



Nagy László

**Miért különbözőek a sejtjeink ha
pontosan ugyanazt az információt
tartalmazzák ?**

Debrecen, 2012. január 17.

www.meetthescientist.hu



Friedrich Miescher



Gregor Mendel



Watson and Crick

Watson and Crick



(Reprinted from *Nature*, Vol. 171, p. 737, April 25, 1953)

MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

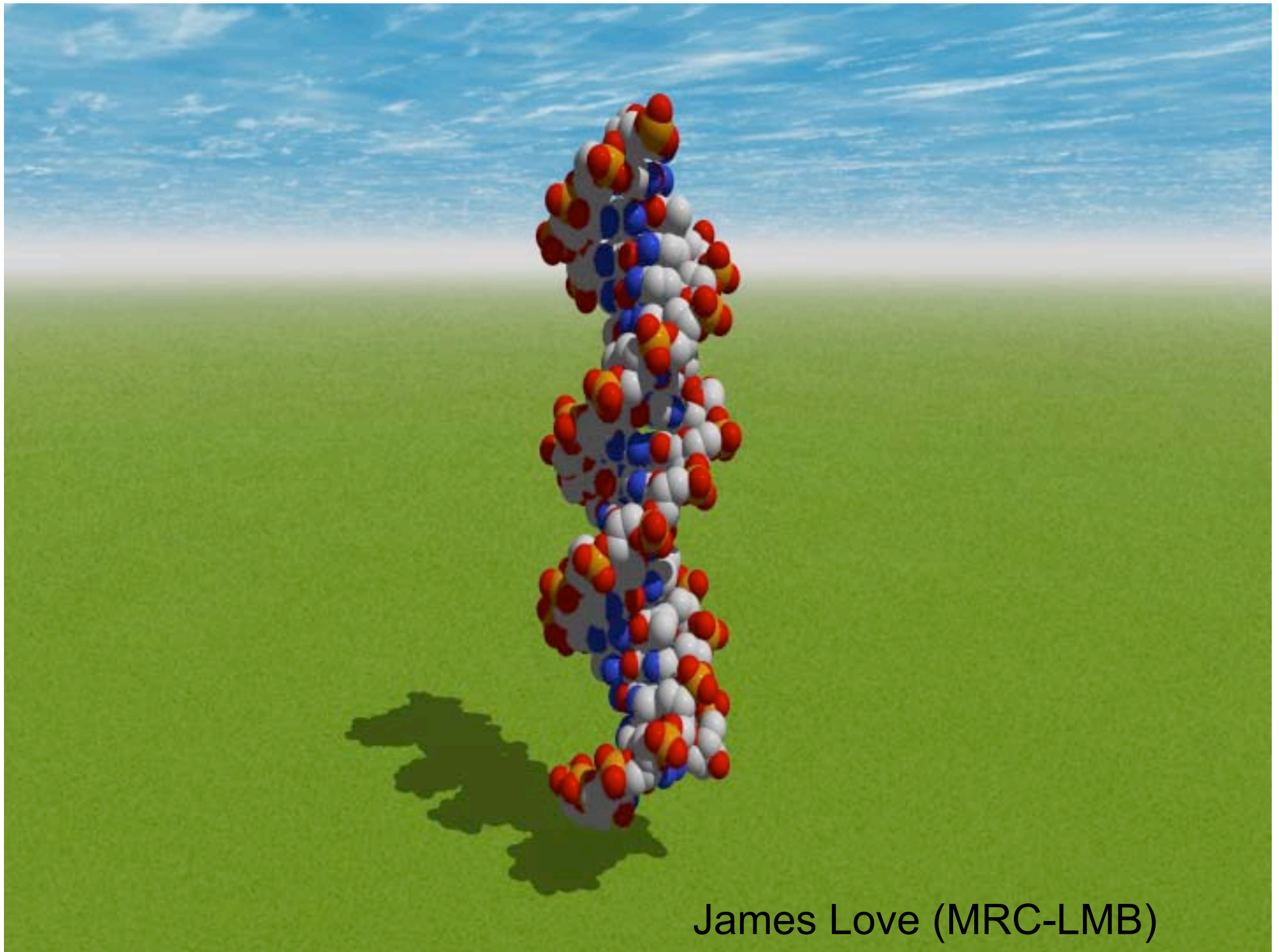
WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey¹. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons:

(1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate di-ester groups joining β -D-deoxyribofuranose residues with 3',5' linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's² model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There is a residue on each chain every 3.4 Å. in the z-direction. We have assumed an angle of 36° between adjacent residues in the same



James Love (MRC-LMB)



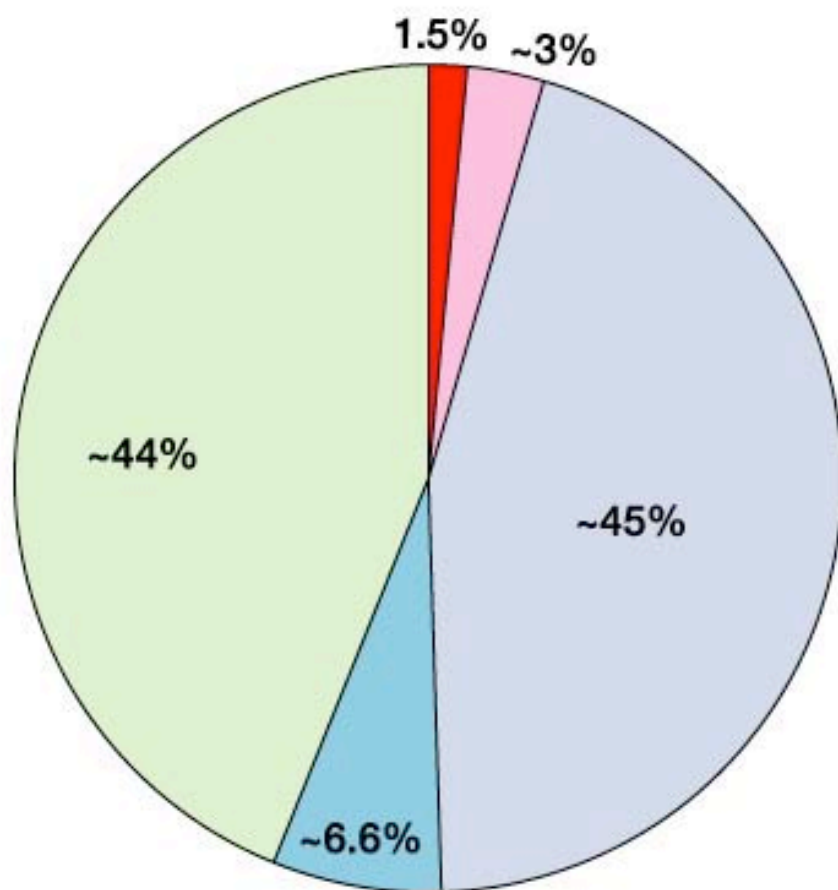
Caption: The sequencing room in the Western Pavilion at the Sanger Centre

© The Wellcome Trust Medical Photographic Library

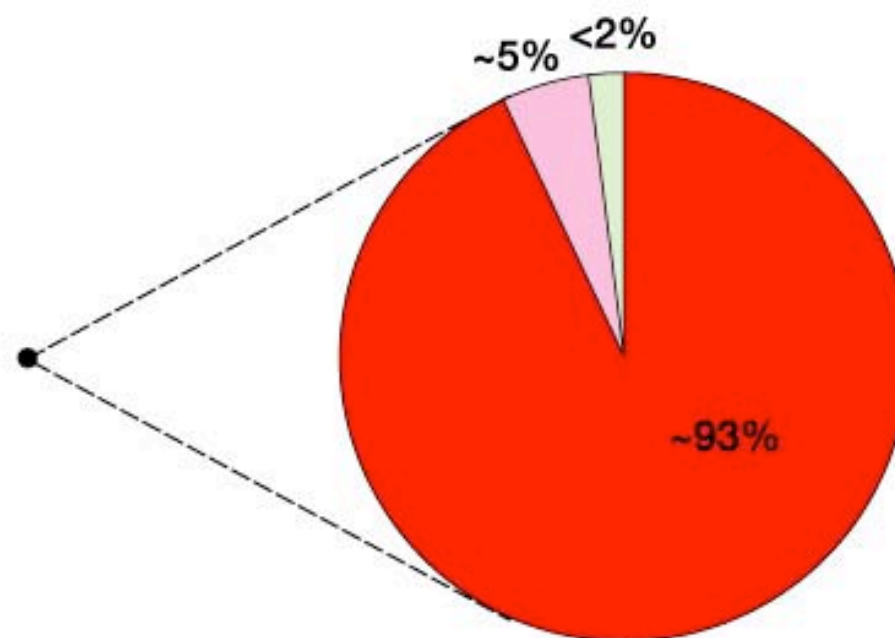
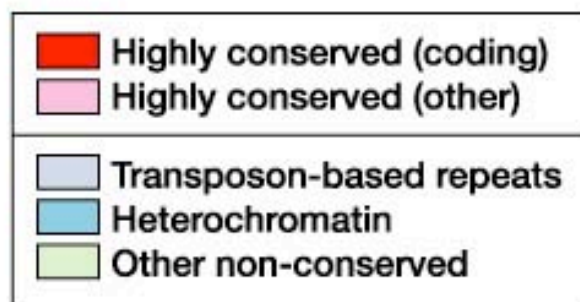
Image for use with the Wellcome Trust genome announcement only, no archiving, no sales, no web use. For further clearance contact j.whiting@wellcome.ac.uk or Tel. +44 (0)20 7611 8347

Collins and Venter





Nuclear genome
(24 linear double-stranded DNA molecules – 3200 Mb; ~30 000 genes)



Mitochondrial genome
(1 circular double-stranded DNA 16.6 kb; 37 genes)

Figure 9-1 Human Molecular Genetics, 3/e. (© Garland Science 2004)

A genomok szabadon hozzáférhetőek

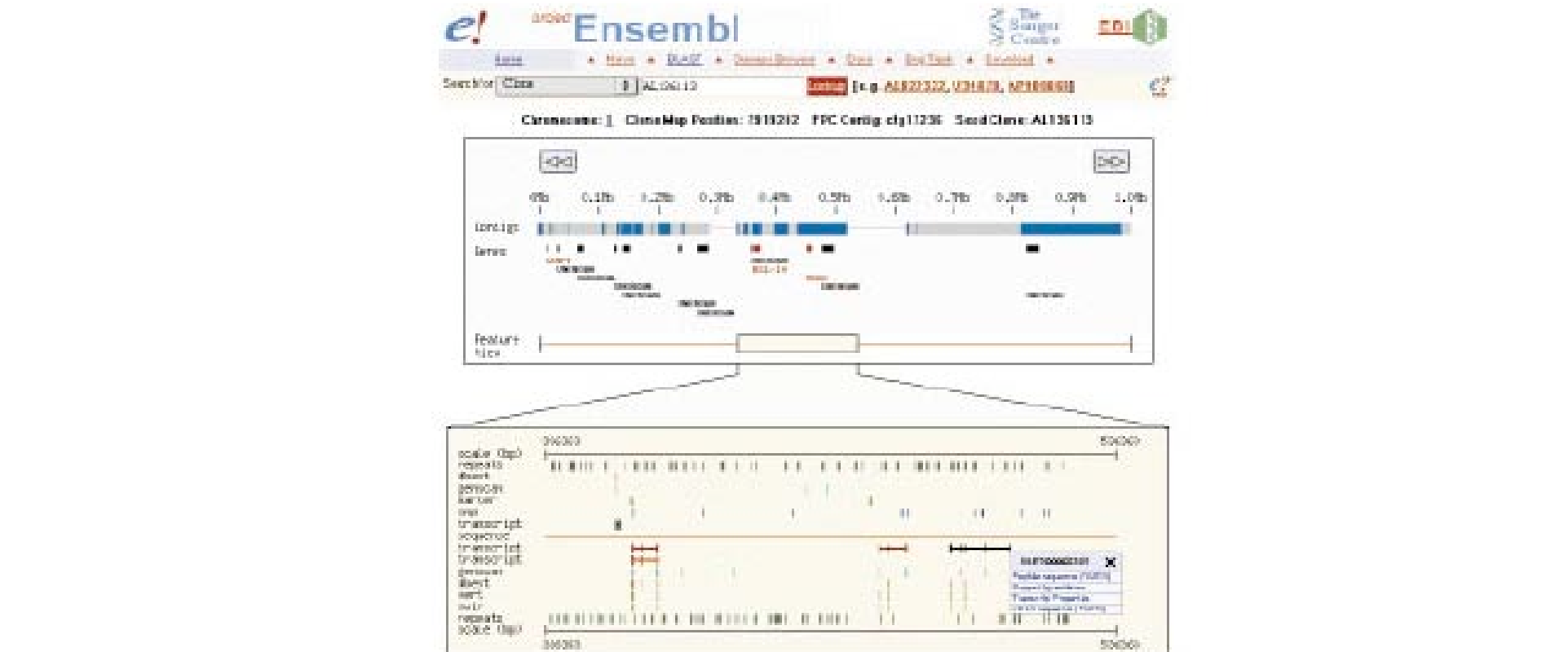
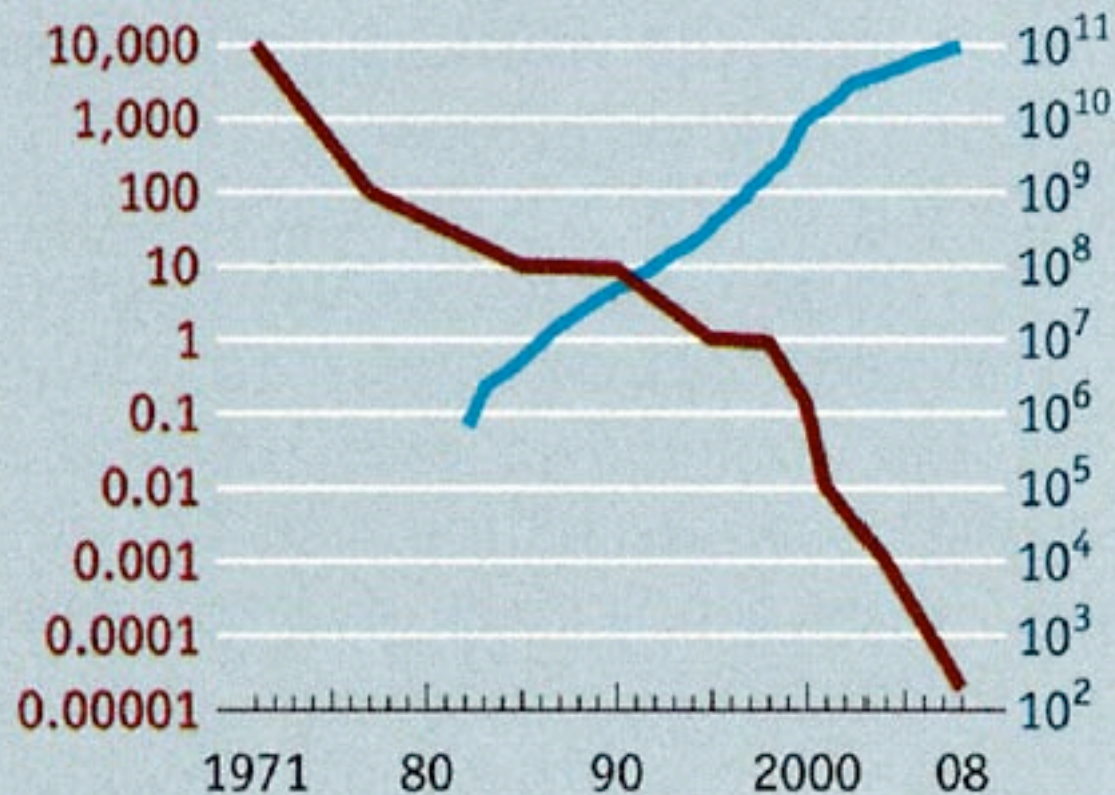


Figure 11 Screen shot from the Genome Browser of Project Ensembl. See <http://www.ensembl.org>.

DNS szekvenálás és a DNS adatbázisok növekedése

Szekvenálás költsége bázispáronként, USD *Bázis pár**



* Növekedés a Genbank
DNS szekvencia adatbankban

Forrás: Raymond Kurzweil



7×10^9

3×10^9



ATTGCTTGGCCAATT
ATTGCTTTGCCAATT

SNP

10 év múlva?



Személyre szabott orvoslás!

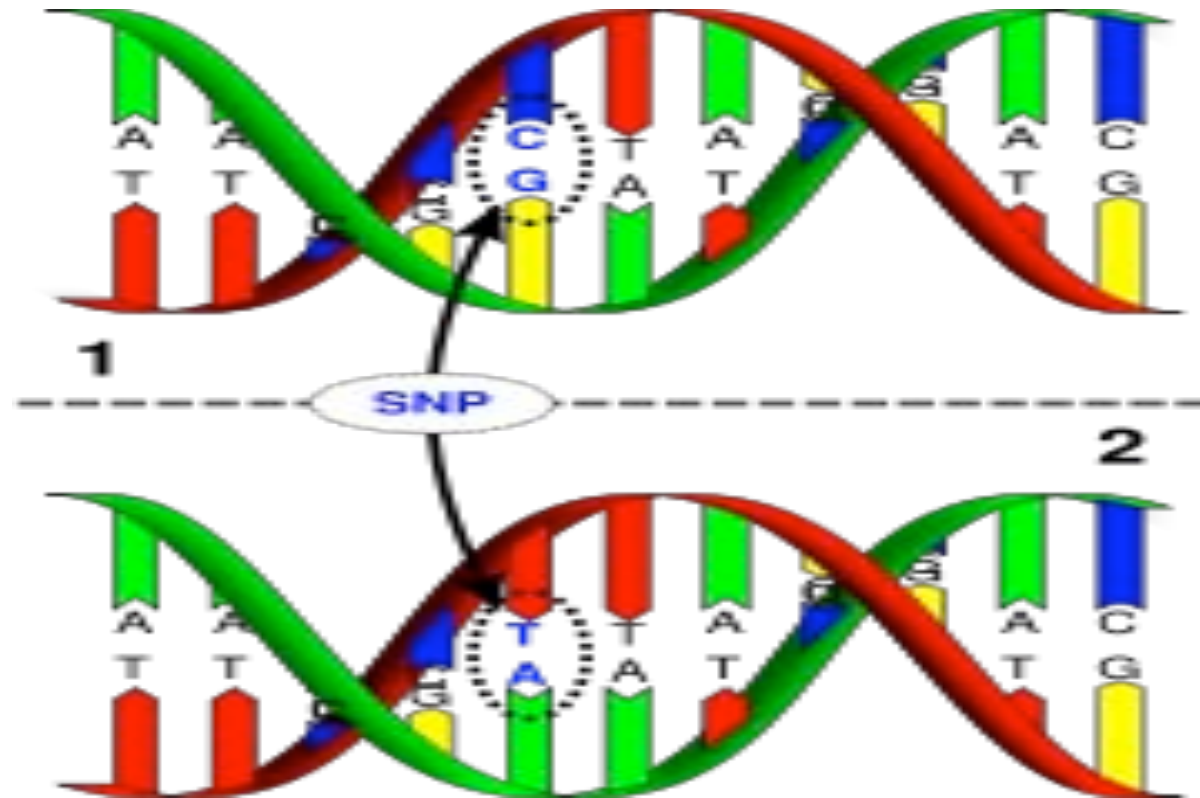
**Fejlett genetikai
diagnosztika**

**Fejlett számítógépes
adatelemzés**

**Szoros
együttműködés orvos
és páciens között**



Egyszerű Nukleotid Polimorfizmus (SNP)?



3,213,401

Génjeink

```
graph TD; A[Génjeink] --> B[Egy gén által öröklött betegség]; A --> C[Több gén által örökített hajlam]; B --> D[Pl. szintévesztés vagy vérzékenység]; C --> E[Pl. szívbetegség vagy cukorbetegség];
```

Egy gén által
öröklött betegség

Több gén által
örökített hajlam

Pl. szintévesztés
vagy
vérzékenység

Pl. szívbetegség
vagy
cukorbetegség



100%

Hajlam!

Mennyibe fog ez kerülni?

Humán Genom Projekt

3 milliárd bázispár
15 év alatt
3 millárd dollár?

Néhány éven belül

3 milliárd bázispár
néhány hét alatt
100 dollár?

Adat, adat, adat

Ha szimplán betűk

61m magas könyvoszlop

vagy

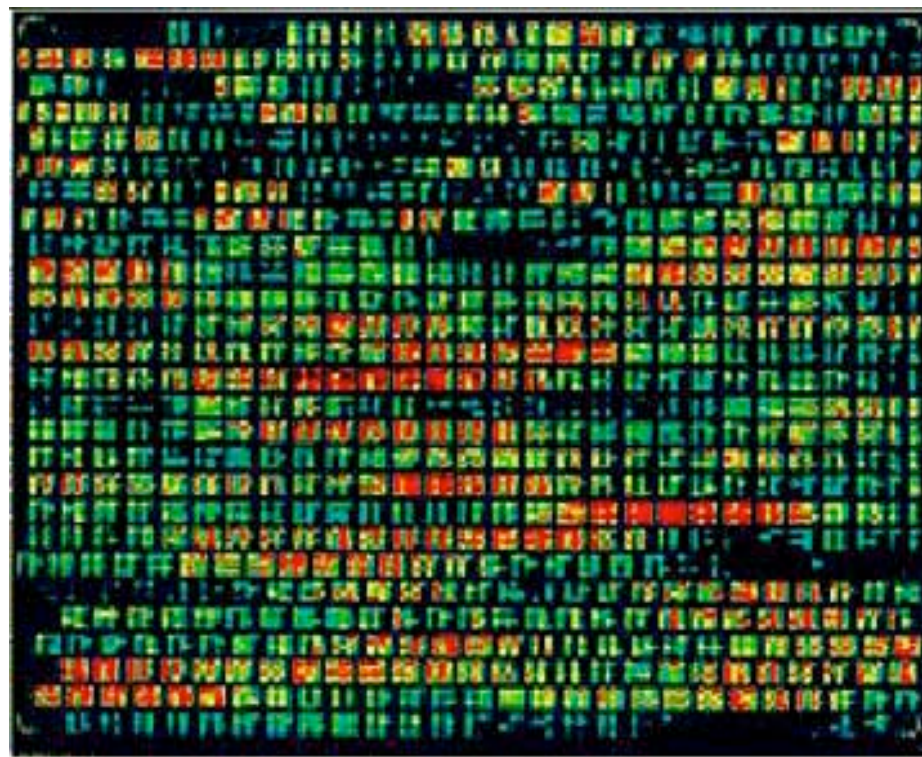
200 telefonkönyv



Adat, adat, adat

Ha képfeldolgozással

30 TeraByte
=
30.000 GigaByte
=
30.000.000 MegaByte



Adat, adat, adat

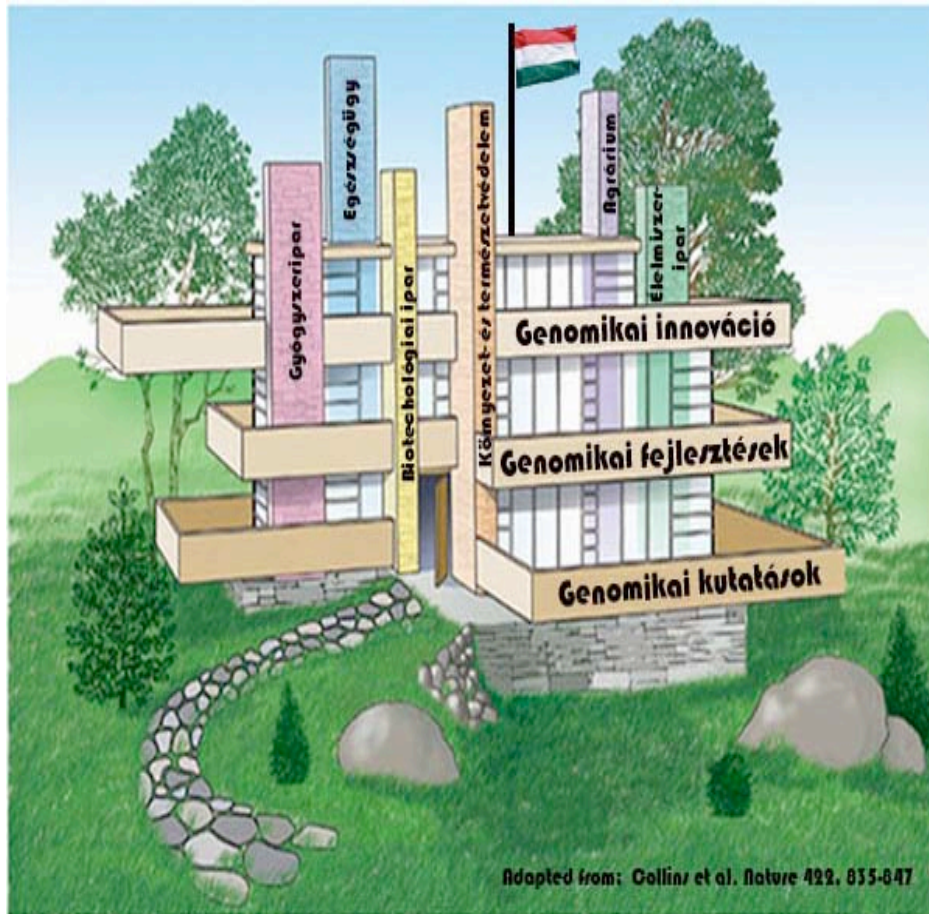
Ha csak a lényeket

20 MegaByte





Genomikai NTP



- Gyógyszeripar
- Egészségügy
- Biotechnológia
- Környezetvédelem
- Természetvédelem
- Mezőgazdaság
- Élelmiszeripar

Ugyanaz a genom, különböző sejtek

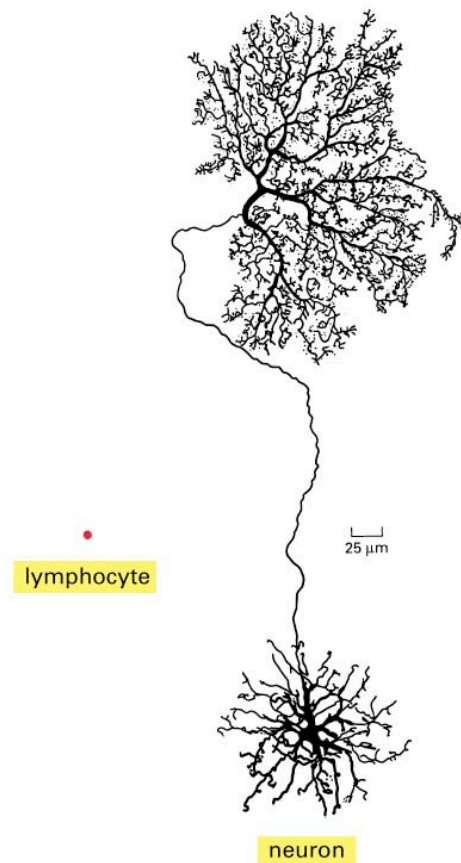


Figure 7-1. Molecular Biology of the Cell, 4th Edition.

Klónozás

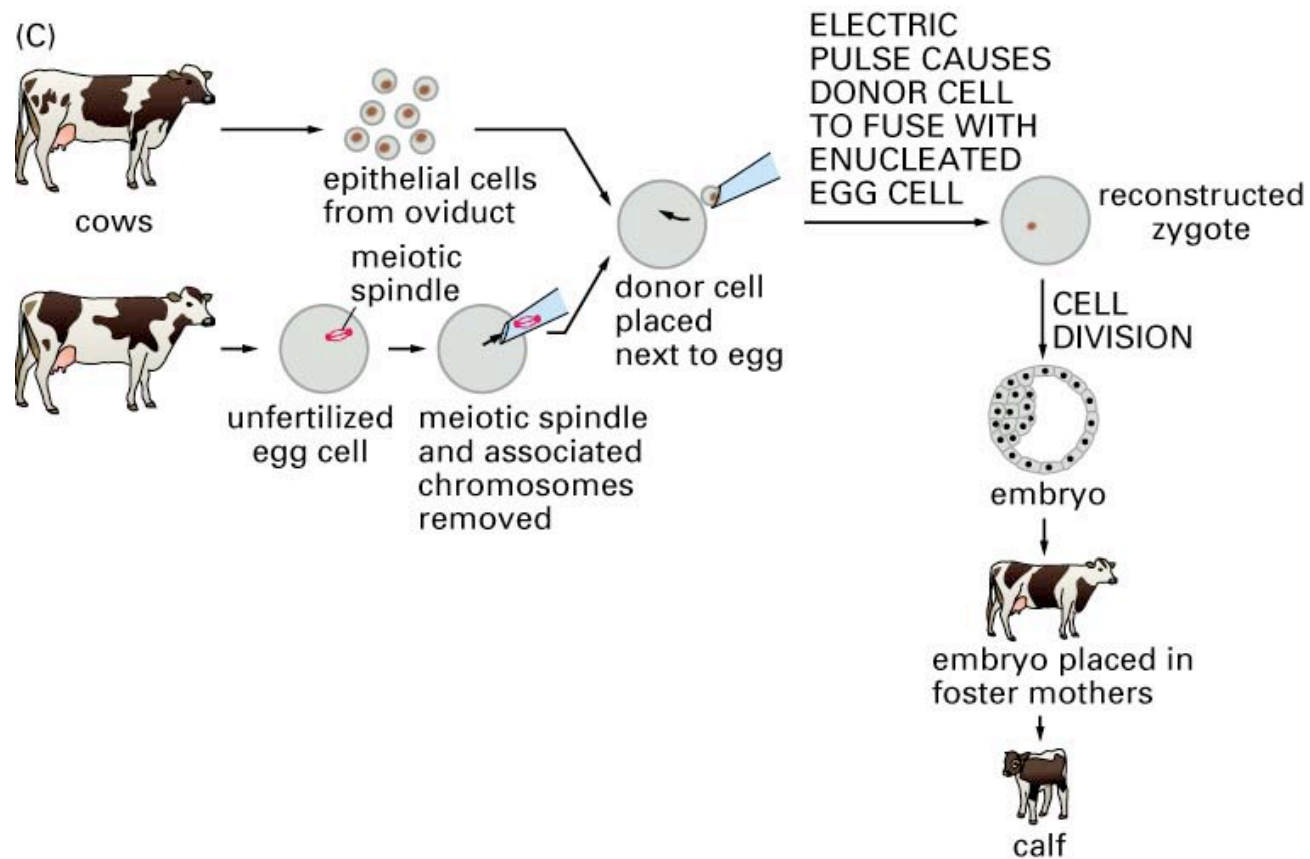
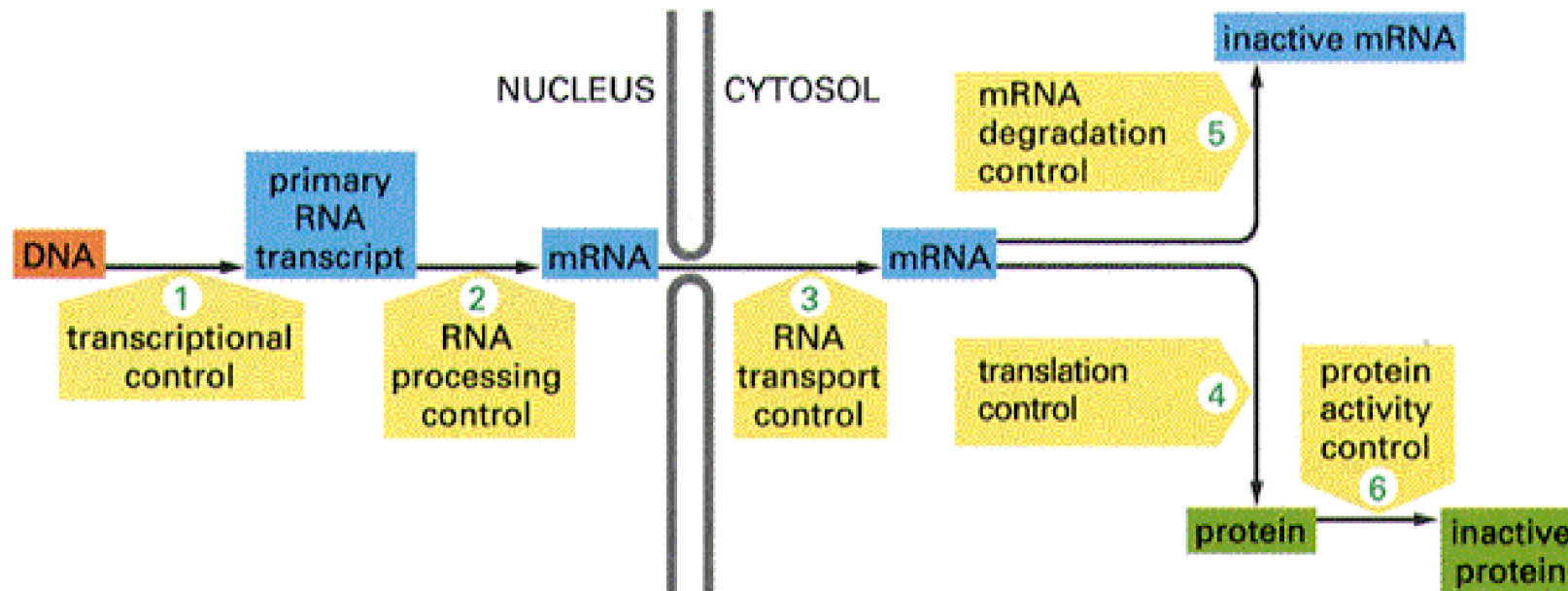
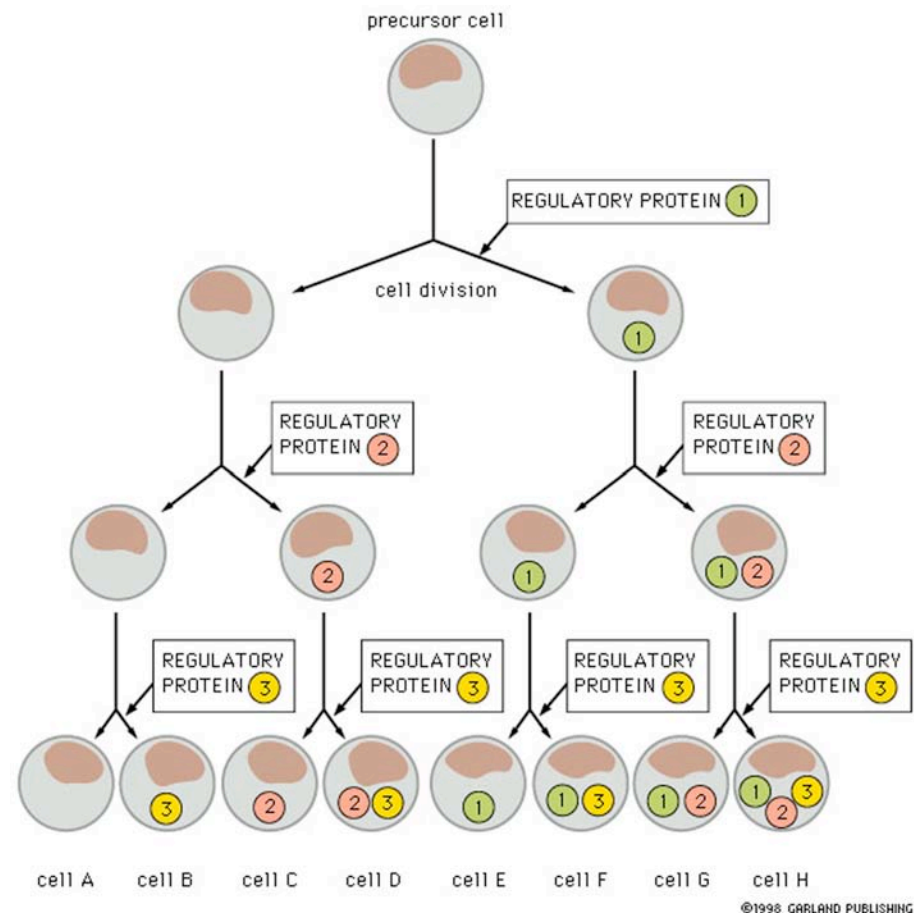


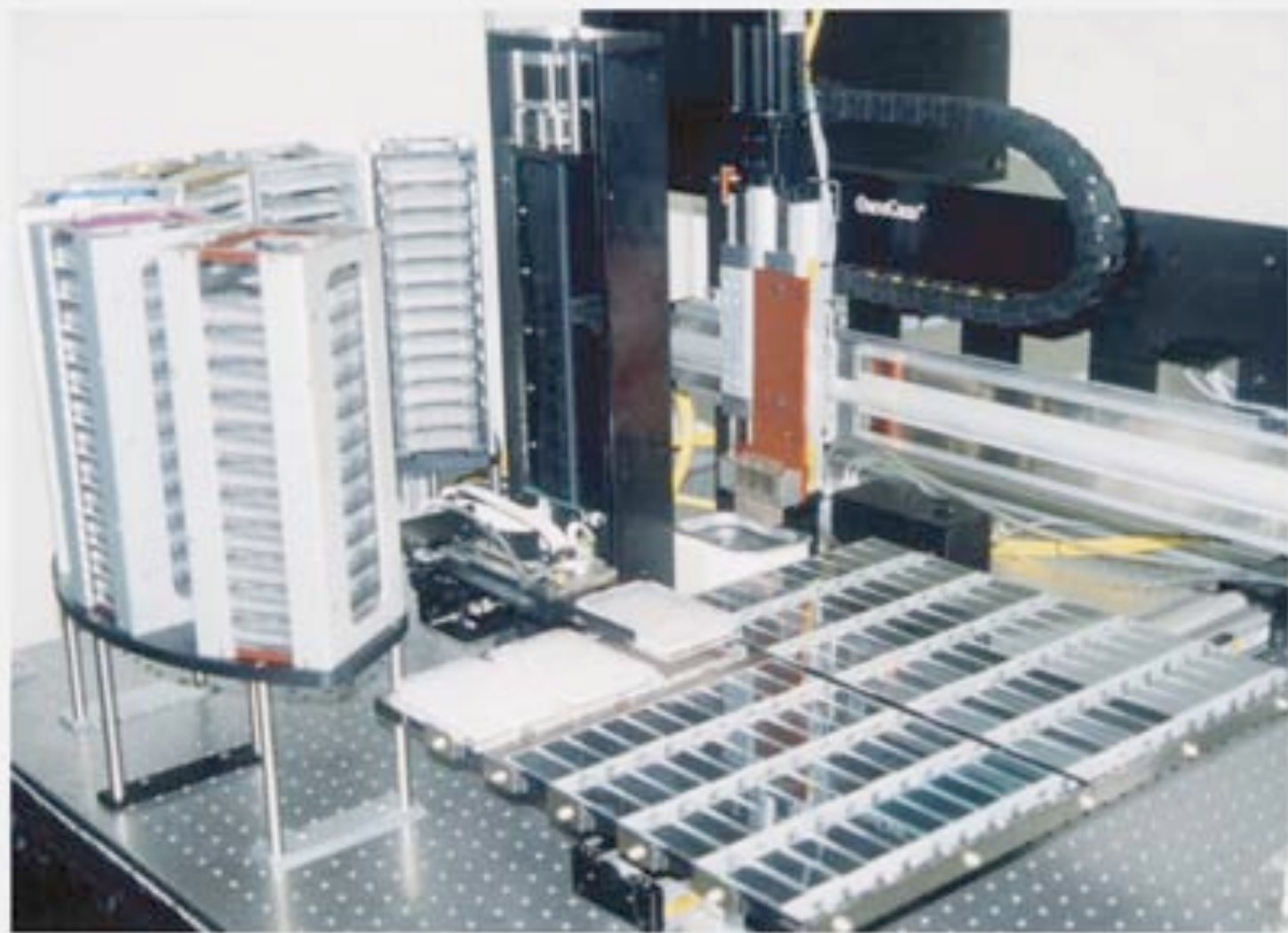
Figure 7-2 part 3 of 3. Molecular Biology of the Cell, 4th Edition.

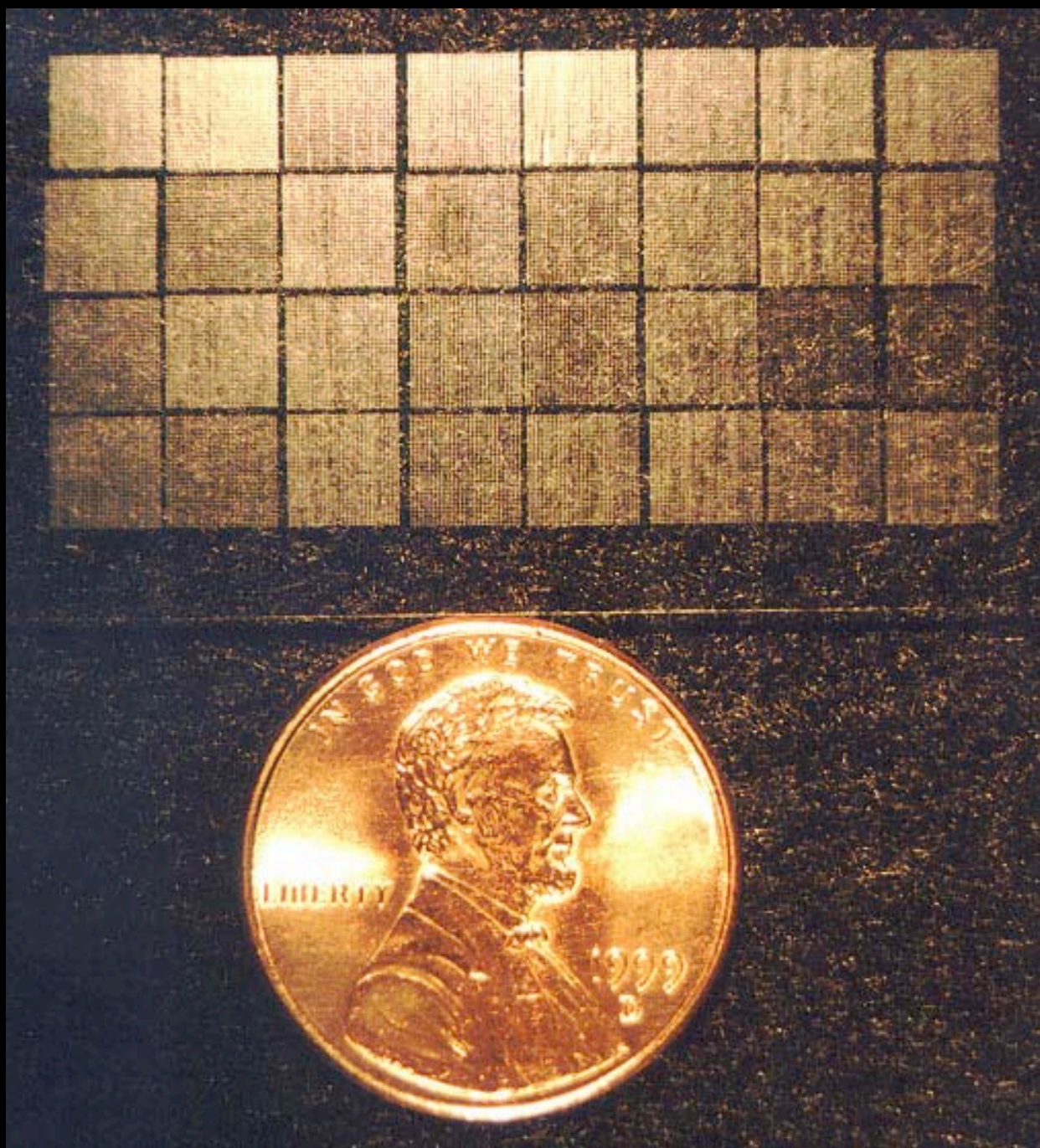
A génkifejeződés szabályozásának szintjei



A sejtek differenciálódása

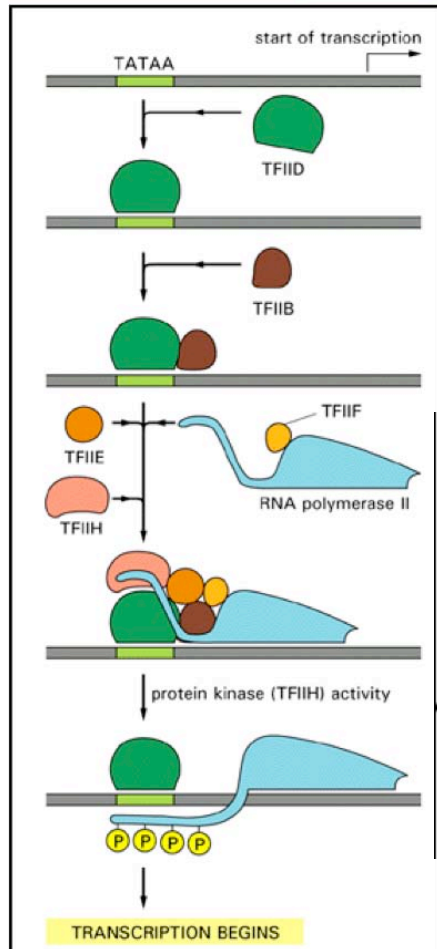




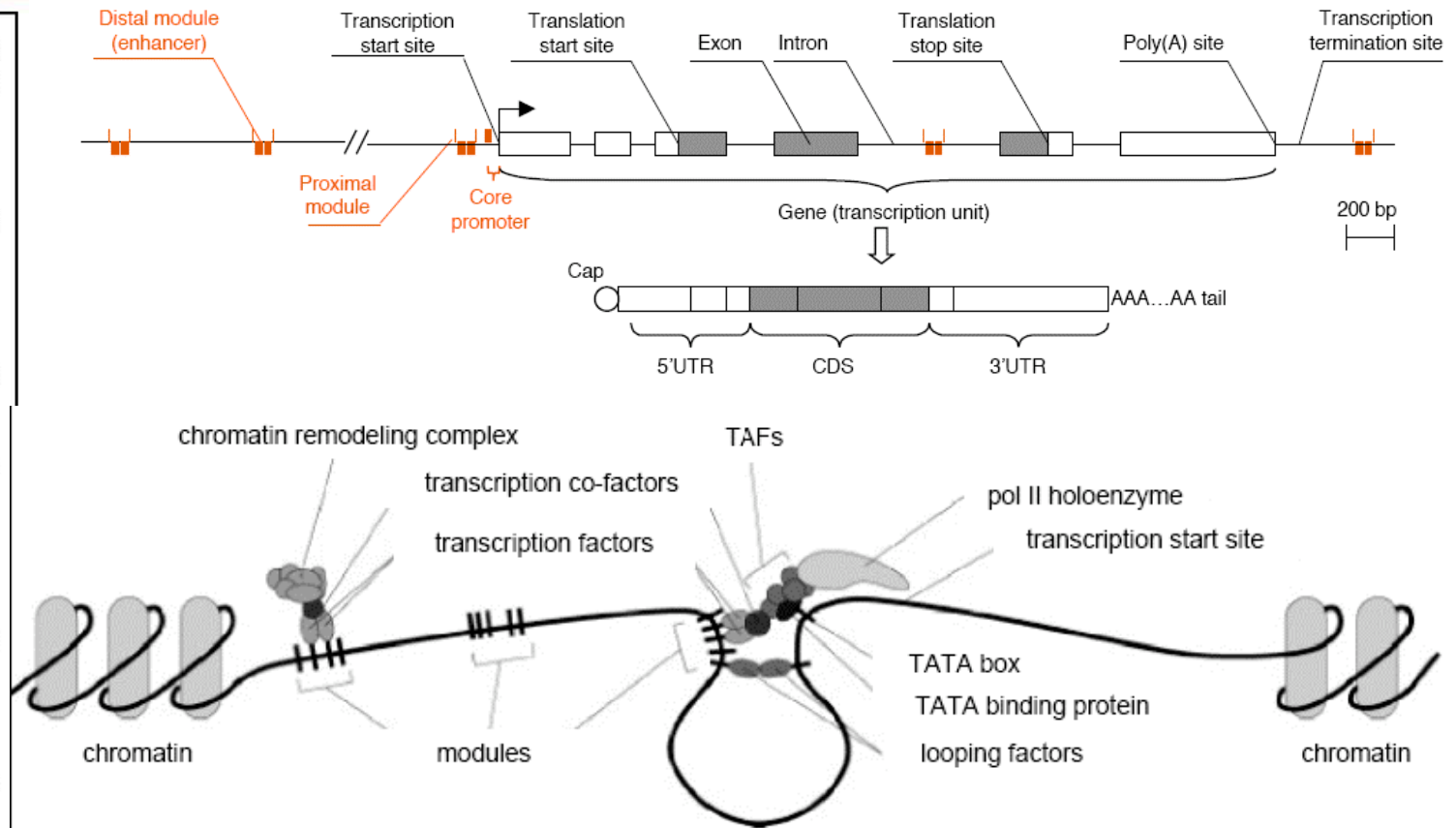




Az eukarióta génátíródás

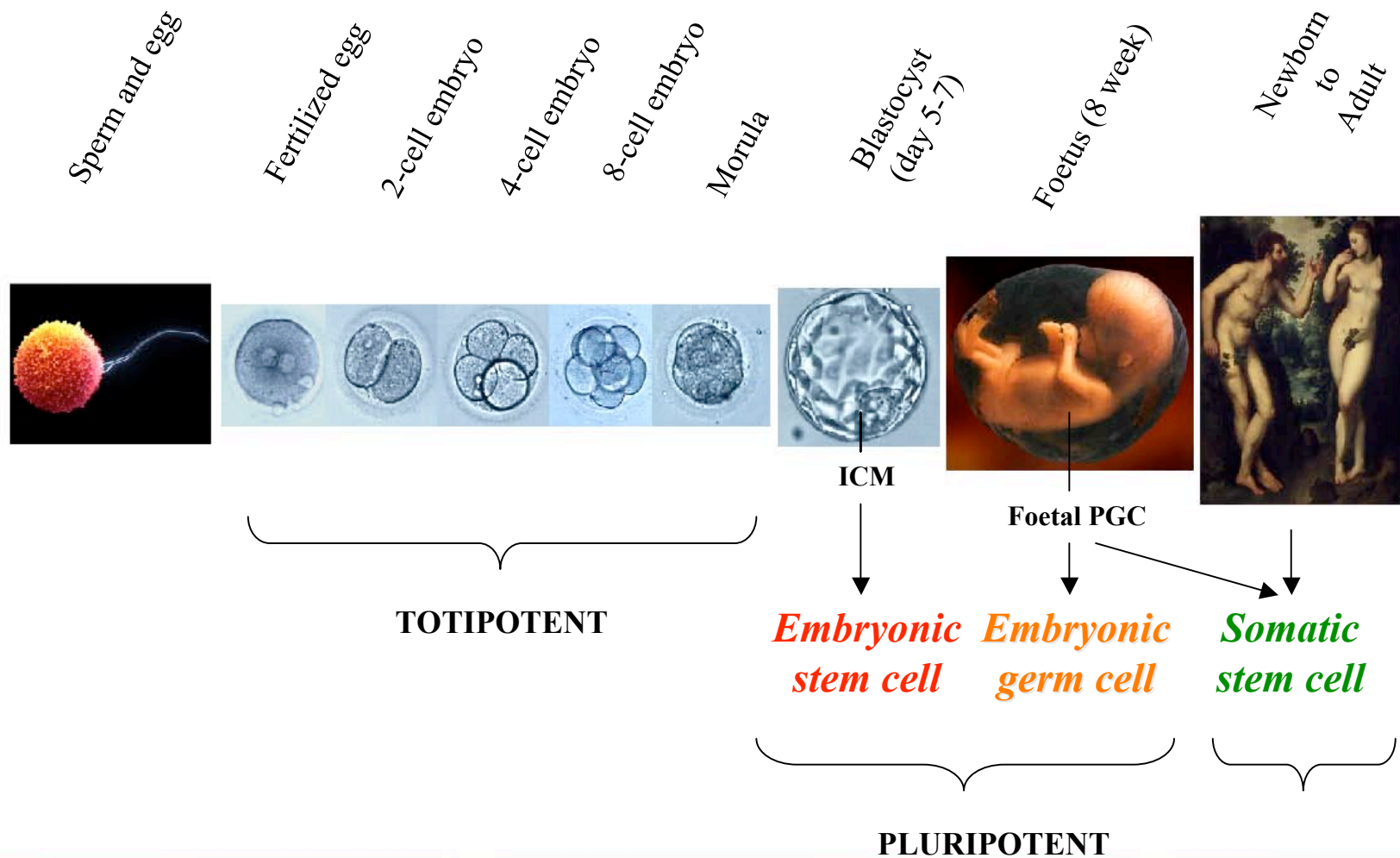


Alberts - Molecular Biology of the Cell 2003



Non-coding (nc) RNAs: rRNA, tRNA, snRNA, snoRNA, miRNA, long ncRNA etc

Az őssejtek forrása



Egér őssejtek izolálása

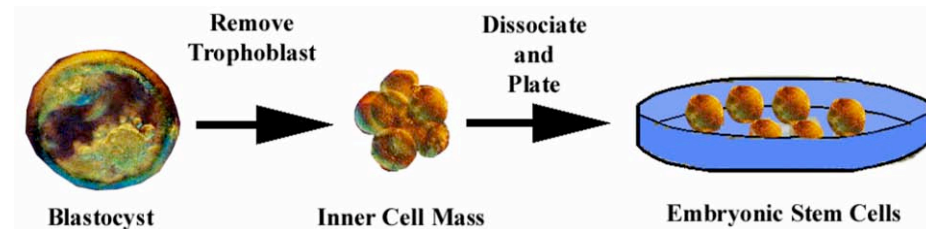
1981



First isolation of embryonic stem cells in mice:

Gail Martin (University of California)

Martin Evans and **M.H. Kaufman** (University of Cambridge)



Emberi őssejtek kinyerése

1981

1998

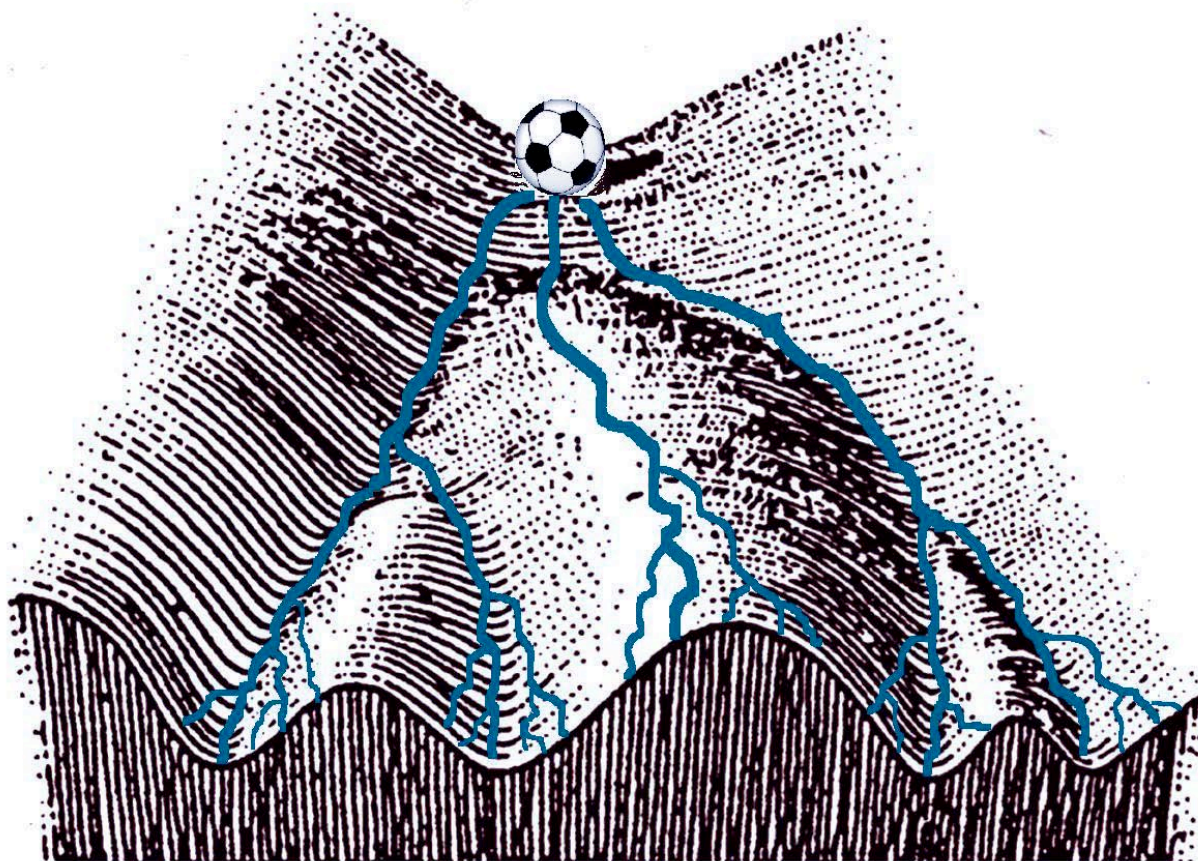


James Thomson and **John Gearhart** isolates cells from the inner cell mass of the early embryo, developing the first human embryonic stem cell lines.

Celebrating
10 Years of hESC Lines



Miért fontosak az összejtek ?



C.H. Waddington (edited)

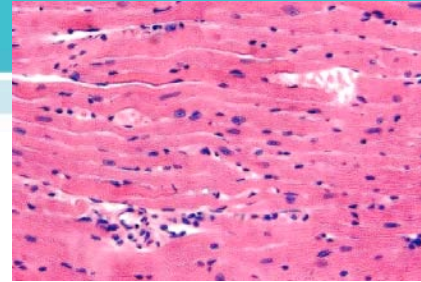
Pancreatic cell



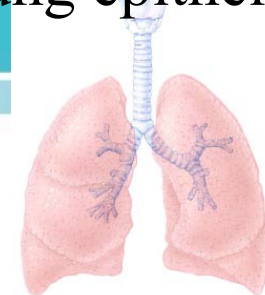
DC



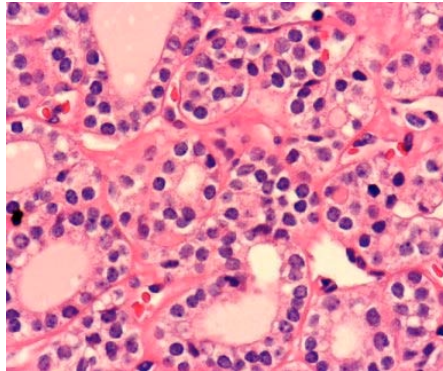
Heart muscle



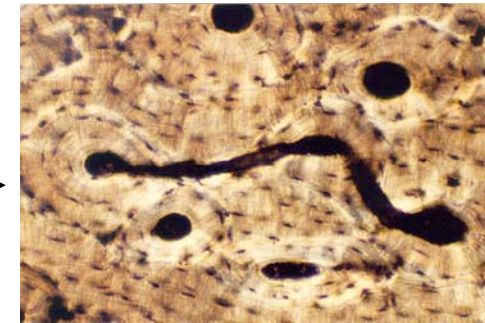
Lung epithel



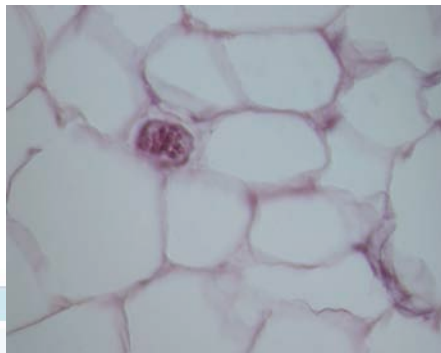
Thyroid follicular



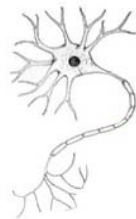
Osteoblast



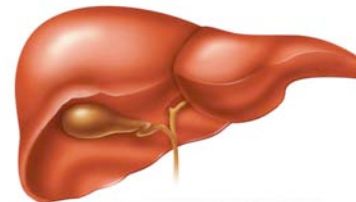
Adipocyte



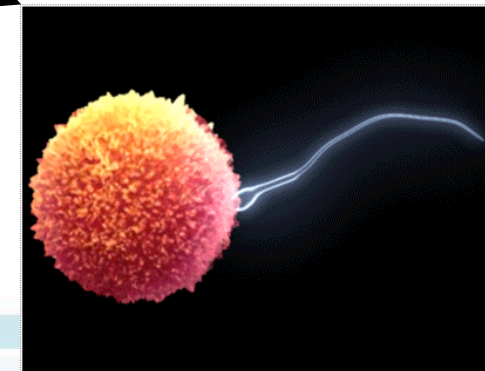
Neuron



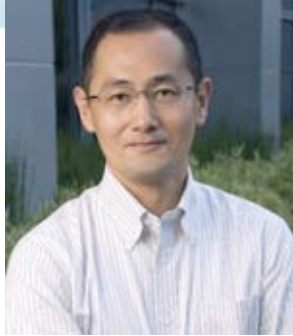
Hepatocyte



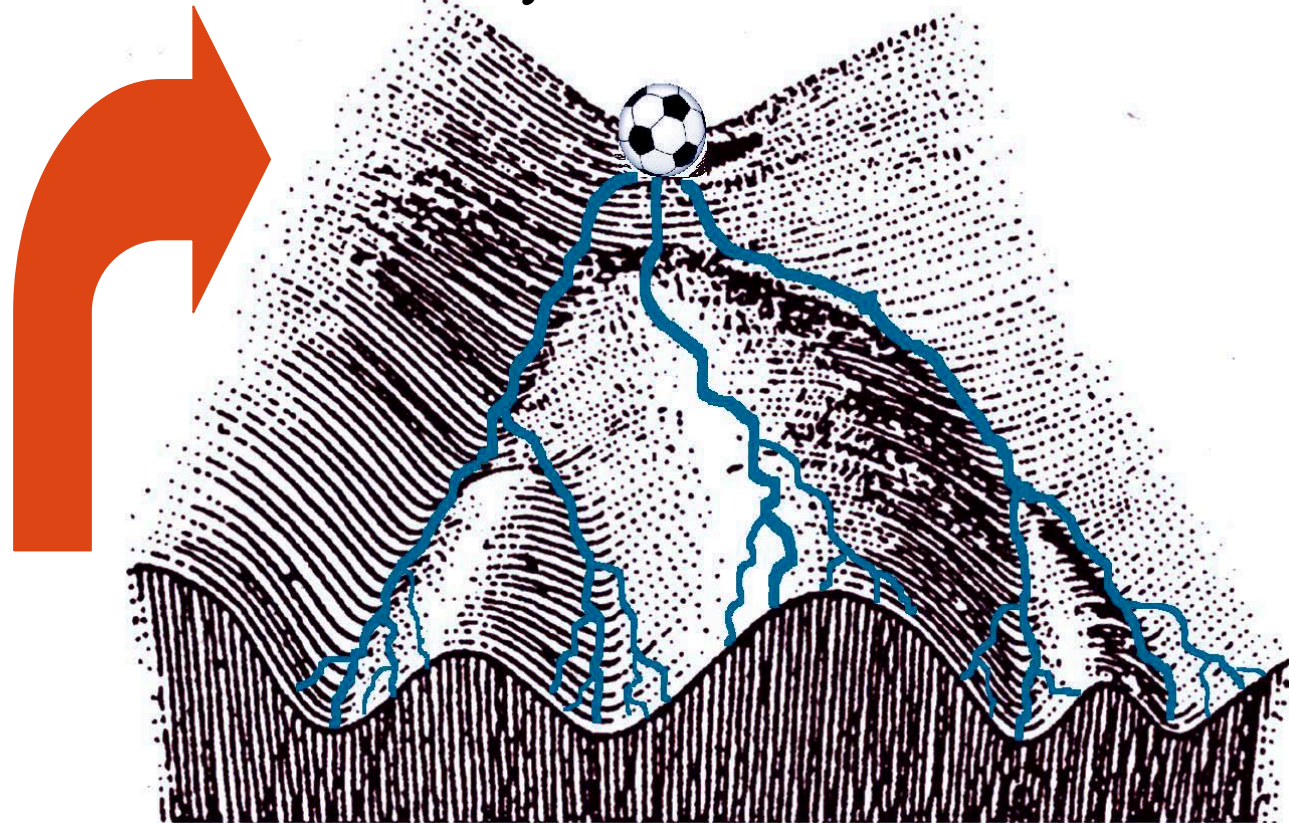
Germ cells



Shinya Yamanaka

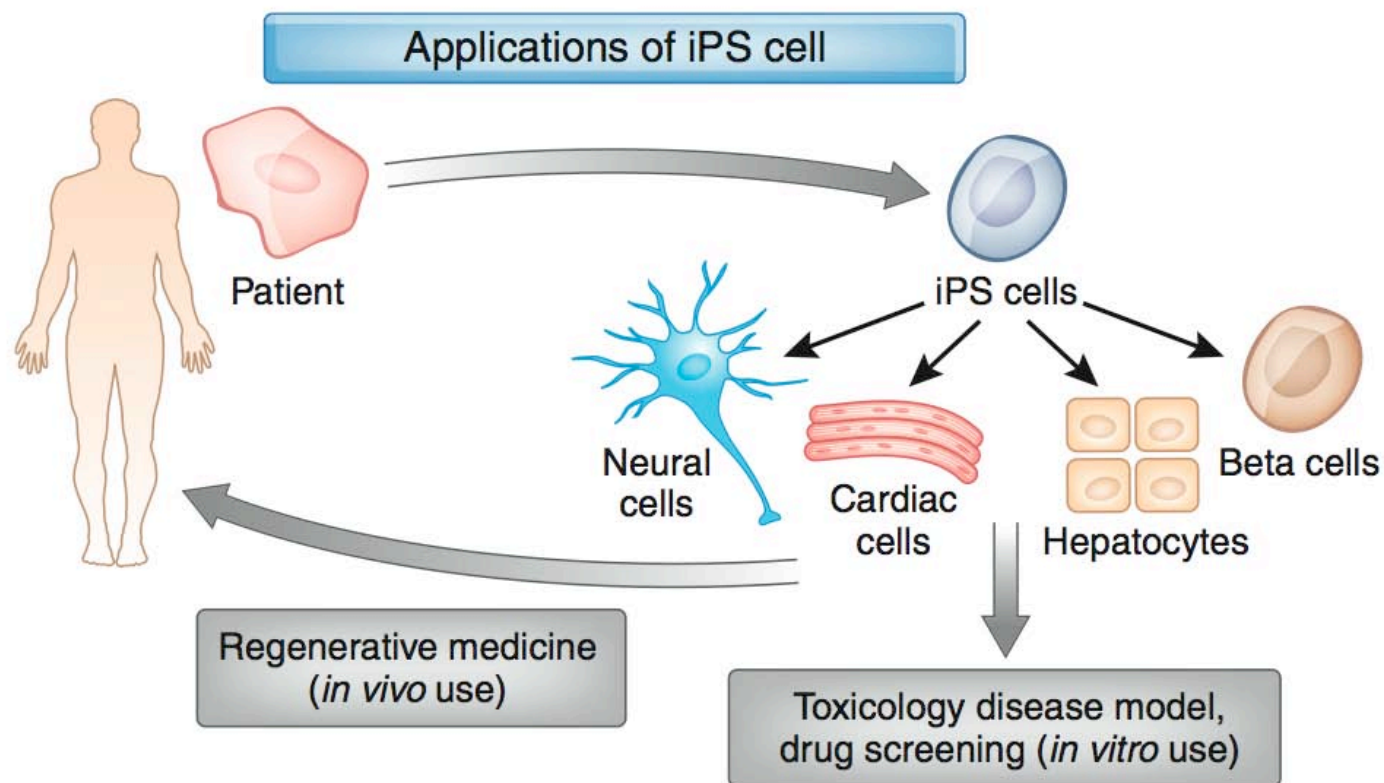


Undifferentiated
embryonic stem cell



Differentiated cell

Indukált pluripotens őssejtek használhatósága





Köszönöm!

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