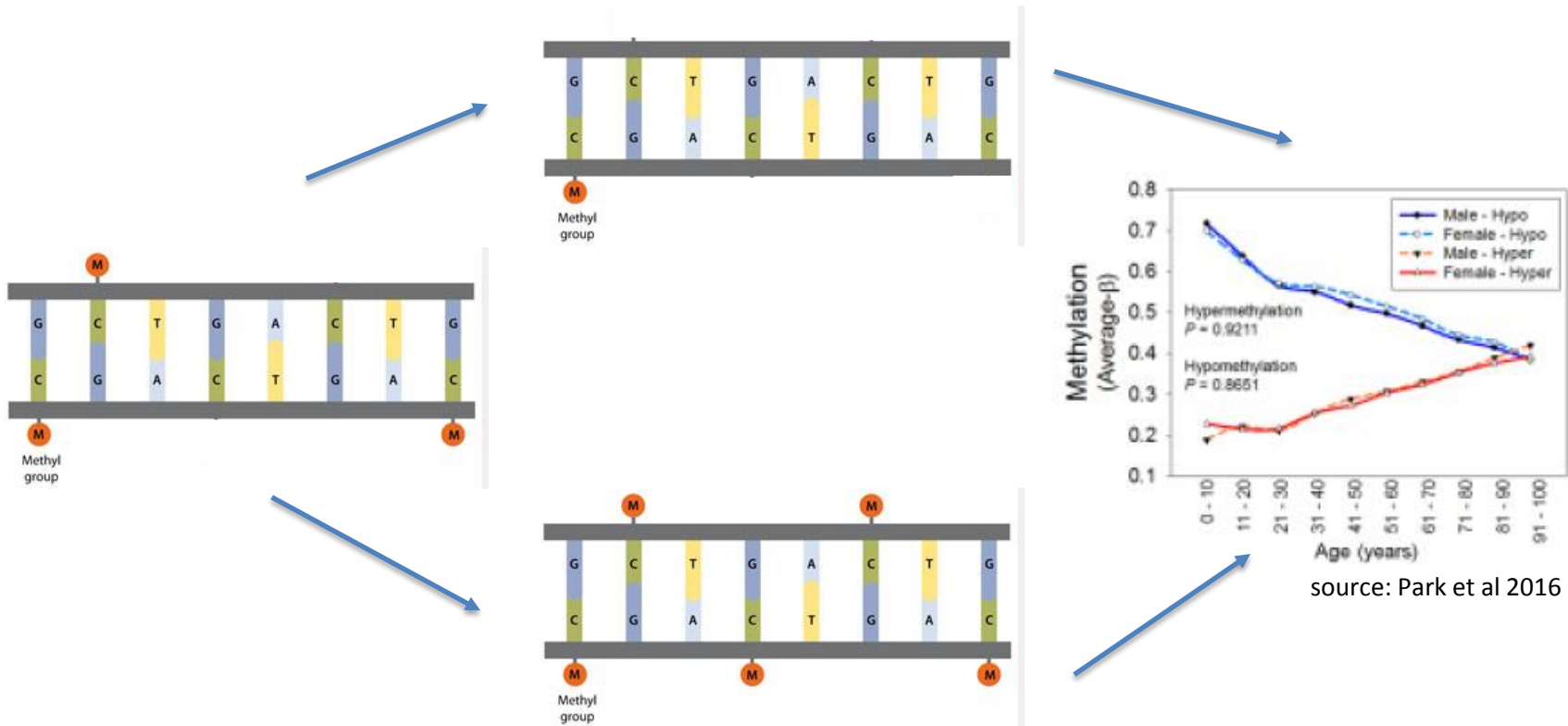
- **DNA methylation:**
 - methyl groups are added to cytosin in certain sequence contexts (CpG)



Age Estimation – Current State



- levels of **DNA methylation at specific sites** change with **age**

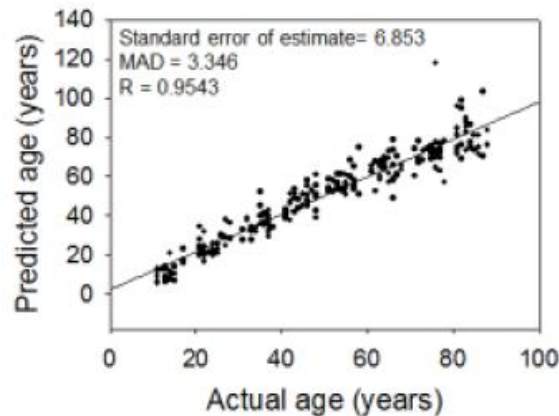


Age Estimation Panels



Author	Year	tissue	markers	R ²	MAD +/- years	RMSE
Bocklandt et al	2011	saliva	EDARADD, NPTX2, Tom1L1	0.85	5.3	
Koch et al	2011	demis, epidermis, cervical smear, T-cells, monocytes	NPTX2, TRIM58, GRIA2, KCNQ1DN, BIRC4bp	0.6	11	
Weidner et al	2014	blood	PDE4C, ITGA2B, ASPA		5.4	7.2
Huang et al	2015	blood	ITGA2B_1, NPTX2_3, NPTX2_4	0.8	7.8	8
Hwan et al	2015	semen	TTCB7, NOX4, cg12837463	0.8	4.2	5.8
Zbiec-Piekarksa et al	2015	blood	ELOVL2, C1orf132, TRIM59 KLF14, FHL2	0.94	4.5	
Bekaert et al	2015	blood, teeth	ASPA, PDE4C, ELOVL2, EDARDD	0.95	3.7	
Park et al	2016	blood	EVOLVL2, ZNF423, CCDC102B,	0.91	3.1	6.3

*(median absolute error)



source: Park et al 2016

Summary



- Currently: Molecular Age Estimation is **feasible from blood samples** holding 3 - 4 year error margins.
- but shows promise for enhancement:
 - focus in research



- GMI provides cutting edge research and technology



- novel panel is currently evaluated in an interlaboratory exercise



**THANK
YOU
FOR
YOUR
ATTENTION!**