



# *От организации хроматина к пониманию функционирования геномов эукариот*

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МГУ имени М.В.Ломоносова

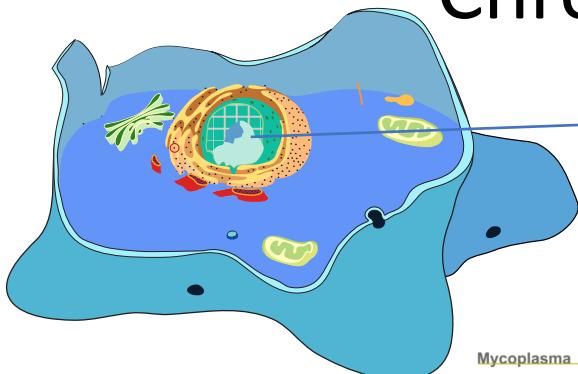
## *Лекция 2.*

*Хроматин: от нуклеосом к  
строению ядра.*

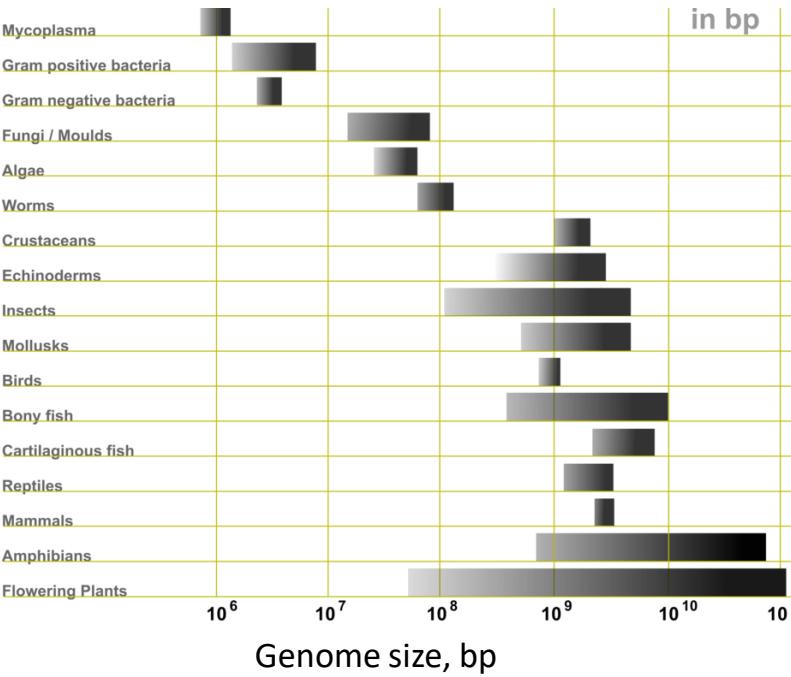
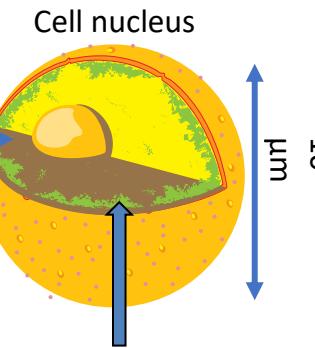
Апрель 2023

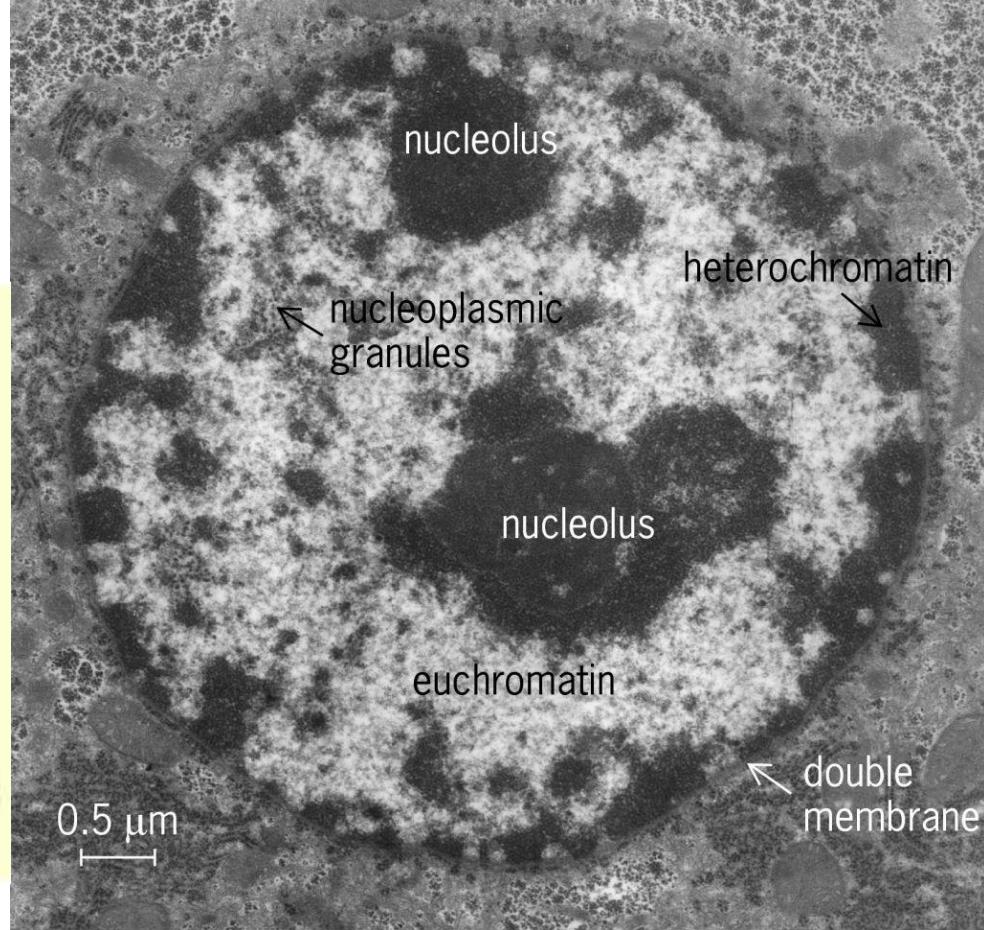
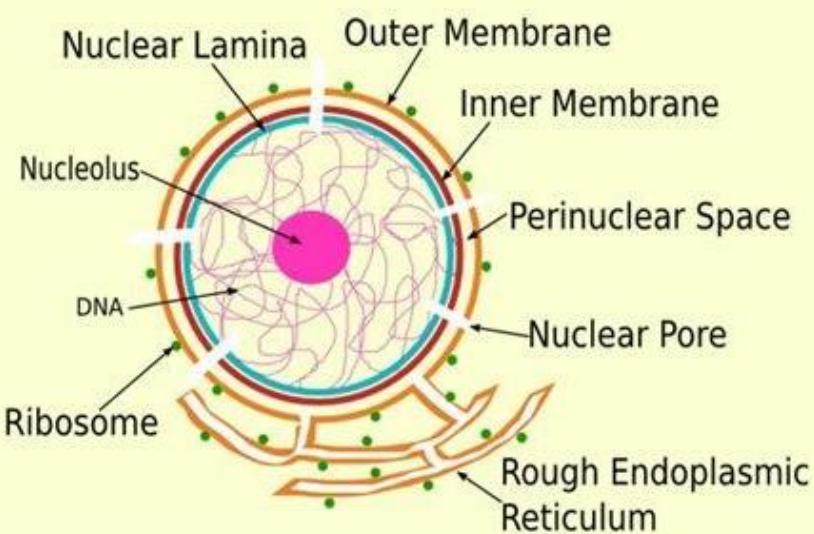
[http://intbio.org/2023\\_chromatin\\_sirius/](http://intbio.org/2023_chromatin_sirius/)

# Chromatin/Хроматин



Eukaryotic cell





# Проблема - неудобные масштабы

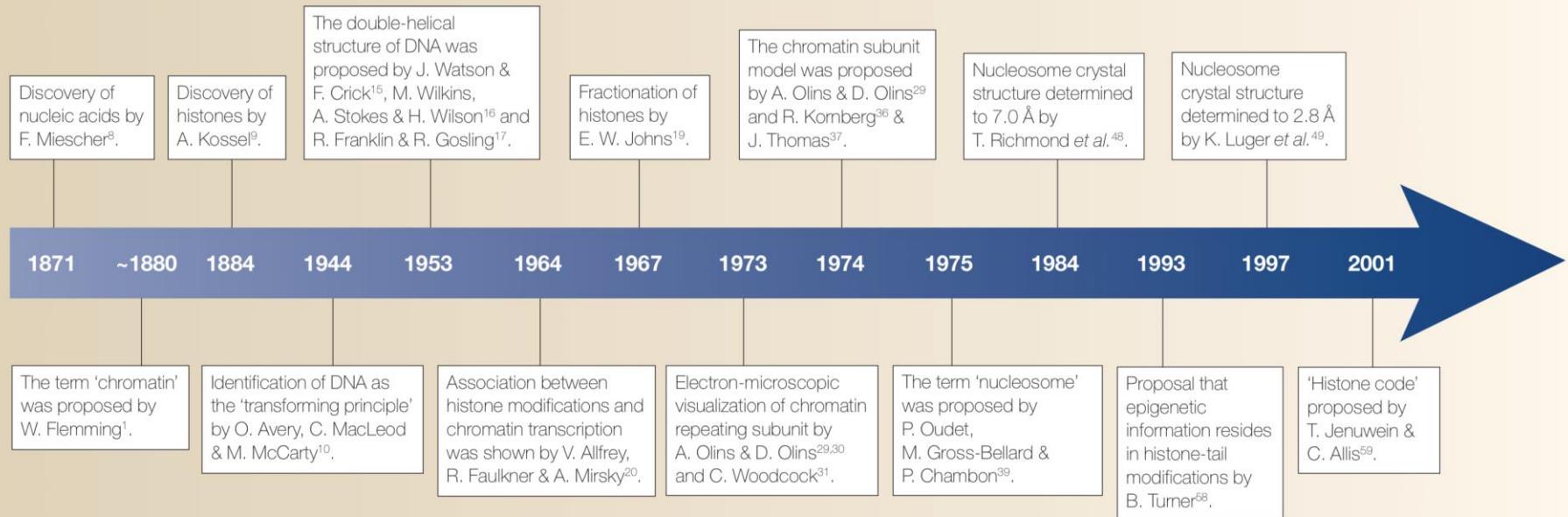
От 10 мкм – работает оптическая микроскопия

До 50 нм – кристаллография, электронная микроскопия, криоЕМ

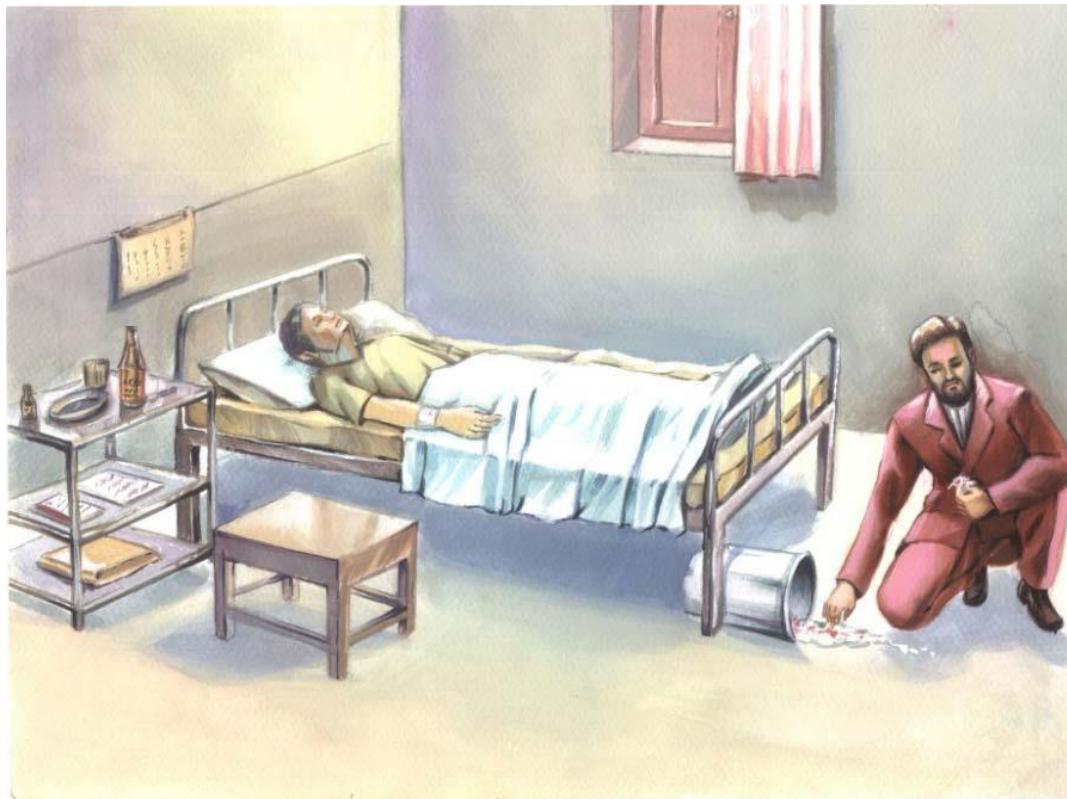
От 50 нм до 10 мкм – масштаб сложно  
поддается изучению

# Немного истории ...

## Timeline | History of chromatin



Ф. Мишер, выделение ядер, анализ нуклина, 1872



# Мишер, выделение ядер, анализ нуклина, 1872

- Исследовал лейкоциты из гноя на повязках раненых
- Анализ компонентов цитоплазмы
- Некоторое вещество выпадало в осадок из раствора при добавлении кислоты и снова растворялось при добавлении щелочи.
- Первый протокол выделения ядер
- **Он провел химический анализ нуклина и обнаружил, что он содержит атомы углерода, водорода, азота, не содержит серу, как белки, но содержит много фосфора (2.5%) - о чем он сообщил в письме к родителям. Сегодня этот препарат признали бы неочищенным хроматином (в чистой ДНК 10% фосфора, в чистом хроматине 4%).**



- Отмывка разбавленным раствором соляной кислотой несколько недель при низких температурах. Далее он показал, что оставшиеся ядра не окрашиваются раствором йода - красителем цитоплазмы того времени.
- Затем он энергично встряхивал ядра в течение длительного периода времени со смесью воды и эфира. Это вызвало растворение липидов в эфире, в то время как ядра, все еще прикрепленные к цитоплазме, собирались на границе вода/эфир. Напротив, чистые ядра без загрязнения цитоплазмы сохранялись в водной фазе. Мишер отфильтровал эти ядра и исследовал их под микроскопом. Он заметил, что таким образом может получить «совершенно чистые ядра с ровным контуром, однородным содержимым, резко очерченным ядрышком, несколько меньшими по сравнению с их первоначальными объемами».
- Впоследствии Мишер экстрагировал изолированные ядра щелочными растворами. При добавлении к ядрам сильно разбавленного (1:100 000) карбоната натрия он заметил, что они значительно набухают и становятся полупрозрачными. Затем Мишер выделил из этих ядер желтый раствор вещества Q. Добавляя уксусную или соляную кислоту в избыtkе, он мог получить нерастворимый хлопьевидный осадок (ДНК). Мишер отметил, что он может снова растворить осадок, добавляя щелочные растворы. Нуклин выделили, но его сильно мало для исследований.
- Вторая версия протокола включала в себя следующее: отмывка лейкоцитов спиртом (удаление липидов), потом обработка пепсином из желудков свиней для очистки от белков цитоплазмы. Уже через несколько часов мелкий серый порошок отделялся от желтой жидкости. Несколько промывок пепсином и получался раствор ядер. При этом ядра, полученные таким способом проявляли те же химические свойства, что и ядра, выделенные соляной кислотой. Далее к этим ядрам он применял протокол щелочной экстракции и при добавлении избытка кислоты получал осадок нуклина.

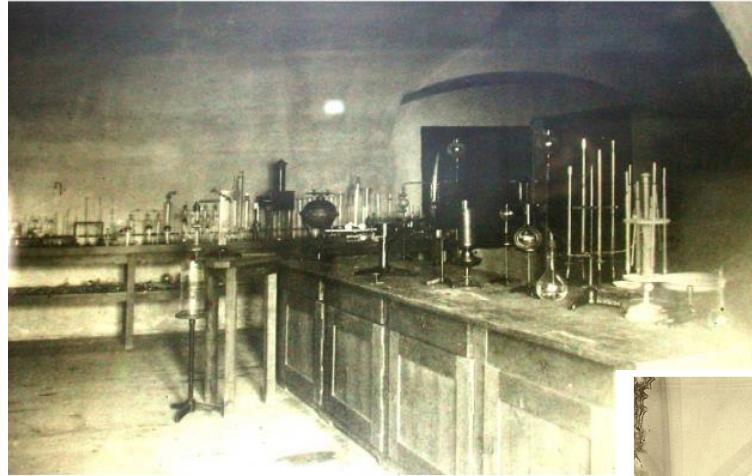
# 1874, Мишер, протамины



Нуклин это кислота, которая связана с основной молекулой, которую он назвал **протамином**. Нуклин с протамином составляют практически всю массу головки сперматозоида

В чистом нуклине из спермы лосося массовая доля P<sub>2</sub>O<sub>5</sub> 22.5%. (22.9% по текущим данным)

# Friedrich Miescher (1844 – 1895)



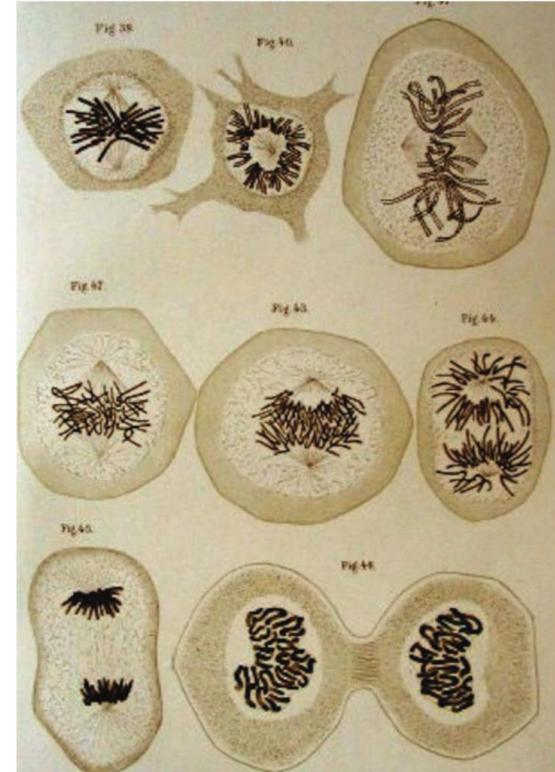
Тюбинген



(Dahm 2005)

# Флемминг, 1879, термин хроматин

Термин хроматин был предложен цитологом Вальтером Флеммингом в 1879-ом году. Флемминг был одним из пионеров микроскопической цитологии. Применив новые материалы (анилиновые краски) он выявил структуры клеток, которые интенсивно окрашивались, и потому были названы им хроматин (от древнегреческого χρῶμα «насыщенность цвета»). Он обнаружил, что хроматин содержит нитевидные структуры, названные позднее хромосомами (название было опубликовано в 1888 году Генрихом Вальдайером). Он обобщил накопленные к тому времени результаты, дополнив их своими открытиями, и в 1882 году опубликовал в пионерской работе «*Zellsubstanz, Kern und Zelltheilung*».



# Альбрехт Коссель (1853 - 1927)

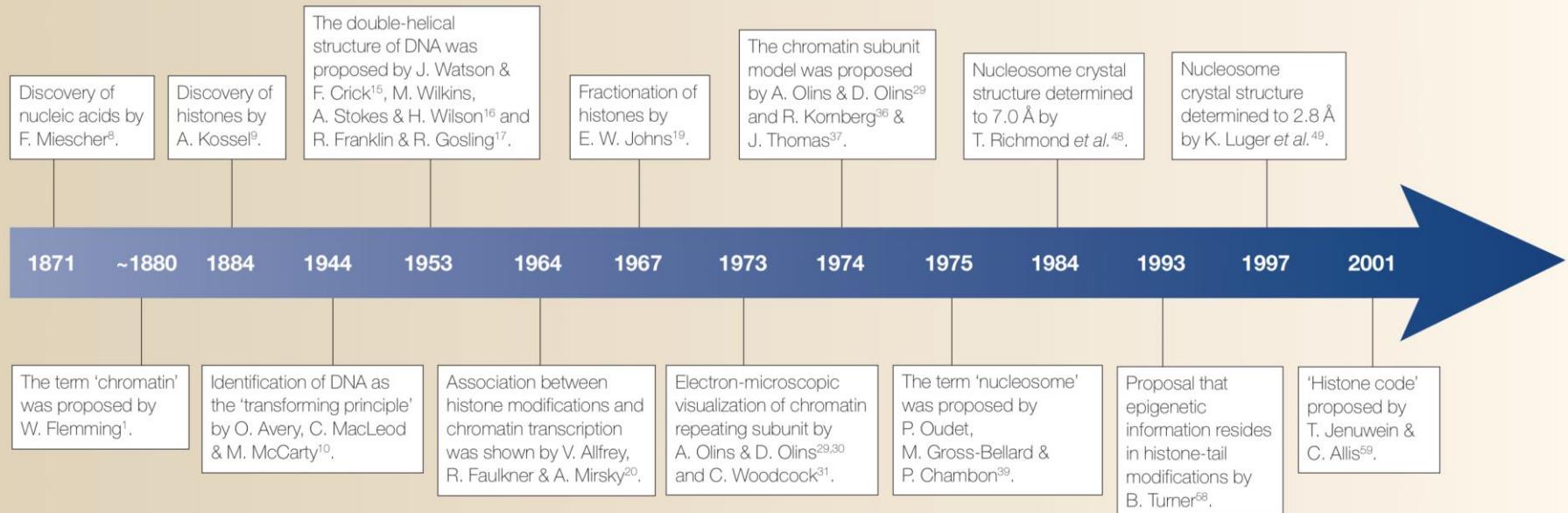
- Обнаружил белки **гистоны**, которые отличаются от протаминов (Kossel, 1884)
- Гистоны не во всех тканях
- Нобелевская премия по физиологии или медицине 10 декабря 1910 года за свои исследования клеточной биологии, химического состава клеточного ядра и за свою работу по выделению и описанию нуклеиновых кислот



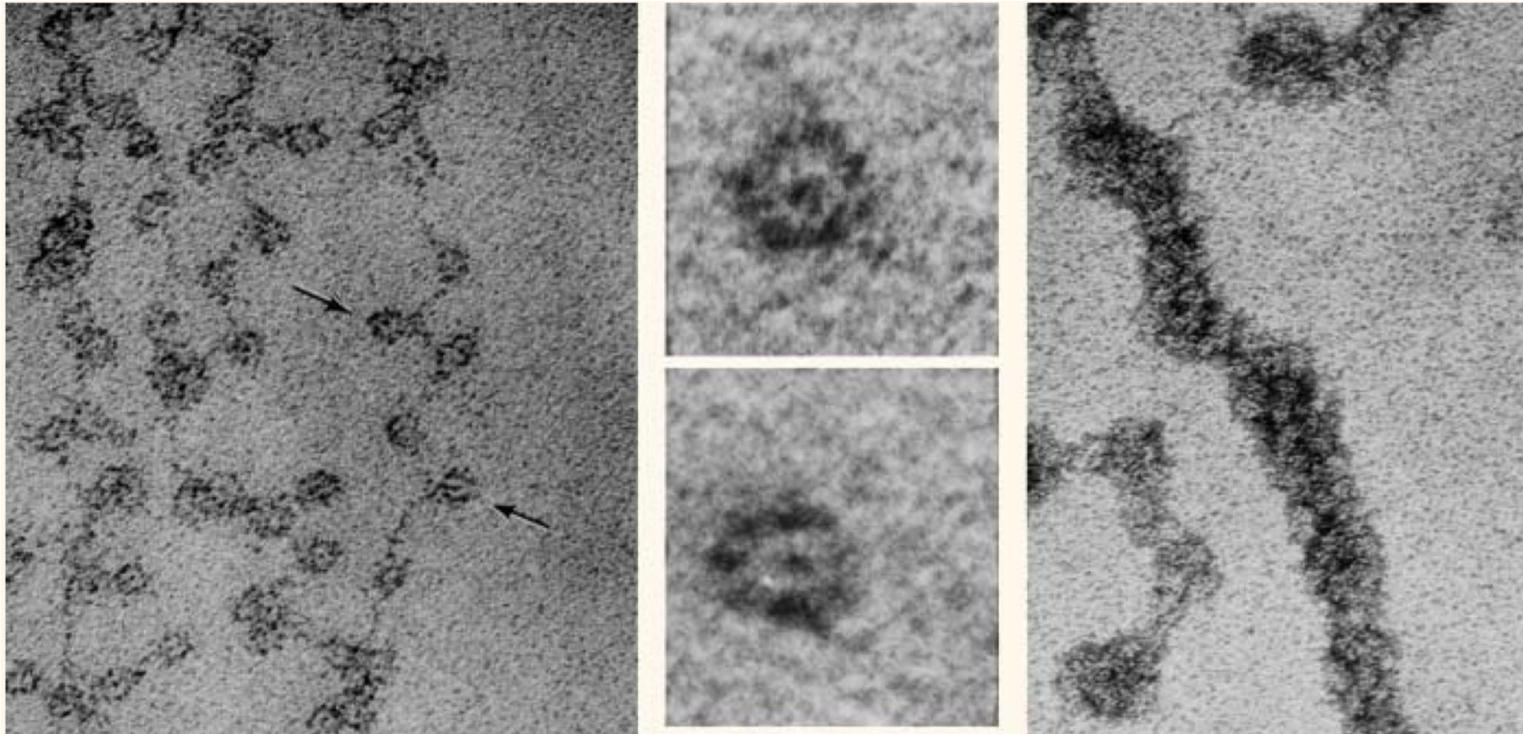
The word "histone" dates from the late 19th century and is derived from the German word "*Histon*", a word itself of uncertain origin, perhaps from Ancient Greek *ἵστημι* (hístēmi, “make stand”) or *ἱστός* (histós, “loom”)

# Немного истории ...

## Timeline | History of chromatin



# 1973 nu-bodies



Don and Ada Olins

Olins, D. E., & Olins, A. L. (2003). Chromatin history: our view from the bridge. *Nature Reviews Molecular Cell Biology*, 4(10), 809–814.

# 1974 nucleosome coposition

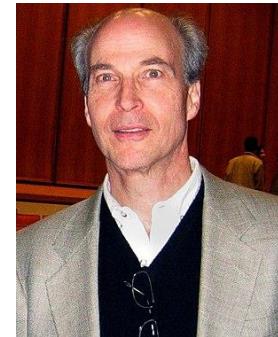
## Chromatin Structure: A Repeating Unit of Histones and DNA

Chromatin structure is based on a repeating unit of eight histone molecules and about 200 DNA base pairs.

These facts lead to two proposals:

- 1) Chromatin structure is based on a repeating unit of two each of F2A1, F3, F2A2, and F2B and about 200 base pairs of DNA.
- 2) A chromatin fiber consists of many such units forming a flexibly jointed chain.

Roger D. Kornberg

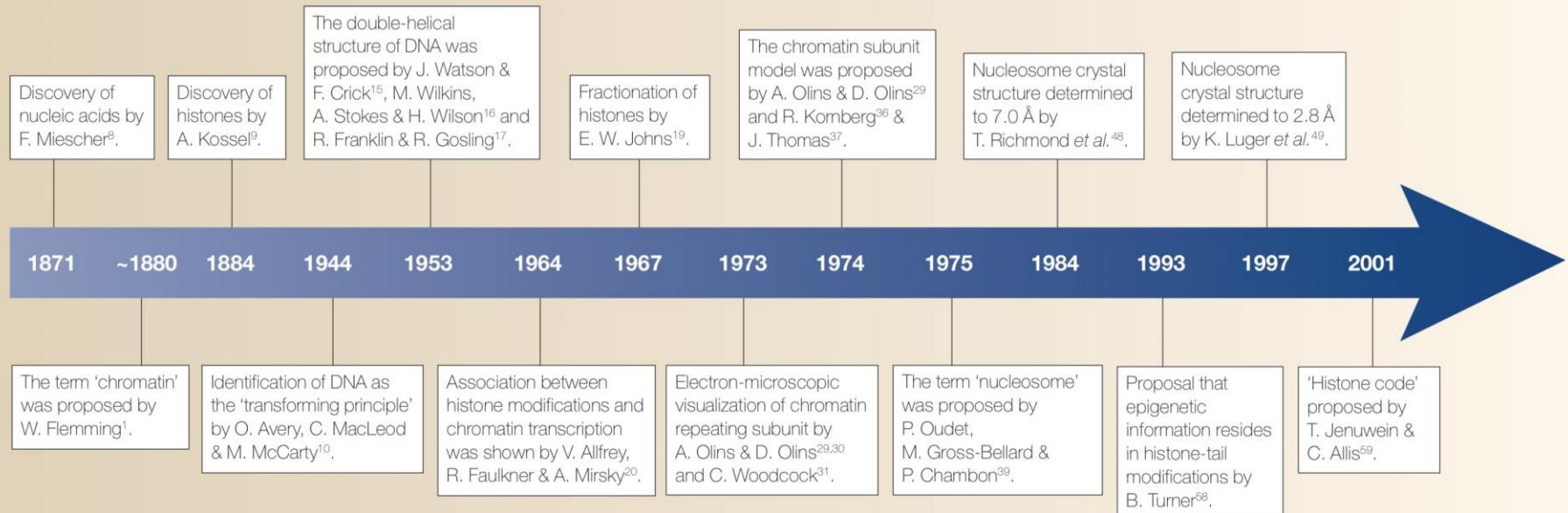


**Roger Kornberg**

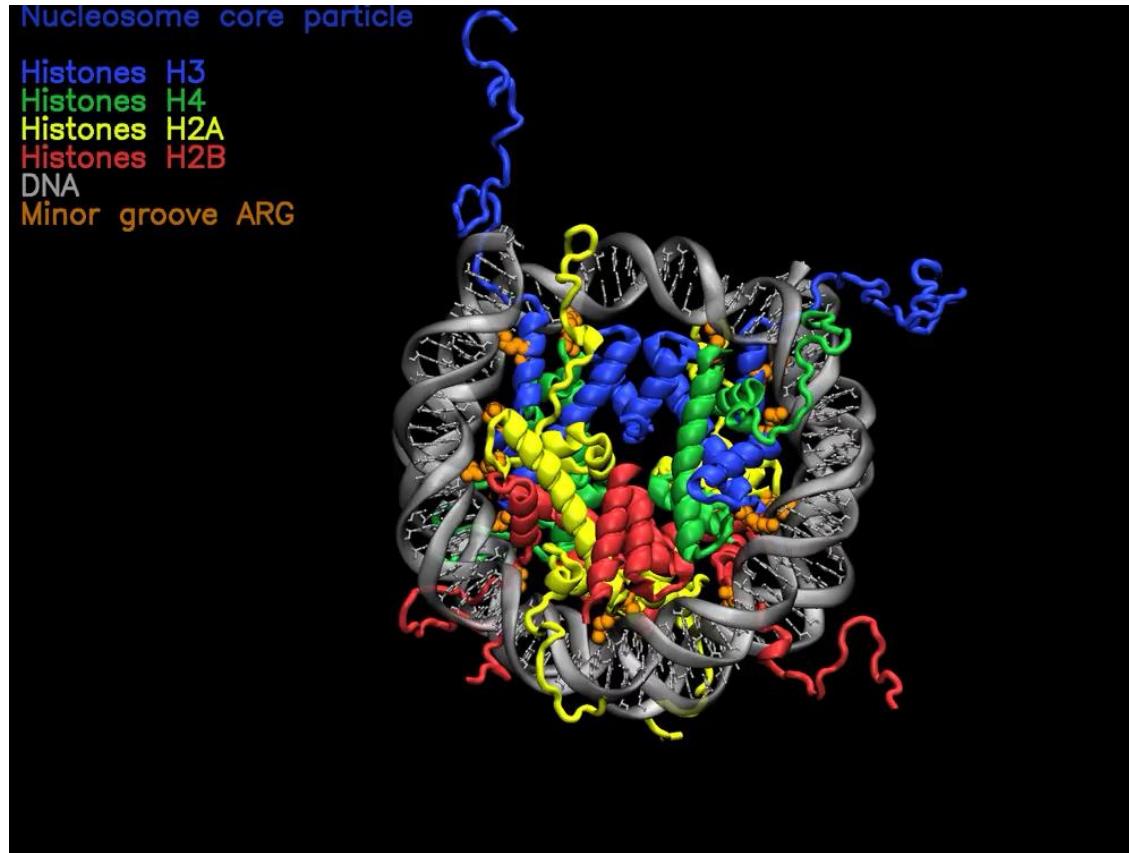
1.  
Kornberg R.D. Chromatin structure: a repeating unit of histones and DNA // Science. American Association for the Advancement of Science, 1974. Vol. 184, № 4139. P. 868–871.

# Немного истории ...

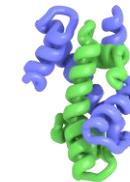
## Timeline | History of chromatin



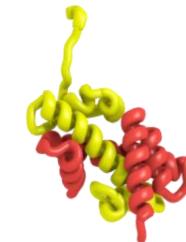
# Nucleosome core structure



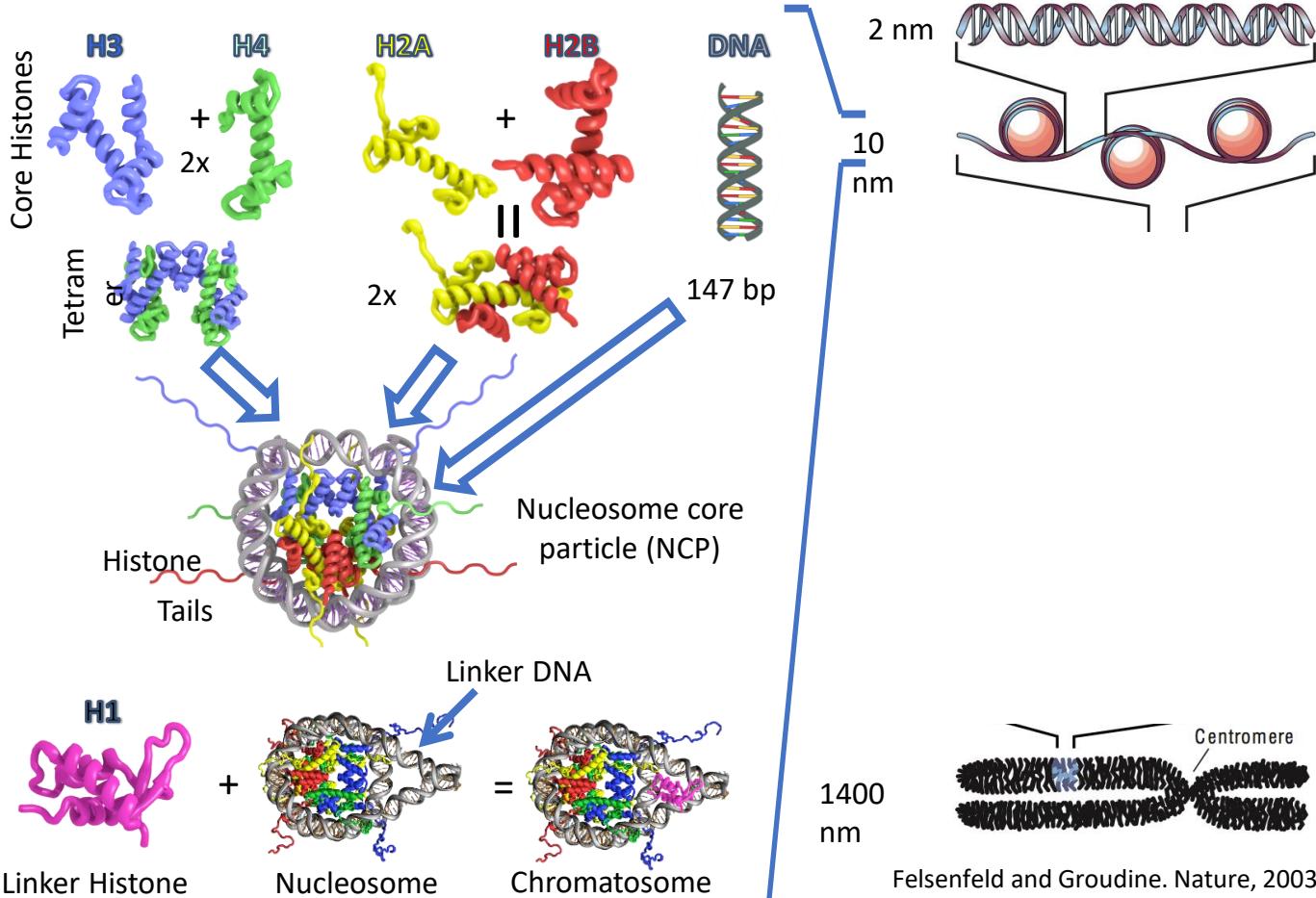
Histone H3-  
H4 dimer



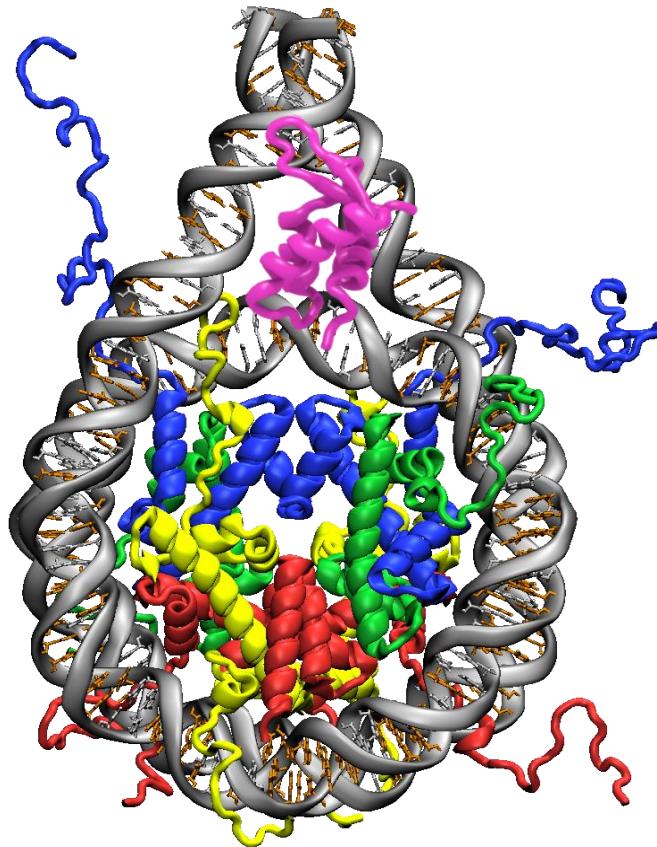
Histone H2A-  
H2B dimer



# Nucleosome structure



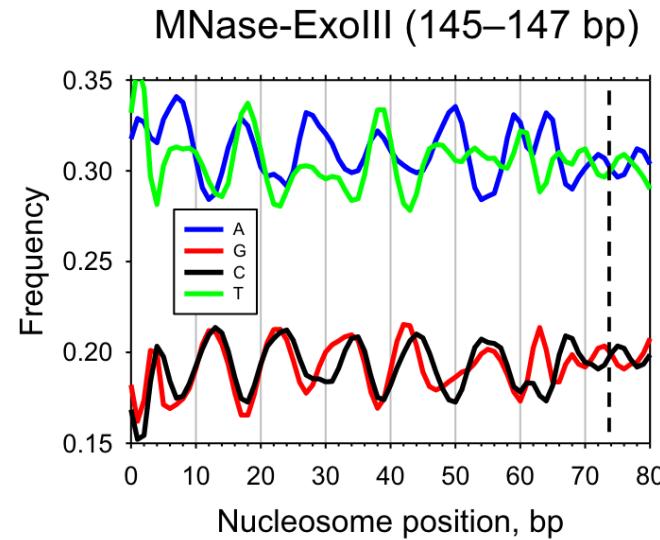
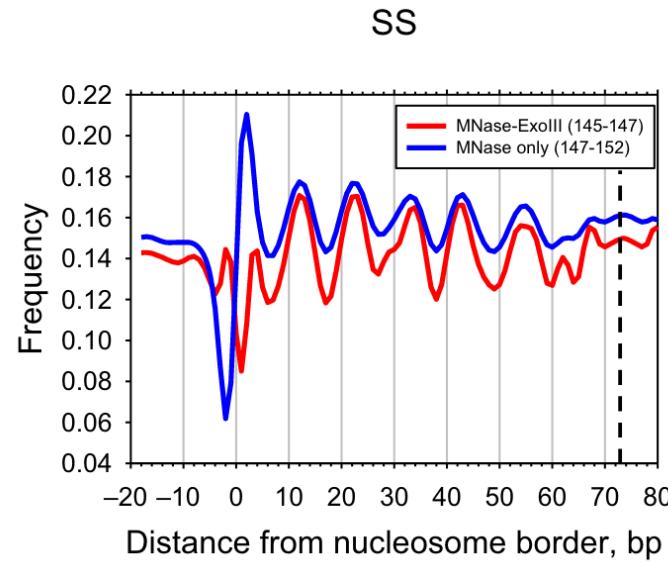
# Хроматосома



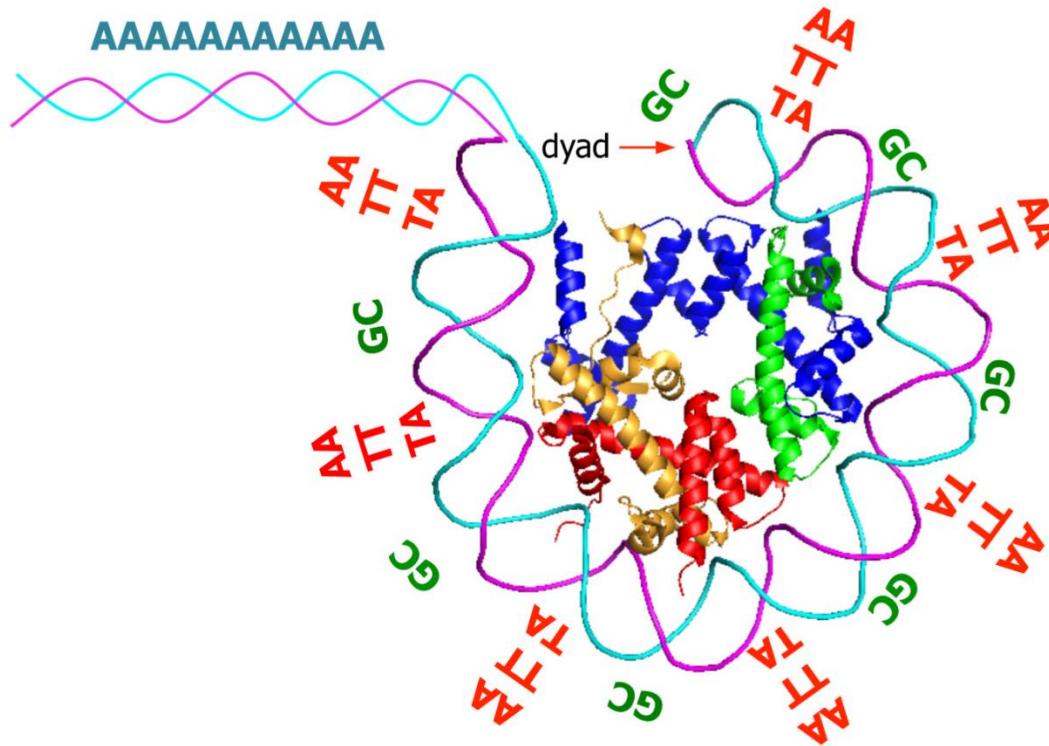


“Plastic” model of a nucleosome  
<https://github.com/molsim/nucLEGO>

# Позиционирование, эффекты indirect readout



Cole, H. A.; Cui, F.; Ocampo, J.; Burke, T. L.; Nikitina, T.; Nagarajavel, V.; Kotomura, N.; Zhurkin, V. B.; Clark, D. J. Novel Nucleosomal Particles Containing Core Histones and Linker DNA but No Histone H1. *Nucleic Acids Res* 2016, 44 (2), 573–581.  
<https://doi.org/10.1093/nar/gkv943>.

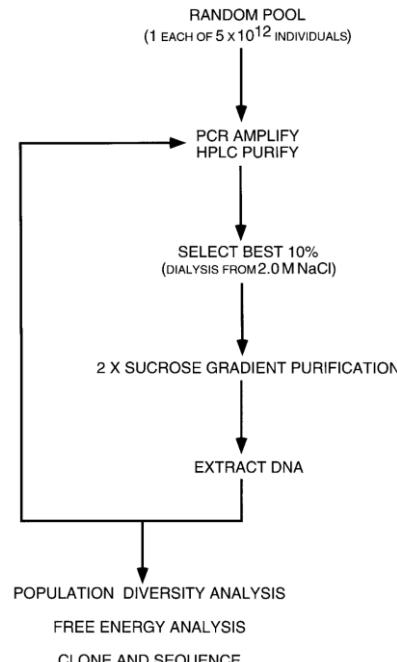


Struhl, K.; Segal, E. Determinants of Nucleosome Positioning.  
*Nat. Struct. Mol. Biol.* **2013**, 20 (3), 267–273.  
<https://doi.org/10.1038/nsmb.2506>.

# 601 Widom sequence – nucleosome positioning sequence

**Table 2.** Free energies of individual clones from round 15

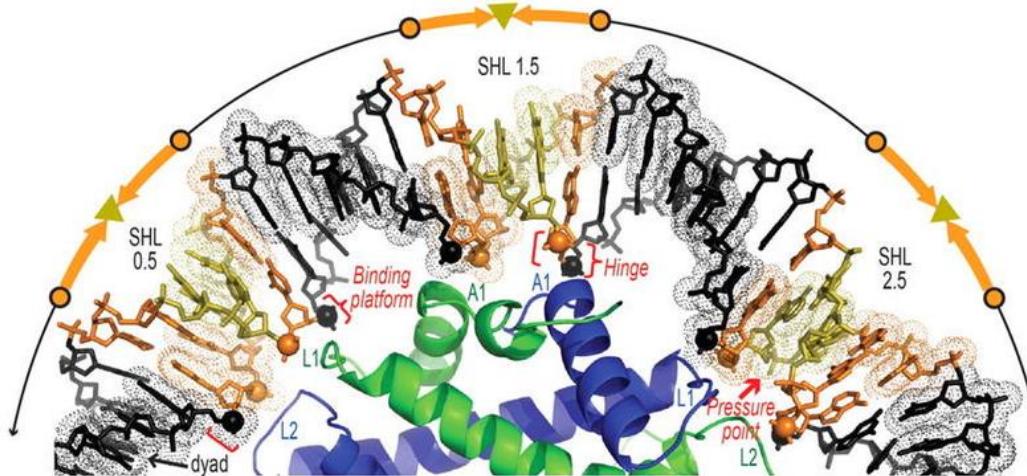
| Clone no. | $\Delta\Delta G^a$ (kcal mol $^{-1}$ )<br>relative to 5S molecule |
|-----------|---|
| 601       | $-2.9 \pm 0.33$ ( $n = 7$ )                                       |
| 603       | $-2.7 \pm 0.31$ ( $n = 6$ )                                       |
| 607       | $-2.5 \pm 0.32$ ( $n = 5$ )                                       |
| 611       | $-2.5 \pm 0.32$ ( $n = 5$ )                                       |
| 612       | $-2.1 \pm 0.48$ ( $n = 5$ )                                       |
| 613       | $-2.3 \pm 0.31$ ( $n = 5$ )                                       |
| 618       | $-2.3 \pm 0.31$ ( $n = 5$ )                                       |
| 623       | $-2.6 \pm 0.31$ ( $n = 6$ )                                       |
| 626       | $-2.8 \pm 0.31$ ( $n = 6$ )                                       |



Lowary, P. T. & Widom, J. New DNA sequence rules for high affinity binding to histone octamer and sequence-directed nucleosome positioning. *J. Mol. Biol.* **276**, 19–42 (1998).

# 601 Widom sequence – nucleosome positioning sequence

A

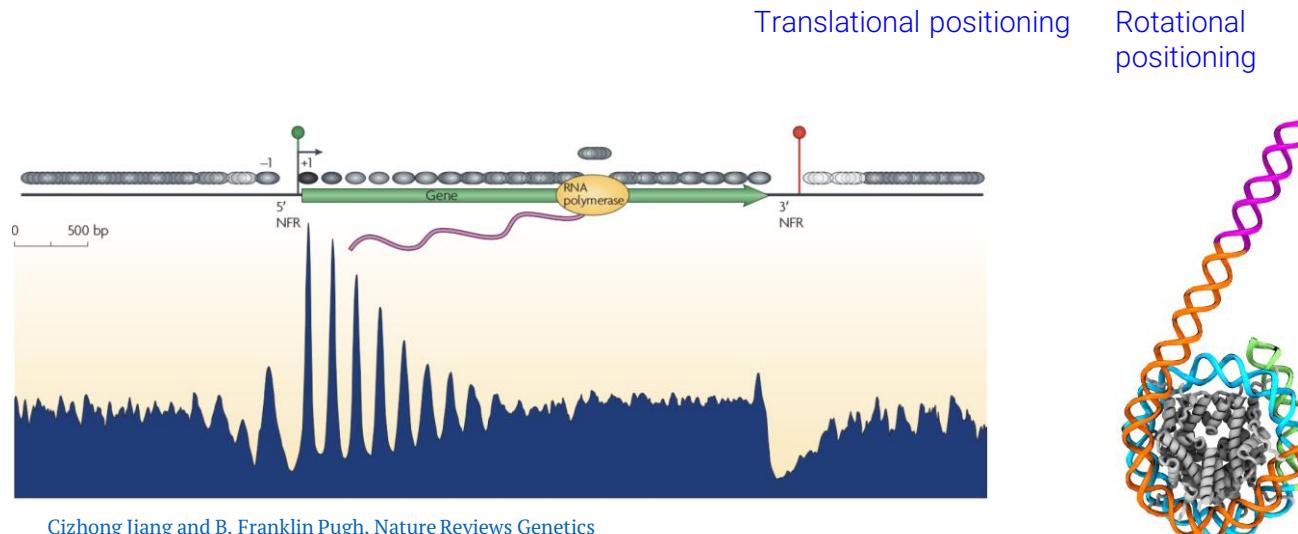
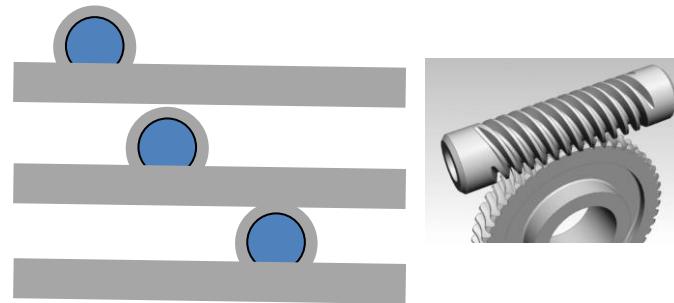


B

|                 | N-tail   | L2~L1 | A1~A1 | L1~L2 | L2~L1 | A1~A1 | L1~L2 | L2~L1 | A1~A1 | L1~L2 | A1~A1 | L1~L2 | N-tail |
|-----------------|--|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--------|
| SHL             | -6.5   | -5.5  | -4.5  | -3.5  | -2.5  | -1.5  | -0.5  | 0.5   | 1.5   | 2.5   | 3.5   | 4.5   | 6.5    |
| -70             | -60  | -50   | -40   | -30   | -20   | -10   | 0     | 10    | 20    | 30    | 40    | 50    | 60     |
| NCP146b         | ATCTCCAAATATCCCTTGGAGTC <sup>*</sup> AGTAATAAGTGCTCAAMCTGCGTTTCACGCCGGAATTCTACTGAATTCTGTGAAGTTTCCTTTGTATGCCAGTTGAGCTGACTTTCTCAGATCCAGGGATAATTGGAGAT            |       |       |       |       |       |       |       |       |       |       |       |        |
| NCP146          | ATCATATACTCAACTGCAGAGTTCTACCAAATGTTGATTTGGAAACTCTCTCATCAAATL <sup>*</sup> GGATGTTCAGCTGAATTCACTGGAGTGAACATGCCCTTTGTATGCCAGTTGAGCTGATATTGTAT                    |       |       |       |       |       |       |       |       |       |       |       |        |
| NCP147          | ATCAATACTCAACTGCAGAGTACTACCAAATGTTGATTTGGAAACTCTCTCATCAAATL <sup>*</sup> GGATGTTCAGCTGAACATGCCCTTTGTATGCCAGTTGAGCTGACTTTCTAACATACCTTTGTAGTAATGCCAGGTGATATTGTAT |       |       |       |       |       |       |       |       |       |       |       |        |
| NCP145          | ATCAATACTCAACTGCAGAGTACTACCAAATGTTGATTTGGAAACTCTCTCATCAAATL <sup>*</sup> GGATGTTCAGCTGAACATGCCCTTTGTATGCCAGTTGAGCTGACTTTCTAACATACCTTTGTAGTAATGCCAGGTGATATTGTAT |       |       |       |       |       |       |       |       |       |       |       |        |
| NCP-TA2         | ATCAATACTCAACTGCAGAGTACTACCAAATGTTGATTTGGAAACTCTCTCATCAAATL <sup>*</sup> GGATGTTCAGCTGAACATGCCCTTTGTATGCCAGTTGAGCTGACTTTCTAACATACCTTTGTAGTAATGCCAGGTGATATTGTAT |       |       |       |       |       |       |       |       |       |       |       |        |
| NCP-TA          | ATCAATACTCAACTGCAGAGTACTACCAAATGTTGATTTGGAAACTCTCTCATCAAATL <sup>*</sup> GGATGTTCAGCTGAACATGCCCTTTGTATGCCAGTTGAGCTGACTTTCTAACATACCTTTGTAGTAATGCCAGGTGATATTGTAT |       |       |       |       |       |       |       |       |       |       |       |        |
| NCP-601R        | ATCGATGAAATATCCCTGCAAGCTC <sup>*</sup> GGAGCTGGGGGTAAATCCCTTGCGGTAAACCGGGGGGGGAATCCTCCCCCGCGTTAAACCGCCAGGGGATTACCTAGCTCCAGCACCGTGTACATATAATTCATCGAT            |       |       |       |       |       |       |       |       |       |       |       |        |
| NCP-601         | ATCAAGATCCGGTGGCGGGCGCTTAAATTCGGSTGTTGACACGCTCTAGCACCGCTTAAACCGACGTAAACCGCGTTCGGCGGTAAACCGCCAGGGGATTACCTAGCTCCAGCACCGTGTACATATAATTCATCGAT                      |       |       |       |       |       |       |       |       |       |       |       |        |
| NCP-601L        | ATCACAAATCCGGTGGCGGGCGCTTAAATTCGGSTGTTGACACGCTCTAGCACCGCTTAAACCGACGTAAACCGCGTTCGGCGGTAAACCGCCAGGGGATTACCTAGCTCCAGCACCGTGTACATATAATTCATCGAT                     |       |       |       |       |       |       |       |       |       |       |       |        |
| Widom consensus | tgcaaggctCTAGtggtgcGTTAAAcgGctgttagccGacCggTTAAACGccacCTAGtgctcgcf   |       |       |       |       |       |       |       |       |       |       |       |        |

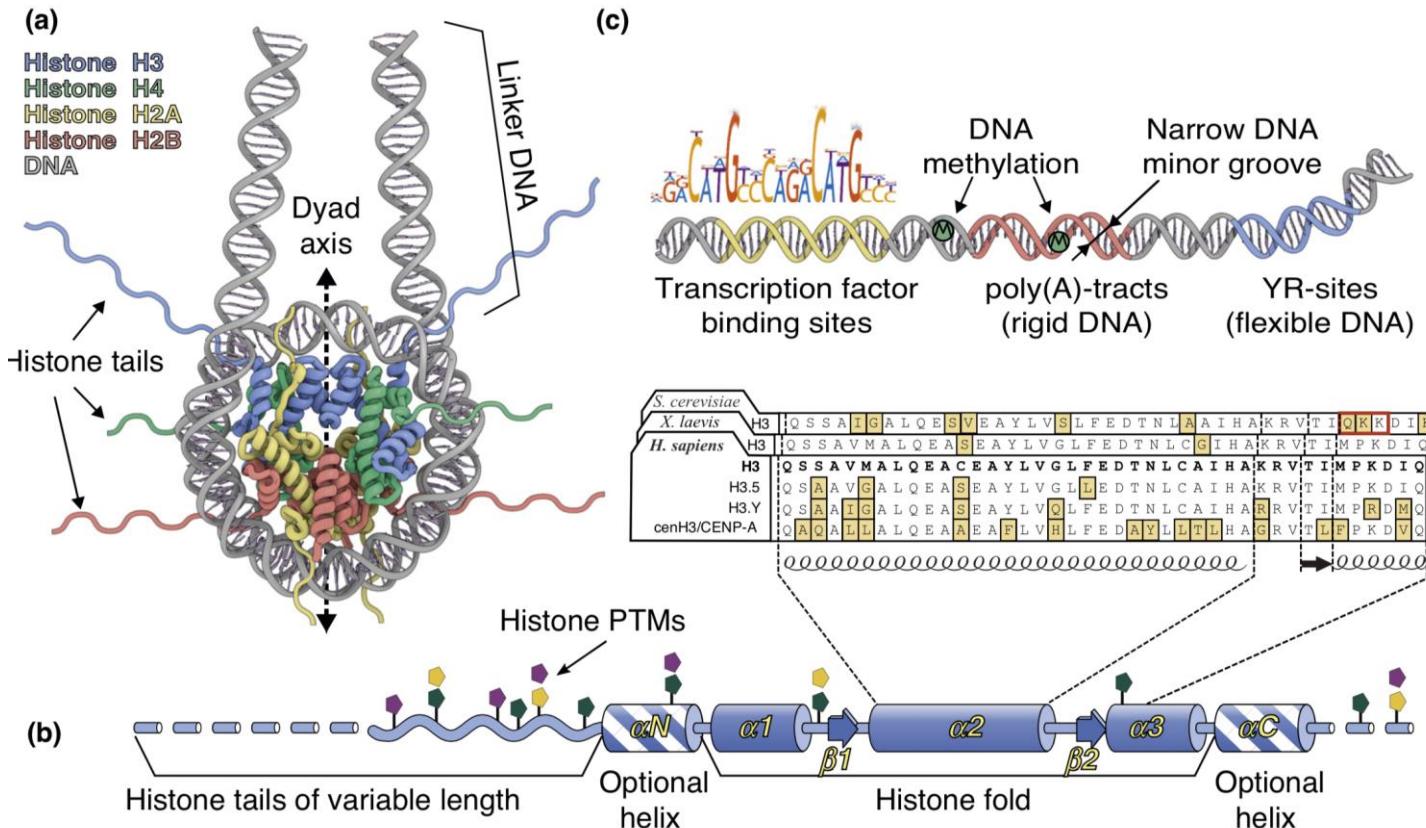
## Nucleosome sliding and positioning

- Nucleosome positioning is important for:
  - Gene expression
  - Binding of TF (including pioneer factors)
- Shifting DNA by 1 bp rotates DNA by 36 degrees



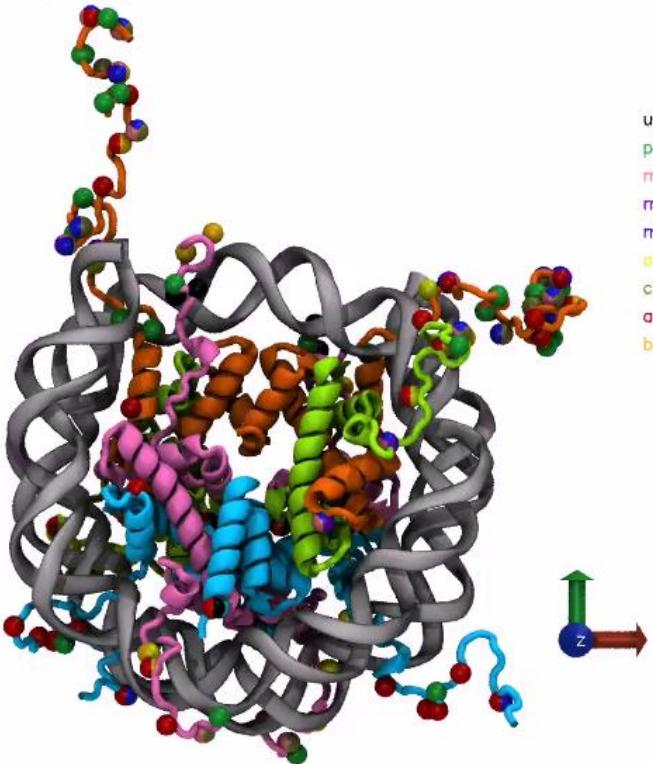
Cizhong Jiang and B. Franklin Pugh, Nature Reviews Genetics

# Nucleosome compositional variability



# Histone post-translational modifications

Nucleosome structure (1KX5)



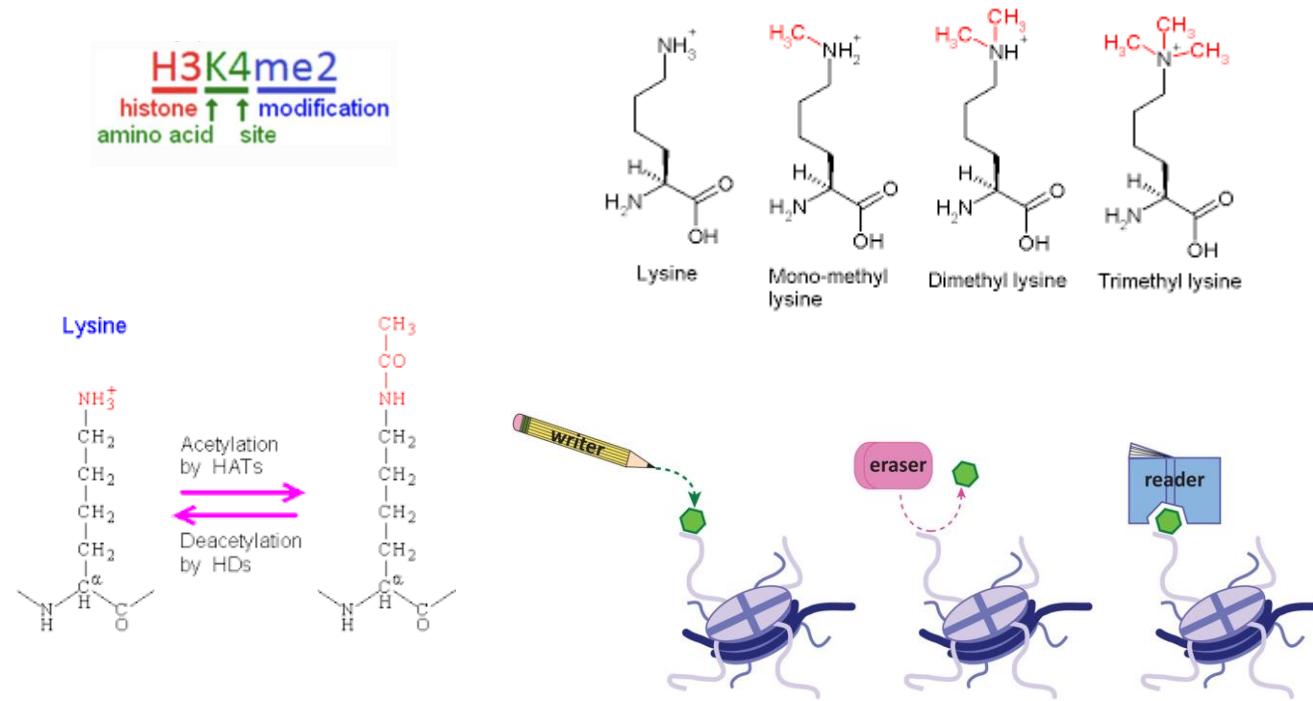
z

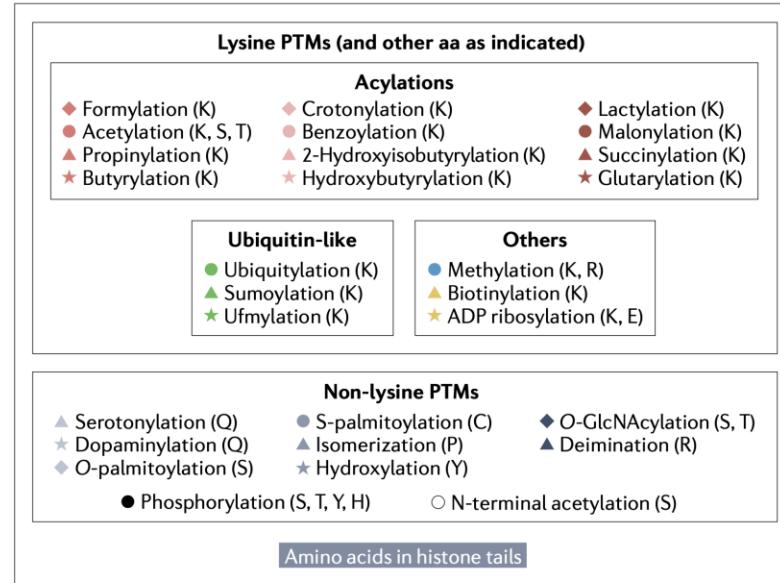
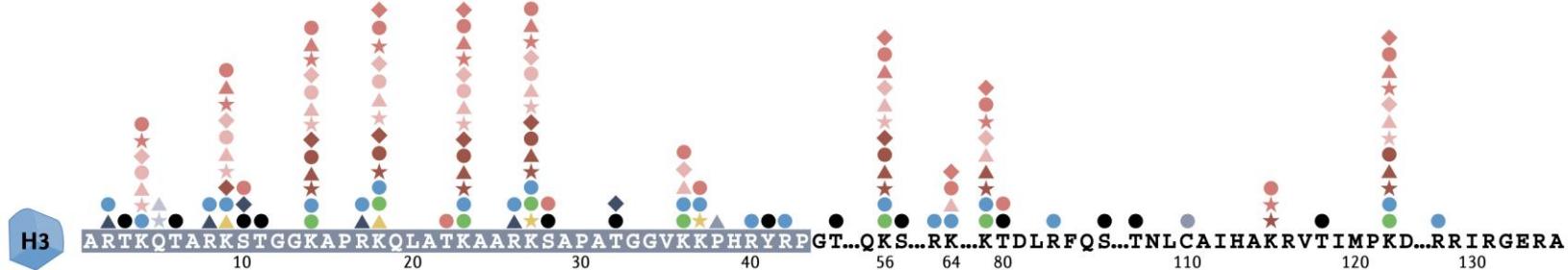
z

z

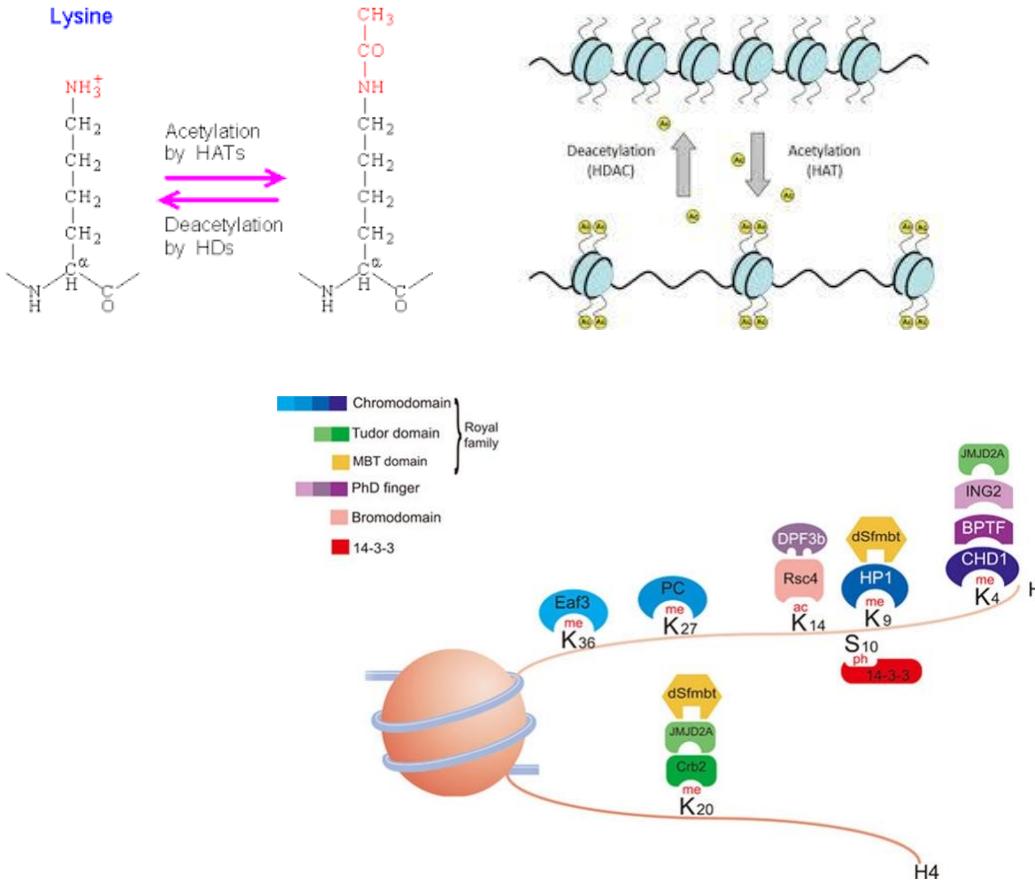
| H2A        | H2B        | H3       | H4       |
|------------|------------|----------|----------|
| H2AS1ph    | H2BK5ac    | H3R2me1  | H4S1ph   |
| H2AR3me2   | H2BK5me1   | H3R2ci   | H4R3me1  |
| H2AR3ci    | H2BK12ac   | H3T3ph   | H4R3ci   |
| H2AK5oc    | H2BS14ph   | H3K4ac   | H4K5ac   |
| H2AK9ac    | H2BK15ac   | H3K4me1  | H4K8ac   |
| H2AK9bio   | H2BK16ac   | H3K4me2  | H4K8bio  |
| H2AK13bio  | H2BK20ac   | H3K4me3  | H4K12ac  |
| H2AK13ar   | H2BK30ar   | H3S6ph   | H4K12bio |
| H2AK119ub  | H2BK46ac   | H3T6ph   | H4K16ac  |
| H2AT120ph  | H2BK120ac  | H3R8ci   | H4K16ar  |
| H2AK121ub  | H2BK120ub  | H3K9ac   | H4K20me1 |
| H2AK125bio | H2AK127bio | H3K9me1  | H4K20me2 |
| H2AK129bio | H2AS137ph  | H3K9me2  | H4K20me3 |
| H2AS139ph  | H2AS139ph  | H3K9me3  | H4K91ac  |
|            | H2AY142ph  | H3K9bio  | H4K91ub  |
|            |            | H3S10ph  |          |
|            |            | H3T11ph  |          |
|            |            | H3K14ac  |          |
|            |            | H3R17me1 |          |
|            |            | H3R17me2 |          |
|            |            | H3R17ci  |          |
|            |            | H3K18oc  |          |
|            |            | H3K18bio |          |
|            |            | H3K23ac  |          |
|            |            | H3R26me1 |          |
|            |            | H3R26ci  |          |
|            |            | H3K27ac  |          |
|            |            | H3K27me1 |          |
|            |            | H3K27me2 |          |
|            |            | H3K27me3 |          |
|            |            | H3K27ar  |          |
|            |            | H3S28ph  |          |
|            |            | H3S31ph  |          |
|            |            | H3K36ac  |          |
|            |            | H3K36me3 |          |
|            |            | H3K36me1 |          |
|            |            | H3K36me2 |          |
|            |            | H3K37ar  |          |
|            |            | H3Y41ph  |          |
|            |            | H3T45ph  |          |
|            |            | H3K56ac  |          |
|            |            | H3K79me1 |          |
|            |            | H3K79me2 |          |

# Histone post-translational modifications





# Effects of histone PTMs



Influence through changes in physical interactions

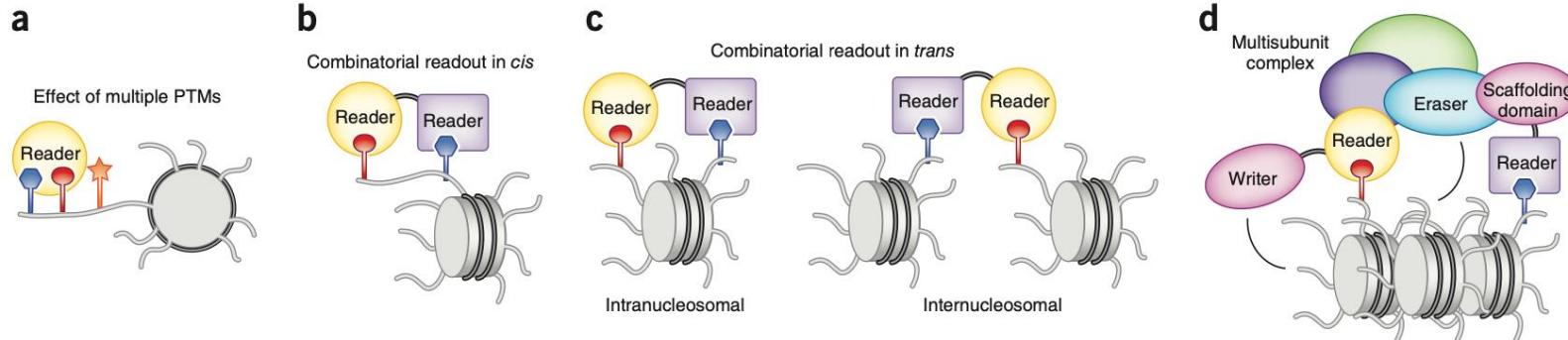
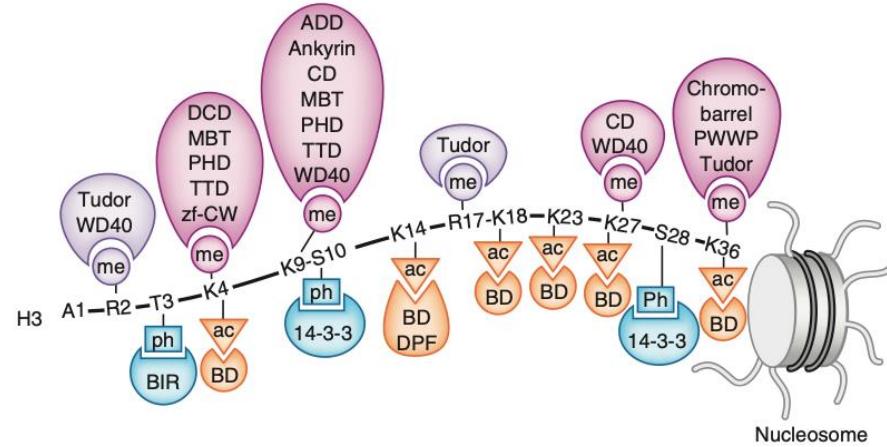
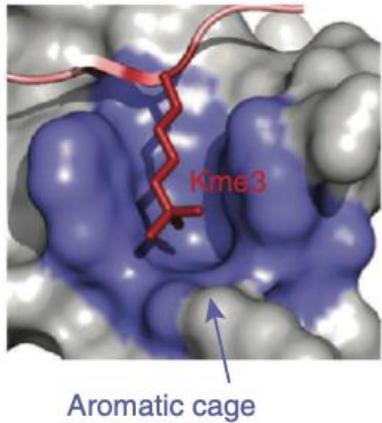
Influence through "effector" domains and proteins

**Table 1 Histone readers and their target PTMs**

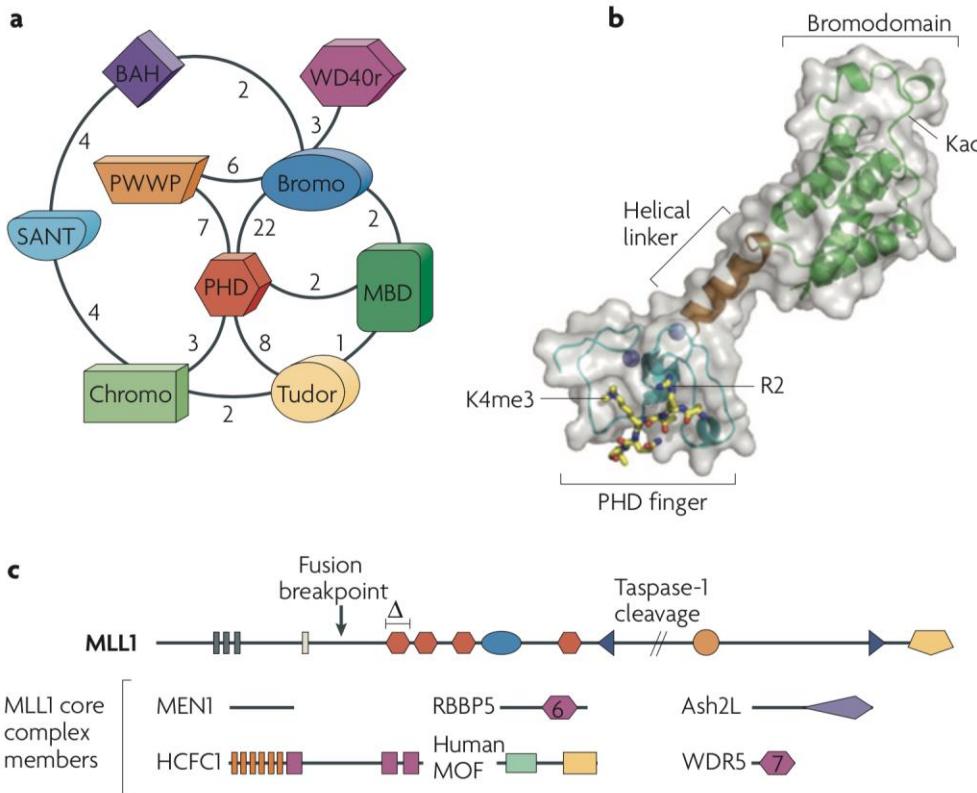
| Recognition of                    | Reader        | Histone PTM                            |
|-----------------------------------|---------------|--|
| Methyllysine                      | ADD           | H3K9me3                                |
|                                   | Ankyrin       | H3K9me2, H3K9me1                       |
|                                   | BAH           | H4K20me2                               |
|                                   | Chromo-barrel | H3K36me3, H3K36me2, H4K20me1, H3K4me1  |
|                                   | Chromodomain  | H3K9me3, H3K9me2, H3K27me3, H3K27me2   |
|                                   | DCD           | H3K4me3, H3K4me2, H3K4me1              |
|                                   | MBT           | H3Kme1, H3Kme2, H4Kme1, H4Kme2         |
|                                   | PHD           | H3K4me3, H3K4me2, H3K9me3              |
|                                   | PWWP          | H3K36me3, H4K20me1, H4K20me3, H3K79me3 |
|                                   | TTD           | H3K4me3, H3K9me3, H4K20me2             |
|                                   | Tudor         | H3K36me3                               |
|                                   | WD40          | H3K27me3, H3K9me3                      |
|                                   | zf-CW         | H3K4me3                                |
| Methylarginine                    | ADD           | H4R3me2s                               |
|                                   | Tudor         | H3Rme2, H4Rme2                         |
|                                   | WD40          | H3R2me2                                |
| Acetyllysine                      | Bromodomain   | H3Kac, H4Kac, H2AKac, H2BKac           |
|                                   | DBD           | H3KacKac, H4KacKac                     |
|                                   | DPF           | H3Kac                                  |
|                                   | Double PH     | H3K56ac                                |
| Phosphoserine or phosphothreonine | 14-3-3        | H3S10ph, H3S28ph                       |
|                                   | BIR           | H3T3ph                                 |
|                                   | Tandem BRCT   | H2AXS139ph                             |
| Unmodified histone                | ADD           | H3un                                   |
|                                   | PHD           | H3un                                   |
|                                   | WD40          | H3un                                   |

# Chromatin readers

Kme3-binding pocket



# Effector domains



Ruthenburg, A. J., et al. (2007). "Multivalent engagement of chromatin modifications by linked binding modules." Nat Rev Mol Cell Biol 8(12): 983-994.

# Human histones (~ 100 genes)

<https://histdb.intbio.org/human/>

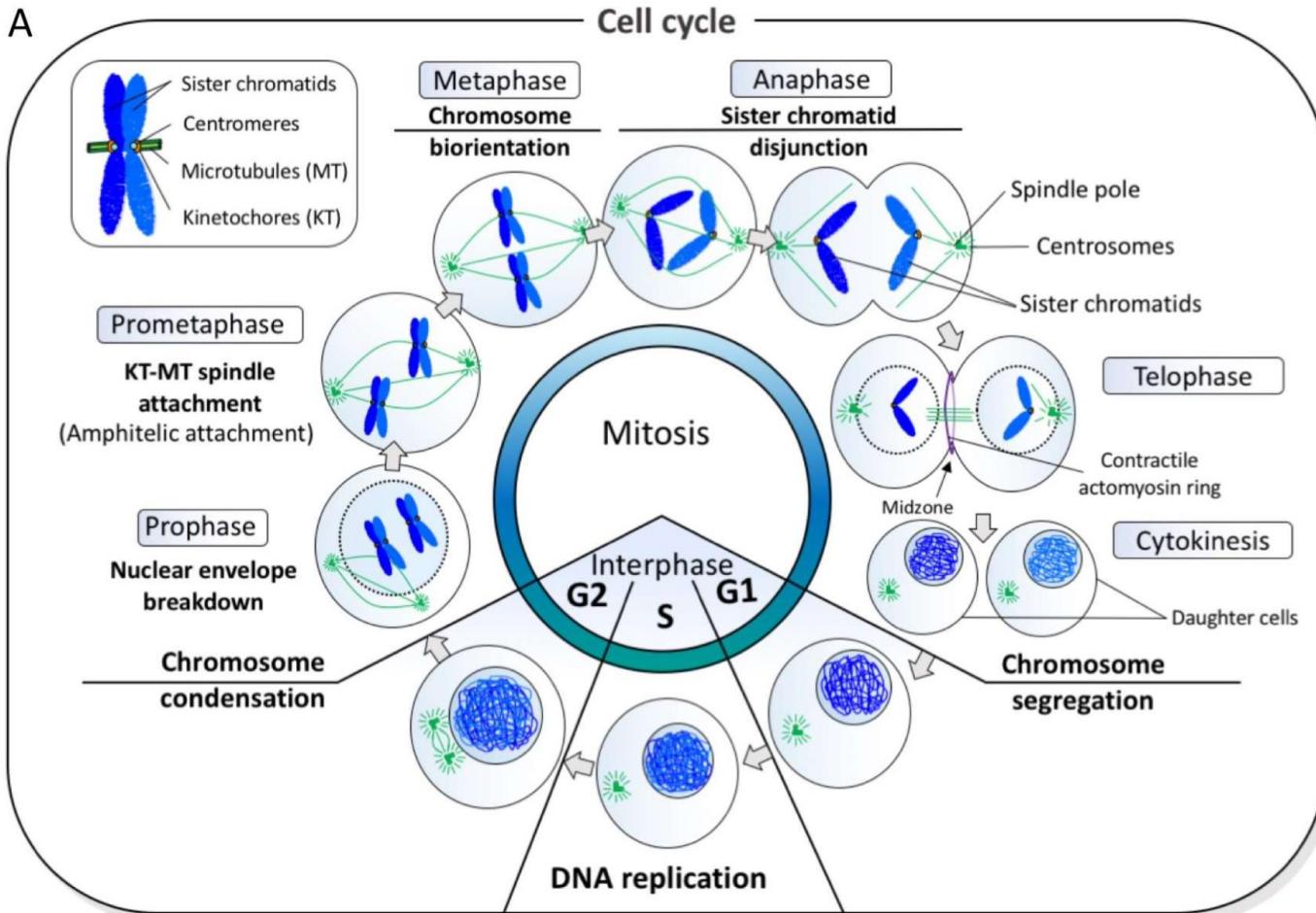
| Histone type | Histone variant | Canonical isoform | HGNC symbol | NCBI gene ID | H2A TS H2A.1      | H2AC1      | 221613 | H2B TS H2B.1    | H2BC1             | 255626     | H3 canonical H3.1 | isoform_1 | H3C1               | 8350      | H4 canonical H4 | isoform_1 | H4C1            | 8359      |       |        |  |
|--------------|-----------------|-------------------|-------------|--------------|-------------------|------------|--------|-----------------|-------------------|------------|-------------------|-----------|--------------------|-----------|-----------------|-----------|-----------------|-----------|-------|--------|--|
| H1           | H1.0            | H1-0              |             | 3005         | H2A canonical H2A | isoform_2  | H2AC4  | 8335            | H2B canonical H2B | isoform_8  | H2BC3             | 3018      | H3 canonical H3.1  | isoform_1 | H3C2            | 8358      | H4 canonical H4 | isoform_1 | H4C2  | 8366   |  |
| H1           | H1.1            | H1-1              |             | 3024         | H2A canonical H2A | isoform_7  | H2AC6  | 8334            | H2B canonical H2B | isoform_1  | H2BC4             | 8347      | H3 canonical H3.1  | isoform_1 | H3C3            | 8352      | H4 canonical H4 | isoform_1 | H4C3  | 8364   |  |
| H1           | H1.2            | H1-2              |             | 3006         | H2A canonical H2A | isoform_9  | H2AC7  | 3013            | H2B canonical H2B | isoform_11 | H2BC5             | 3017      | H3 canonical H3.1  | isoform_1 | H3C4            | 8351      | H4 canonical H4 | isoform_1 | H4C4  | 8360   |  |
| H1           | H1.3            | H1-3              |             | 3007         | H2A canonical H2A | isoform_2  | H2AC8  | 3012            | H2B canonical H2B | isoform_1  | H2BC6             | 8344      | H3 canonical H3.1  | isoform_1 | H3C6            | 8353      | H4 canonical H4 | isoform_1 | H4C5  | 8367   |  |
| H1           | H1.4            | H1-4              |             | 3008         | H2A canonical H2A | isoform_1  | H2AC11 | 8969            | H2B canonical H2B | isoform_1  | H2BC7             | 8343      | H3 canonical H3.1  | isoform_1 | H3C7            | 8968      | H4 canonical H4 | isoform_1 | H4C6  | 8361   |  |
| H1           | H1.5            | H1-5              |             | 3009         | H2A canonical H2A | isoform_10 | H2AC12 | 85235           | H2B canonical H2B | isoform_1  | H2BC8             | 8339      | H3 canonical H3.1  | isoform_1 | H3C8            | 8355      | H4 canonical H4 | isoform_2 | H4C7  | 8369   |  |
| H1           | TS H1.6         | H1-6              |             | 3010         | H2A canonical H2A | isoform_1  | H2AC13 | 8329            | H2B canonical H2B | isoform_2  | H2BC9             | 8345      | H3 canonical H3.1  | isoform_1 | H3C10           | 8357      | H4 canonical H4 | isoform_1 | H4C8  | 8365   |  |
| H1           | TS H1.7         | H1-7              |             | 341567       | H2A canonical H2A | isoform_8  | H2AC14 | 8331            | H2B canonical H2B | isoform_1  | H2BC10            | 8346      | H3 canonical H3.1  | isoform_1 | H3C11           | 8354      | H4 canonical H4 | isoform_1 | H4C9  | 8294   |  |
| H1           | OO H1.8         | H1-8              |             | 132243       | H2A canonical H2A | isoform_1  | H2AC15 | 8330            | H2B canonical H2B | isoform_4  | H2BC11            | 8970      | H3 canonical H3.1  | isoform_1 | H3C12           | 8356      | H4 canonical H4 | isoform_1 | H4C10 | 8363   |  |
| H1           | OO H1.8         | H1-8              |             | 132243       | H2A canonical H2A | isoform_1  | H2AC17 | 8336            | H2B canonical H2B | isoform_4  | H2BC11            | 8970      | H3 canonical H3.1  | isoform_1 | H3C13           | 653604    | H4 canonical H4 | isoform_1 | H4C13 | 8368   |  |
| H1           | TS H1.9(?)      | H1-9P             |             | 373861       | H2A canonical H2A | isoform_3  | H2AC18 | 8337            | H2B canonical H2B | isoform_9  | H2BC11            | 8970      | H3 canonical H3.2  | isoform_1 | H3C14           | 126961    | H4 canonical H4 | isoform_1 | H4C14 | 8370   |  |
| H1           | H1.10           | H1-10             |             | 8971         | H2A canonical H2A | isoform_3  | H2AC19 | 723790          | H2B canonical H2B | isoform_12 | H2BC12            | 85236     | H3 canonical H3.2  | isoform_1 | H3C15           | 333932    | H4 canonical H4 | isoform_1 | H4C15 | 554313 |  |
|              |                 |                   |             |              | H2A canonical H2A | isoform_6  | H2AC20 | 8338            | H2B canonical H2B | isoform_7  | H2BC13            | 8340      | H3 H3.Y1           | H3Y1      | 391769          |           | H4 canonical H4 | isoform_1 | H4-16 | 121504 |  |
|              |                 |                   |             |              | H2A canonical H2A | isoform_4  | H2AC21 | 317772          | H2B canonical H2B | isoform_5  | H2BC14            | 8342      | H3 H3.Y2           | H3Y2      | 340096          |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.J(?)      | H2AJ       |        | 55766           | H2B canonical H2B | isoform_10 | H2BC15            | 8341      | H3 canonical H3(?) | H3-2      | 440686          |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A canonical H2A | isoform_5  | H2AW   | 92815           | H2B canonical H2B | isoform_14 | H2BC15            | 8341      | H3 H3.3            | H3-3A     | 3020            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2AX          | H2AX       |        | 3014            | H2B canonical H2B | isoform_10 | H2BC15            | 8341      | H3 H3.3            | H3-3A     | 3020            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.Z1        | H2AZ1      |        | 3015            | H2B canonical H2B | isoform_14 | H2BC15            | 8341      | H3 H3.3            | H3-3A     | 3020            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.Z1        | H2AZ1      |        | 3015            | H2B canonical H2B | isoform_15 | H2BC17            | 8348      | H3 H3.3            | H3-3B     | 3021            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.Z2        | H2AZ2      |        | 94239           | H2B canonical H2B | isoform_6  | H2BC18            | 440689    | H3 H3.3            | H3-3B     | 3021            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.Z2        | H2AZ2      |        | 94239           | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 H3.3            | H3-3B     | 3021            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.Z2        | H2AZ2      |        | 94239           | H2B canonical H2B | isoform_6  | H2BC18            | 440689    | H3 H3.3            | H3-3B     | 3021            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.Z2        | H2AZ2      |        | 94239           | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 H3.4            | H3-4      | 8290            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A macroH2A.1    | macroH2A.1 |        | MACROH2A1 9555  | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 H3.5            | H3-5      | 440093          |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A macroH2A.1    | macroH2A.1 |        | MACROH2A1 9555  | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A macroH2A.1    | macroH2A.1 |        | MACROH2A1 9555  | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A macroH2A.1    | macroH2A.1 |        | MACROH2A1 9555  | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A macroH2A.1    | macroH2A.1 |        | MACROH2A1 9555  | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A macroH2A.2    | macroH2A.2 |        | MACROH2A2 55506 | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A macroH2A.2    | macroH2A.2 |        | MACROH2A2 55506 | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.B.1       | H2AB1      |        | 474382          | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.B.2       | H2AB2      |        | 474381          | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.B.2       | H2AB2      |        | 83740           | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2A H2A.P         | H2AP       |        | 25763           | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |
|              |                 |                   |             |              | H2B TS H2B.1      | H2BC1      |        | 255626          | H2B canonical H2B | isoform_13 | H2BC18            | 440689    | H3 cenH3           | CENPA     | 1058            |           |                 |           |       |        |  |

Epigenetics & Chromatin

A standardized nomenclature  
for mammalian histone genes

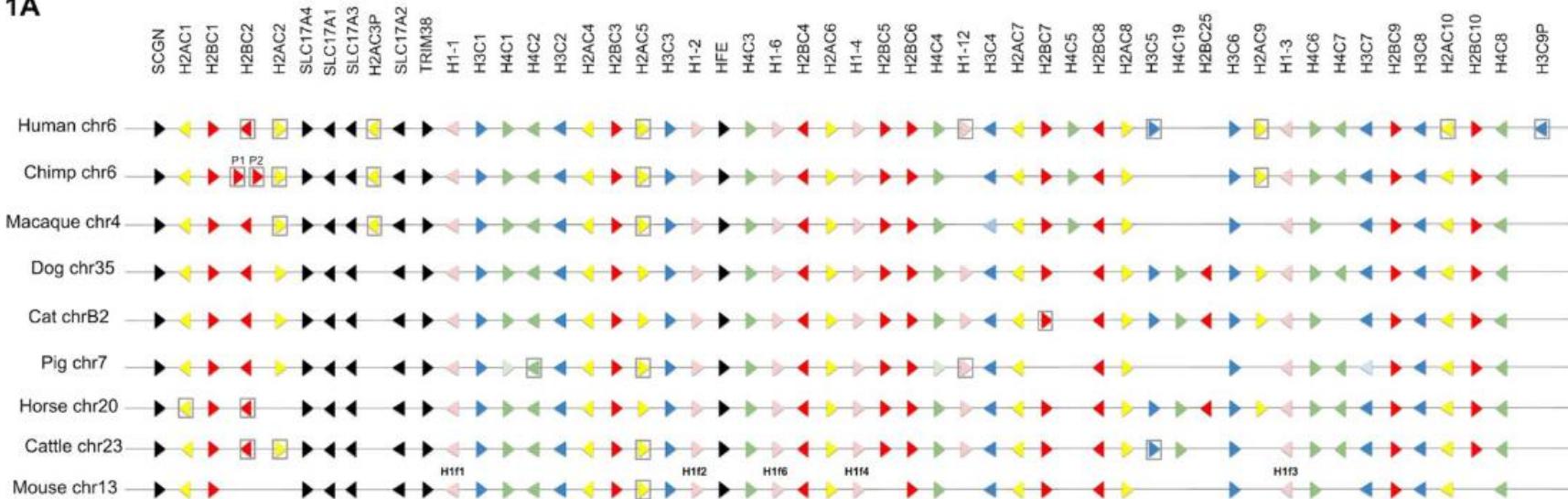
Ruth L. Seal<sup>1,2\*</sup>, Paul Denny<sup>1</sup>, Elspeth A. Bruford<sup>1,2</sup>, Anna K. Gribkova<sup>3</sup>, David Landsman<sup>4</sup>, William F. Marzluff<sup>5</sup>, Monica McAndrews<sup>6</sup>, Anna R. Panchenko<sup>7</sup>, Alexey K. Shaytan<sup>3</sup> and Paul B. Talbert<sup>8</sup>





# Канонические гистоны (replication dependent)

1A



Нарабатываются в S-фазу, не имеет polyA хвоста,  
регулируются на пост-транскрипционном уровне.

# Histone locus body

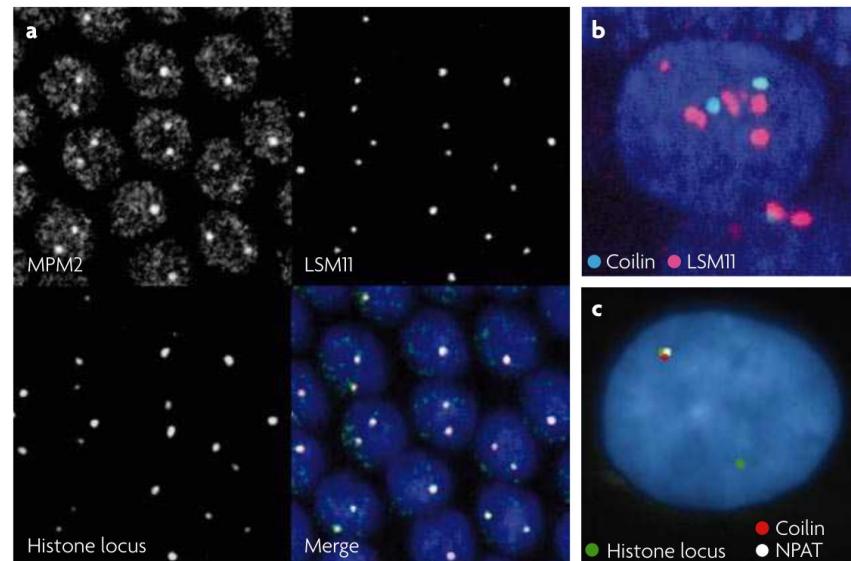
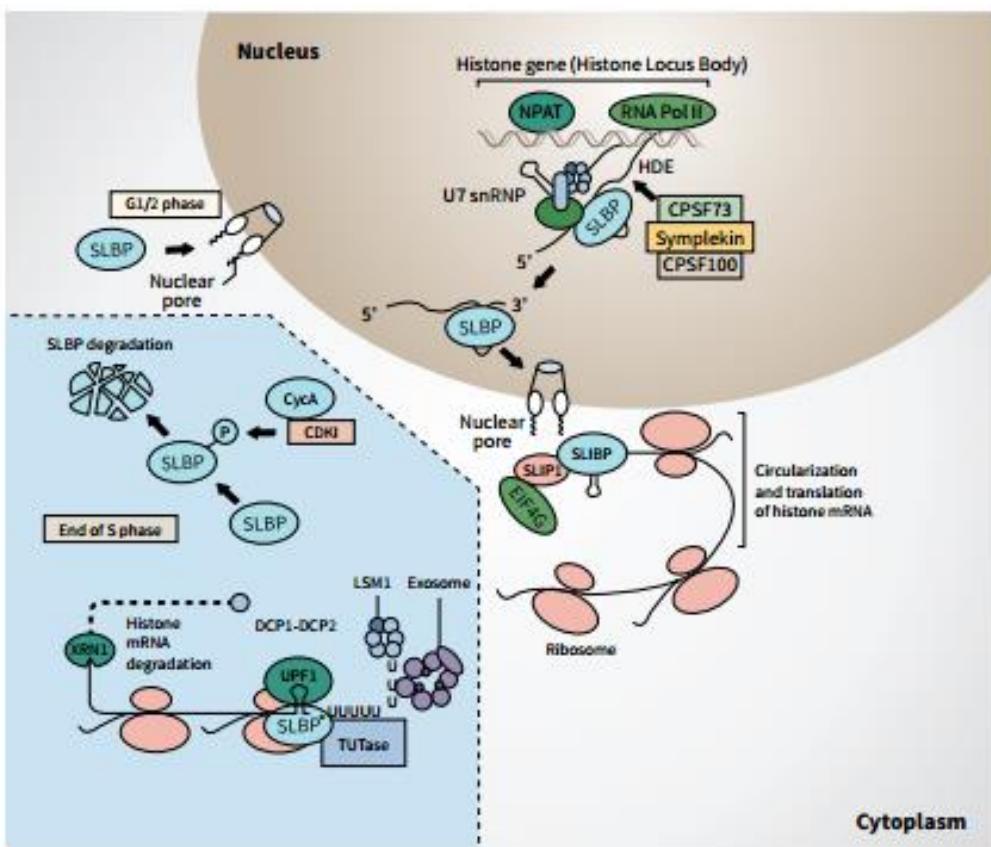


Figure 3 | The Cajal body and the histone locus body (HLB). a | HLB in *Drosophila*

# Гистоновые варианты (replication independent)

- Находятся вне генных кластеров, Экспрессируются в течение всего клеточного цикла, Замещают канонические варианты.

**Histone type: H3**

|   |           |
|---|-----------|
| <b>canonical H3</b>   | 28 / 3746 |
| Alternate names: ca H3  |           |
| Taxonomic span: Eukaryotes                                      |           |
| <br>  |           |
| <b>cenH3</b>  | 14 / 429  |
| Alternate names: CENP-A, cid, CNA1, CNP1, Cse4,<br>HCP-3, HTR12 |           |
| Taxonomic span: Eukaryotes                                      |           |
| <br>  |           |
| <b>H3.3</b>   | 15 / 1180 |
| Alternate names: hv2, soH3-1, soH3-2                            |           |
| Taxonomic span: Eukaryotes                                      |           |
| <br>  |           |
| <b>H3.5</b>   | 2 / 2419  |
| Alternate names: <i>None</i>                                    |           |
| Taxonomic span: Hominids  |           |
| <br>  |           |
| <b>H3.Y</b>   | 8 / 136   |
| Alternate names: H3.X   |           |
| Taxonomic span: Primates  |           |
| <br>  |           |
| <b>TS H3.4</b>  | 2 / 4014  |
| Alternate names: H3.1t  |           |
| Taxonomic span: Mammals   |           |

**Histone type: H2A**

|   |           |
|---|-----------|
| <b>canonical H2A</b>  | 37 / 8462 |
| Alternate names: ca H2A   |           |
| Taxonomic span: Eukaryotes  |           |
| <br>  |           |
| <b>H2A.1</b>  | 2 / 1326  |
| Alternate names: TH2A, TS H2A.1   |           |
| Taxonomic span: Mammals   |           |
| <br>  |           |
| <b>H2A.B</b>  | 15 / 285  |
| Alternate names: H2A.Bbd, H2A.Lap1(mouse)   |           |
| Taxonomic span: Mammals   |           |
| <br>  |           |
| <b>H2A.L</b>  | 17 / 257  |
| Alternate names: H2A.Lap2, H2A.Lap3, H2A.L, H2A.L2  |           |
| Taxonomic span: Certain mammals   |           |
| <br>  |           |
| <b>H2A.P</b>  | 11 / 141  |
| Alternate names: CXorf27, H2A.Lap4, HIP17,<br>Huntingtin-interacting protein M, HYPM                  |           |
| Taxonomic span: Placentalia   |           |
| <br>  |           |
| <b>H2A.W</b>  | 9 / 2062  |
| Alternate names: H2A with SPK motifs  |           |
| Taxonomic span: Plants  |           |
| <br>  |           |
| <b>H2A.X</b>  | 23 / 2487 |
| Alternate names: member X   |           |
| Taxonomic span: Eukaryotes except nematode  |           |
| <br>  |           |
| <b>H2A.Z</b>  | 26 / 5462 |
| Alternate names: D2, H2A.V, H2A.Z, H2A.Z-1, H2A.Z-2,<br>H2A.Zc, H2Av, H2AvD, H2Zp, H1, member Z       |           |
| Taxonomic span: Eukaryotes  |           |
| <br>  |           |
| <b>macroH2A</b>   | 10 / 2436 |
| Alternate names: macroH2A1, macroH2A1.1,<br>macroH2A1.2, macroH2A2, macroH2A2.1,<br>macroH2A2.2, mH2A |           |
| Taxonomic span: Vertebrates(?)  |           |

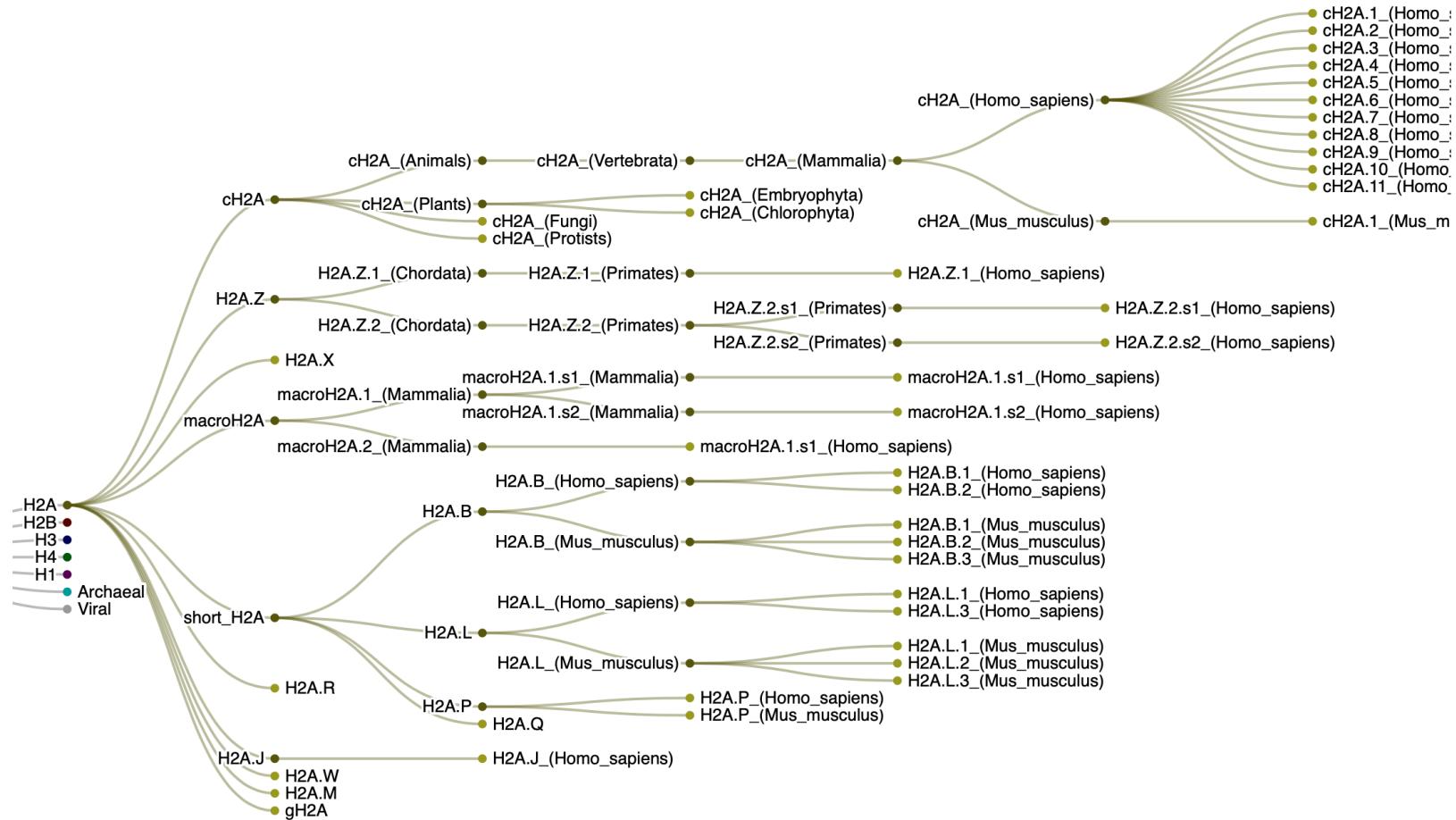
**Histone type: H4**

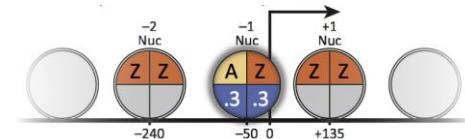
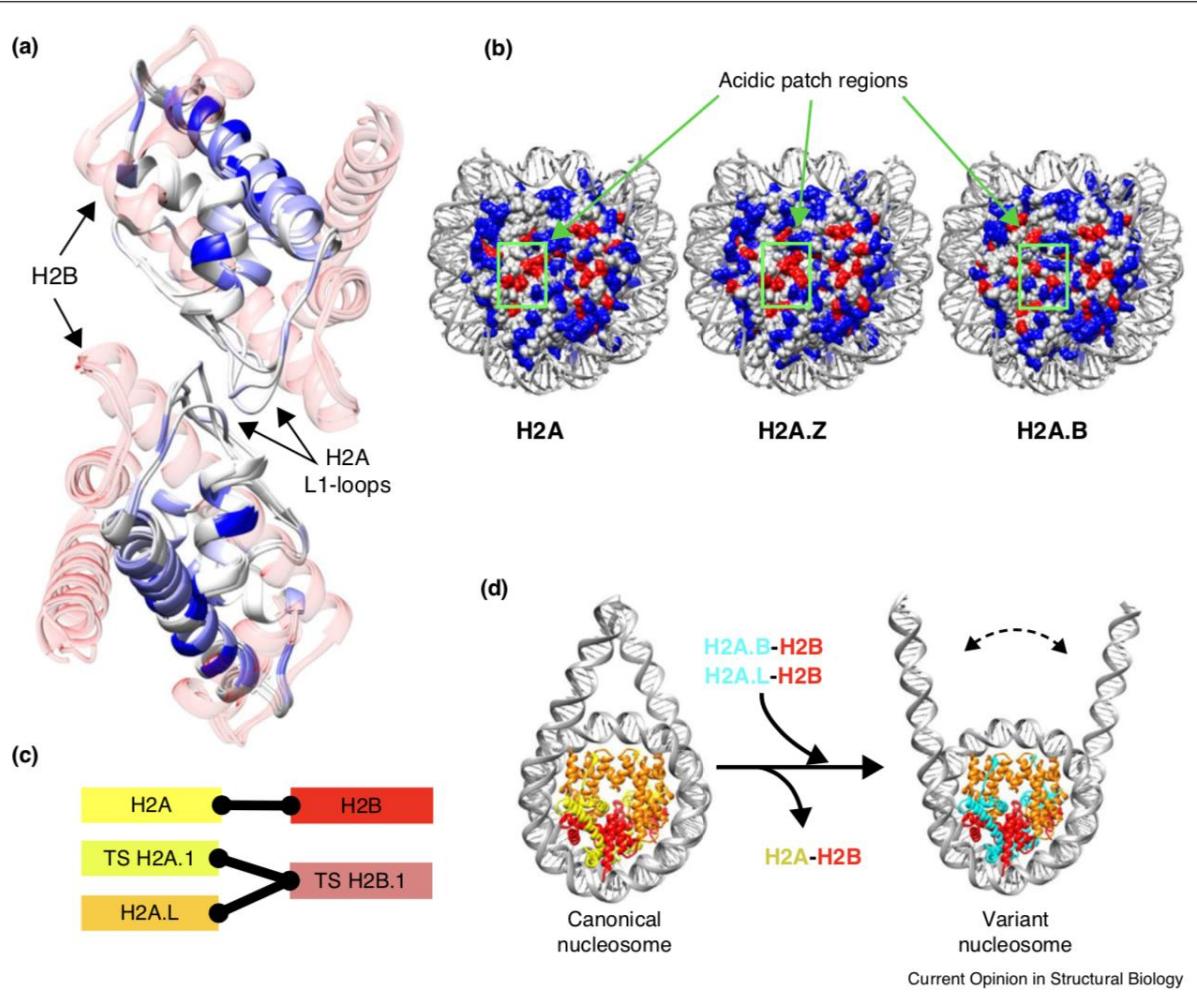
|                            |            |
|----------------------------|------------|
| <b>canonical H4</b>        | 14 / 15978 |
| Alternate names: ca H4     |            |
| Taxonomic span: Eukaryotes |            |

**Histone type: H2B**

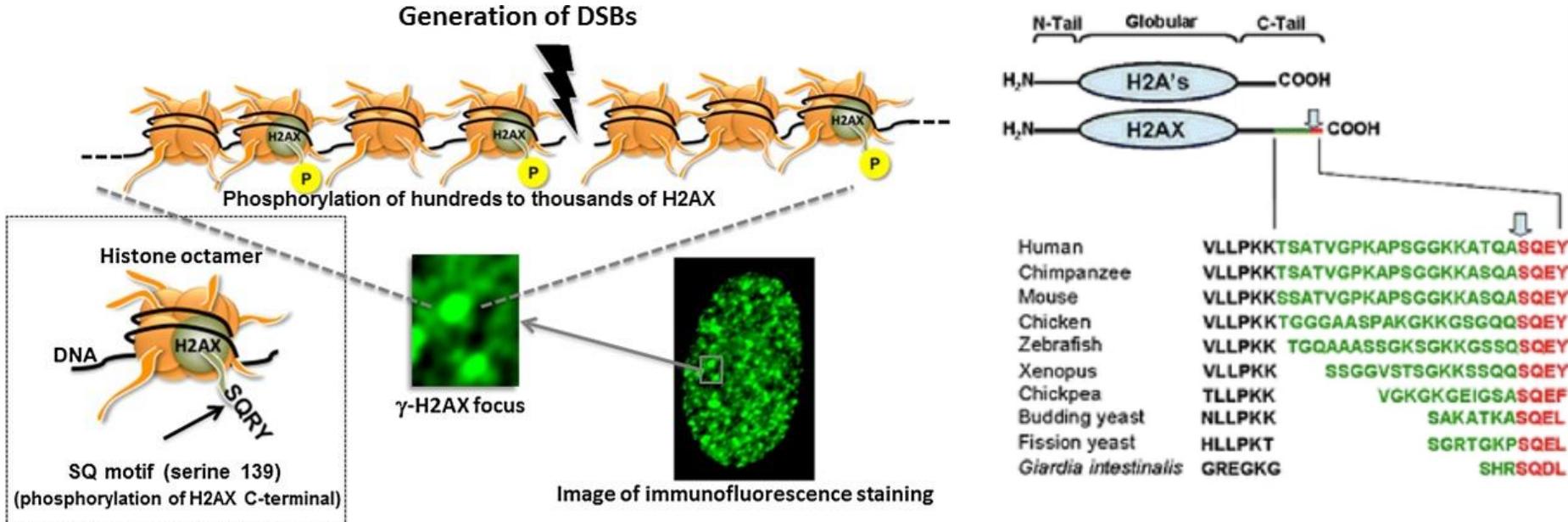
|  |            |
|--|------------|
| <b>canonical H2B</b>   | 29 / 13275 |
| Alternate names: ca H2B                                      |            |
| Taxonomic span: Eukaryotes                                   |            |
| <br>   |            |
| <b>H2B.1</b>   | 3 / 658    |
| Alternate names: H2B.1, hTS2B, TH2B, TS H2B.1                |            |
| Taxonomic span: Mammals                                      |            |
| <br>   |            |
| <b>H2B.W</b>   | 6 / 389    |
| Alternate names: H2BFWT, member W, type W-T                  |            |
| Taxonomic span: Mammals                                      |            |
| <br>   |            |
| <b>H2B.Z</b>   | 2 / 371    |
| Alternate names: H2Bv  |            |
| Taxonomic span: Apicomplexa                                  |            |
| <br>   |            |
| <b>sperm H2B</b>   | 5 / 80     |
| Alternate names: cleavage H2B, early H2B                     |            |
| Taxonomic span: Echinodermata(?)                             |            |
| <br>   |            |
| <b>subH2B</b>  | 11 / 122   |
| Alternate names: H2BL1, subH2Bv                              |            |
| Taxonomic span: Primates, rodents, marsupials, and<br>bovids |            |

# Гистоновые варианты H2A



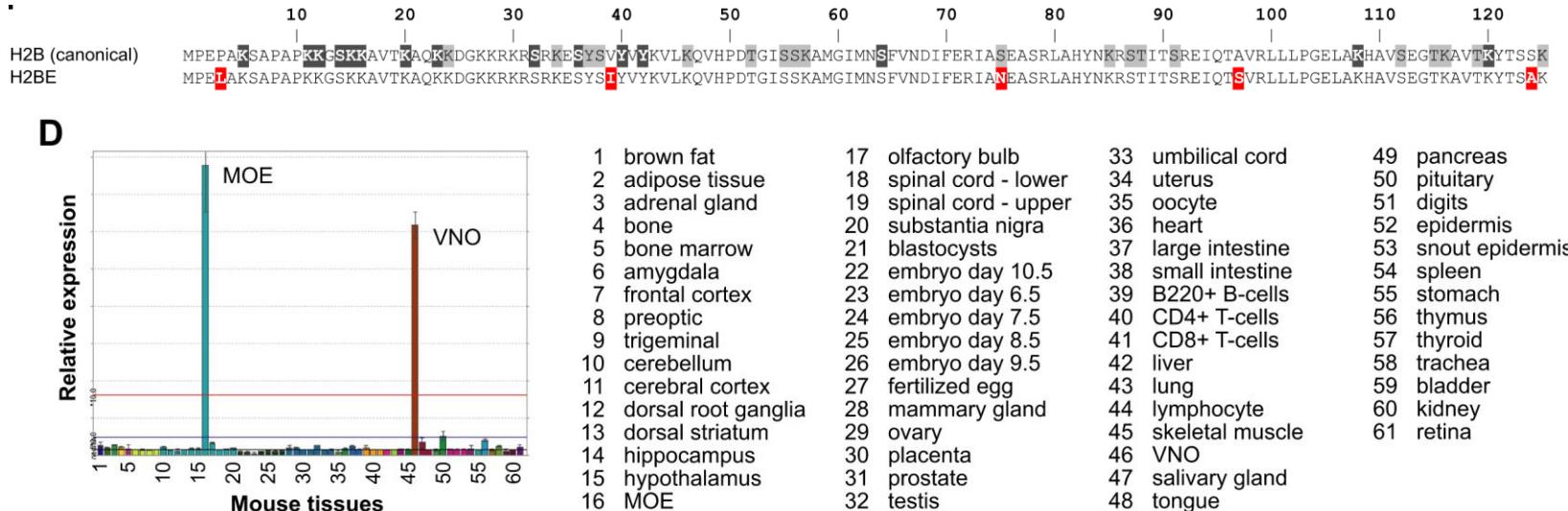


# H2A.X – маркер повреждений ДНК



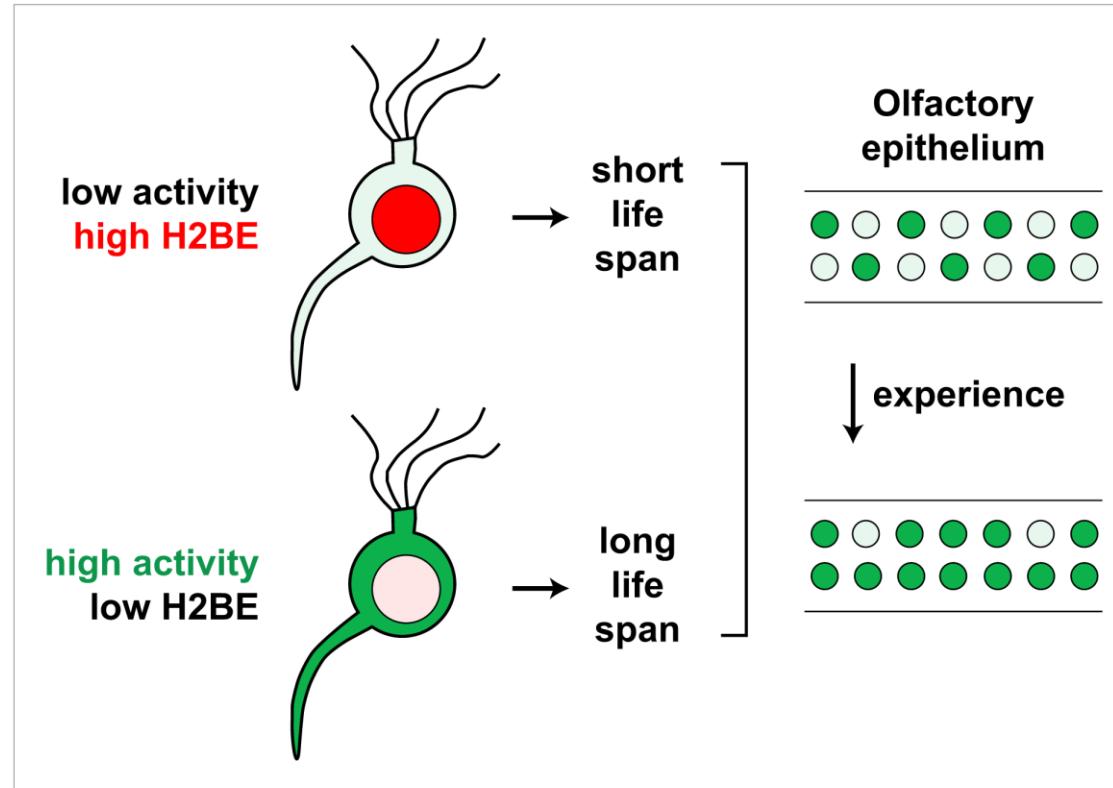
# Разнообразие и функции вариантов у млекопитающих

- Варианты гистонов активно эволюционируют
- Есть варианты встречающиеся только у приматов (H3.Y), у гоминид (H3.5)
- Обладают специфической экспрессией (пример H2B.E у мышей)



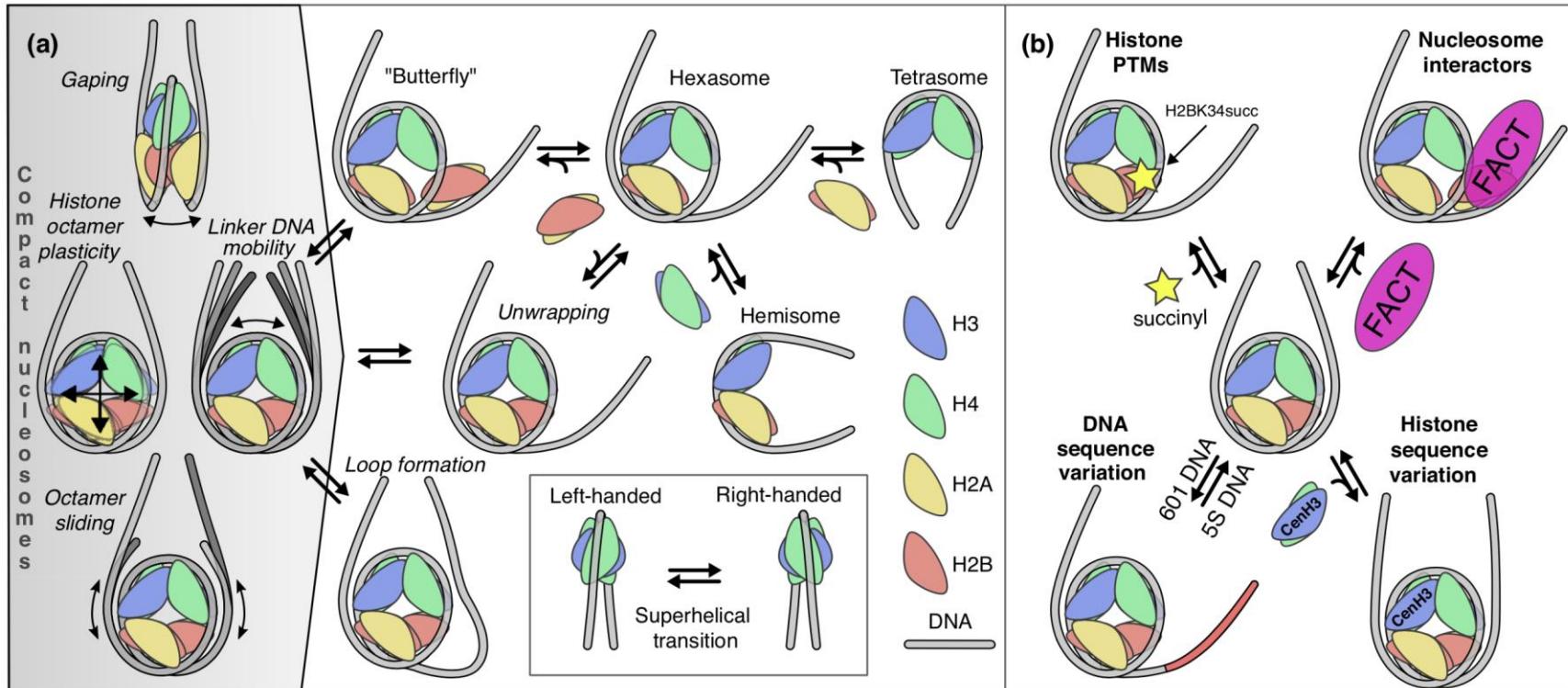
Santoro, S. W.; Dulac, C. The Activity-Dependent Histone Variant H2BE Modulates the Life Span of Olfactory Neurons. *Elife* 2012, 1, e00070. <https://doi.org/10.7554/eLife.00070>.

# H2B.E – участвует в регуляции жизни обонятельных нейронов



**Figure 12.** Model for the effects of neuronal activity on H2BE expression level, life span and resulting neuronal representation.

# Nucleosome structural variability

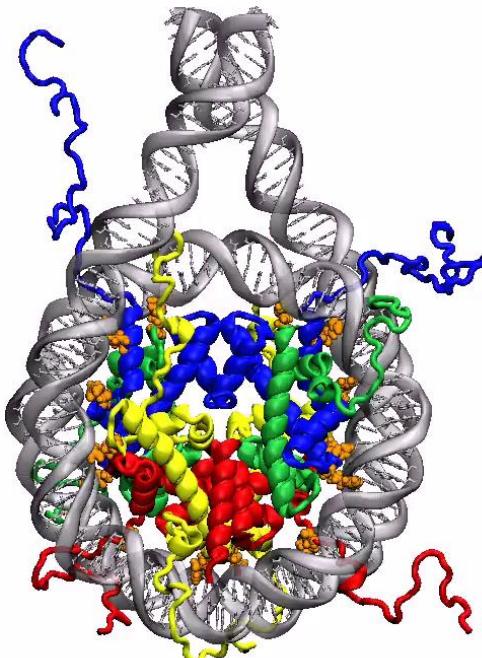


# Nucleosome dynamics

MD simulations of nucleosome with linker DNA (1000 ns)

Histones H3  
Histones H4  
Histones H2A  
Histones H2B  
DNA  
Min groove ARGs

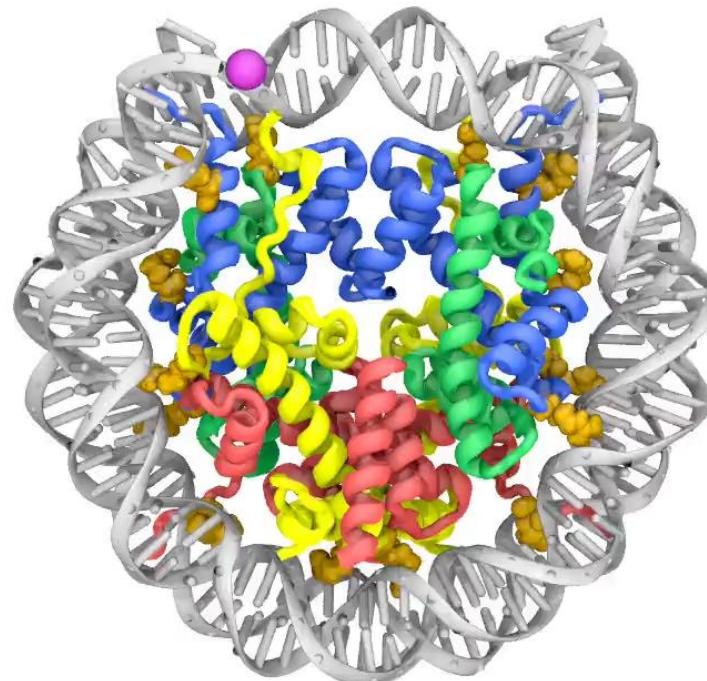
Time: 0.0 ns



Shaytan, A. K.; Armeev, G. A.; Gonçalves, A.; Zhurkin, V. B.; Landsman, D.; Panchenko, A. R. Coupling between Histone Conformations and DNA Geometry in Nucleosomes on a Microsecond Timescale: Atomistic Insights into Nucleosome Functions. *Journal of Molecular Biology* **2016**, 428(1), 221–237. <https://doi.org/10.1016/j.jmb.2015.12.004>.

$NCP_{145}^{tt}$

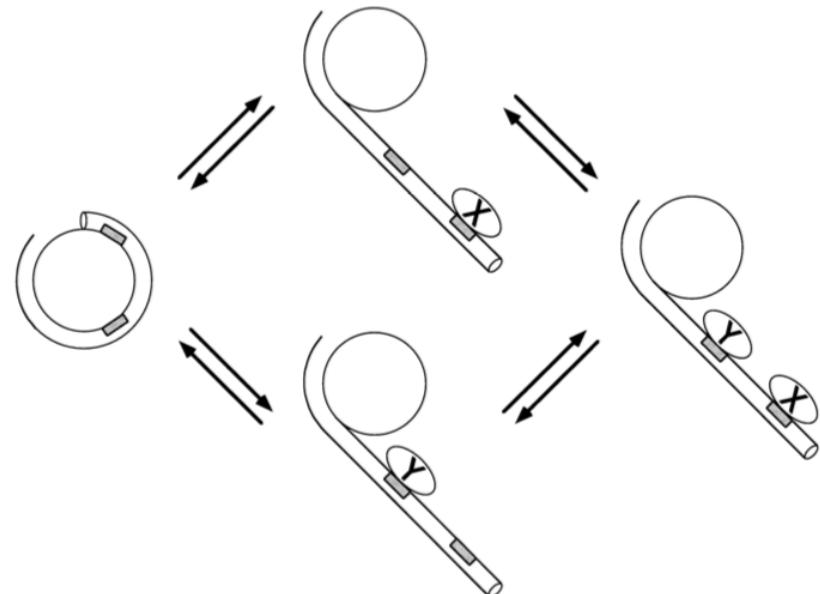
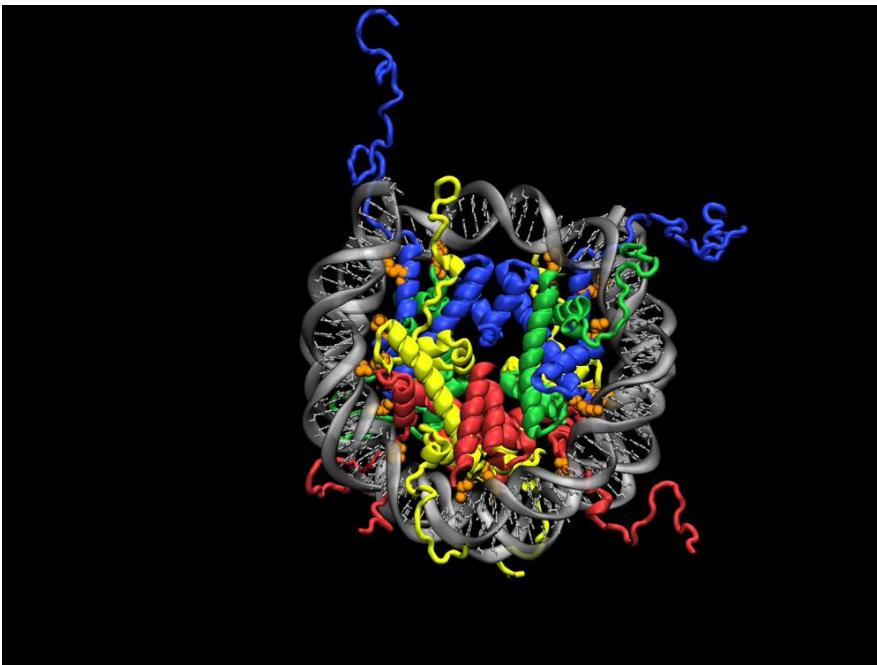
Histones H3  
Histones H4  
Histones H2A  
Histones H2B  
Min groove ARG  
DNA  
05'DNA chain I



Time: 0.0 ns

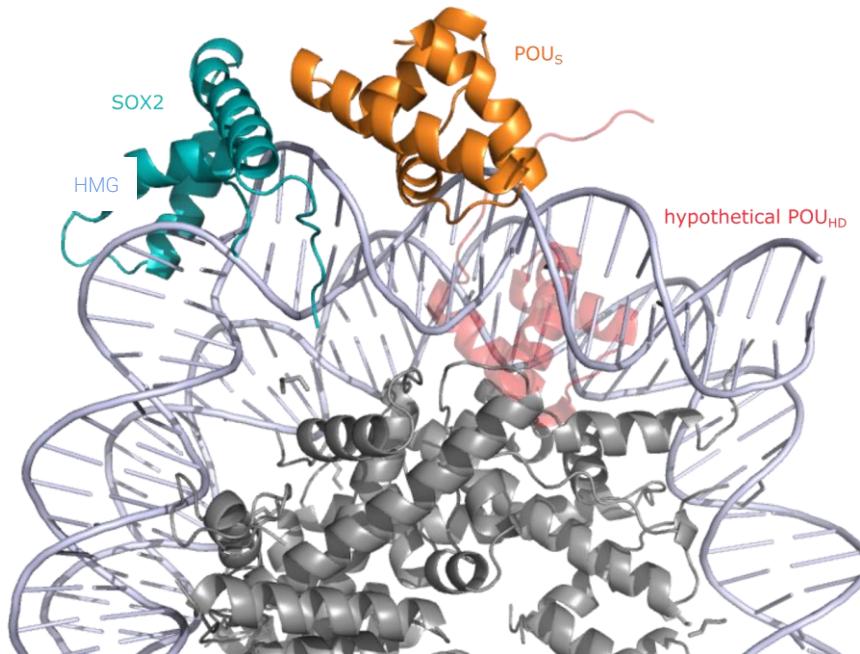
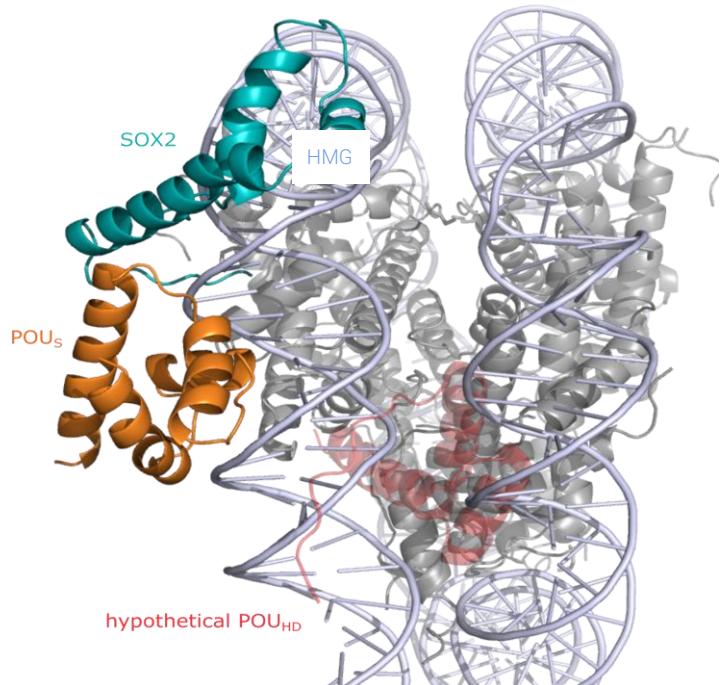
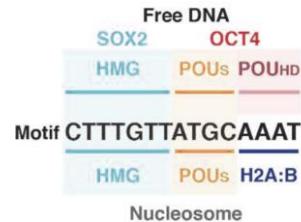
Armeev, G.A., Kniazeva, A.S., Komarova, G.A., Kirpichnikov, M.P. and Shaytan, A.K. (2021) Histone dynamics mediate DNA unwrapping and sliding in nucleosomes. *Nat Commun.*, 12.

## DNA unwrapping and transcription factor binding



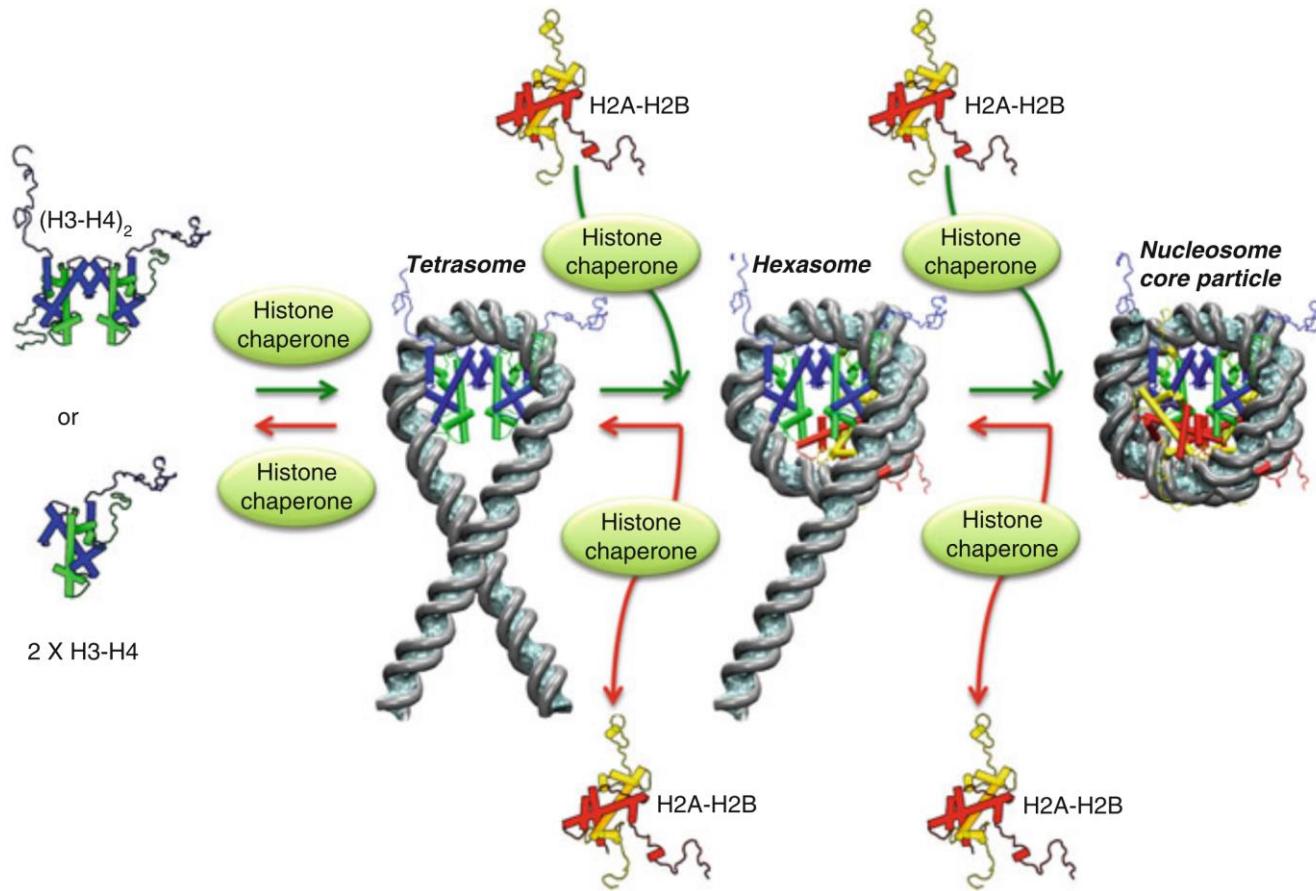
Polach, K. J. and J. Widom (1995). "Mechanism of protein access to specific DNA sequences in chromatin: a dynamic equilibrium model for gene regulation." *J Mol Biol* **254**(2): 130-149.

# Пионерные факторы и нуклеосомы



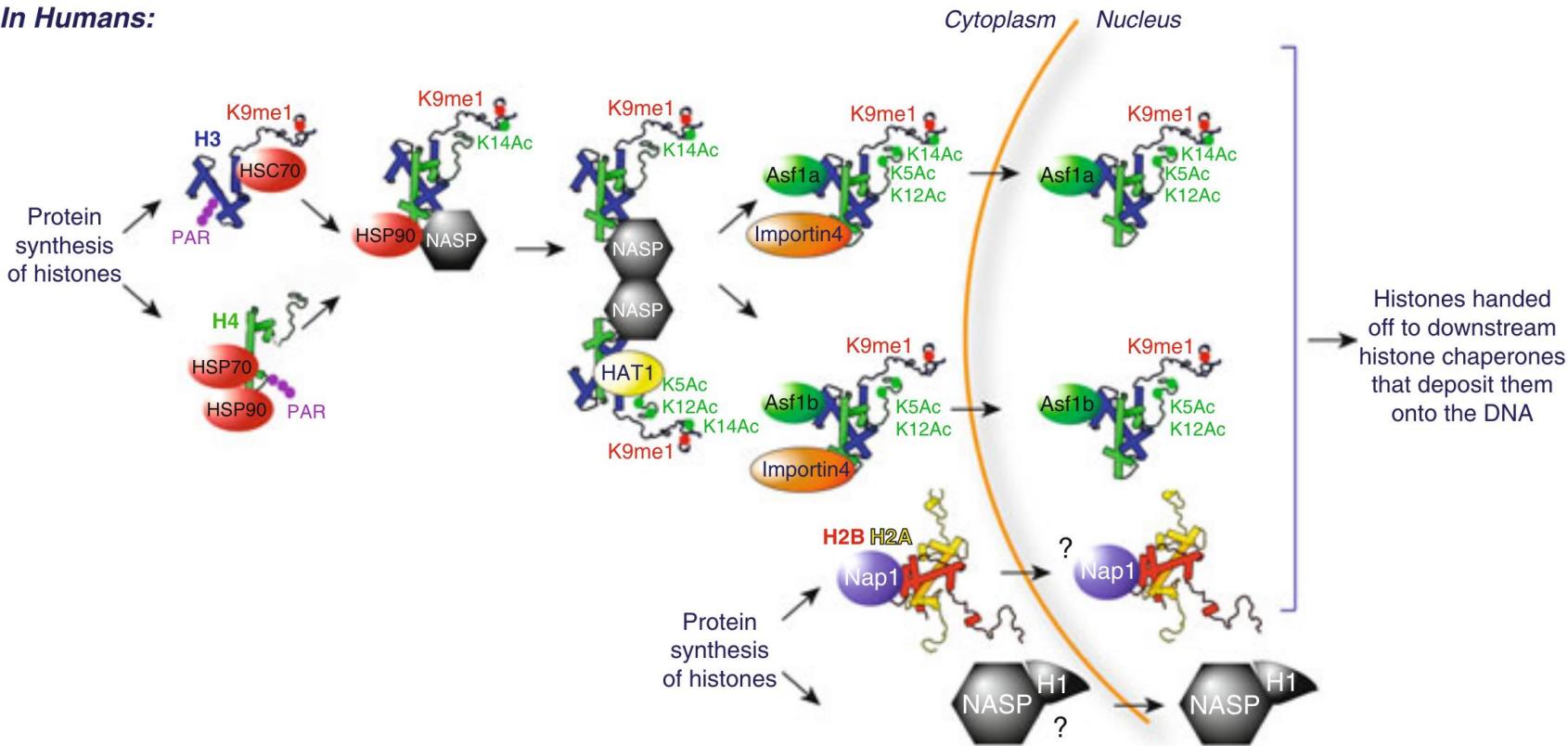
буй + POU<sub>HD</sub> из 1gt0,  
выровнен по POU<sub>S</sub>

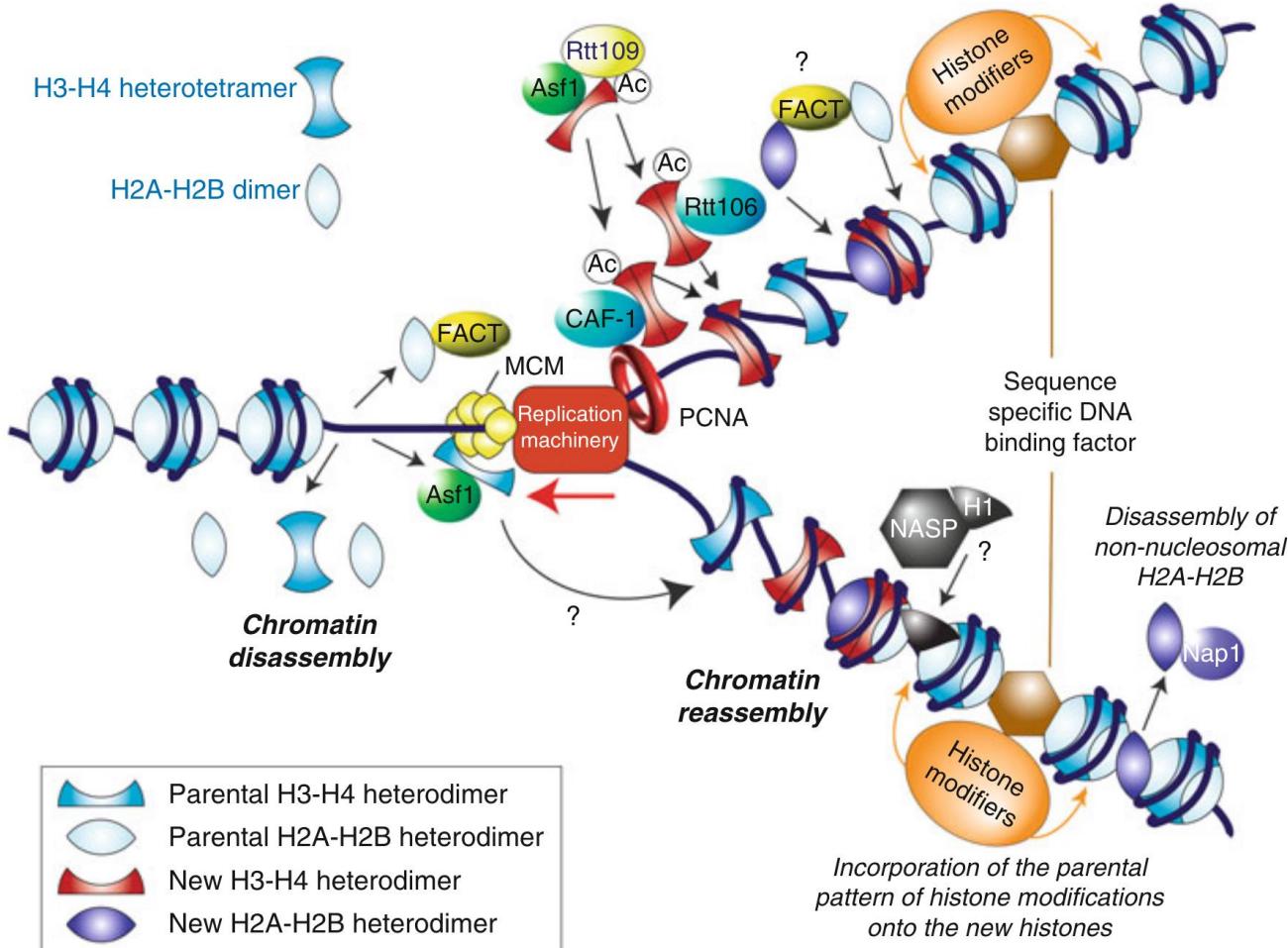
# Сборка нуклеосом



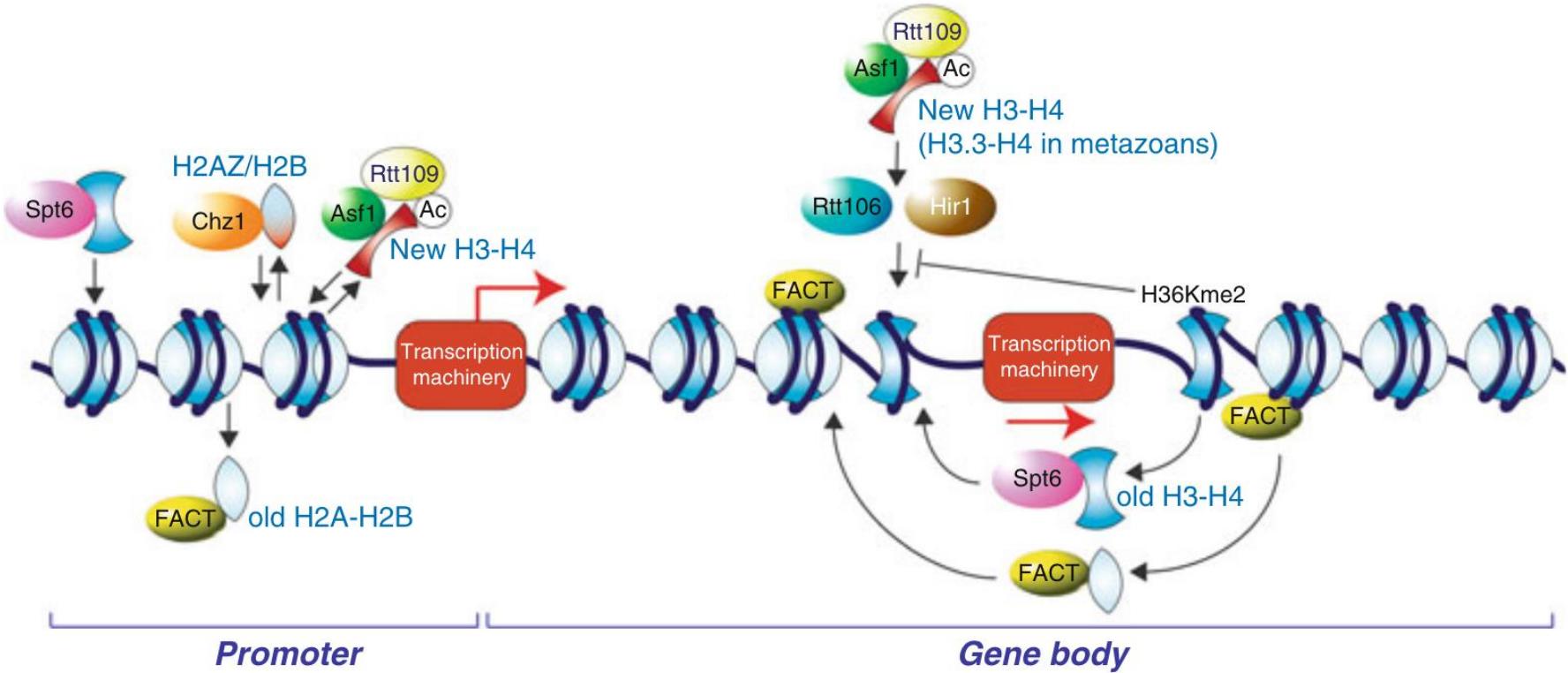
# Шапероны гистонов

In Humans:



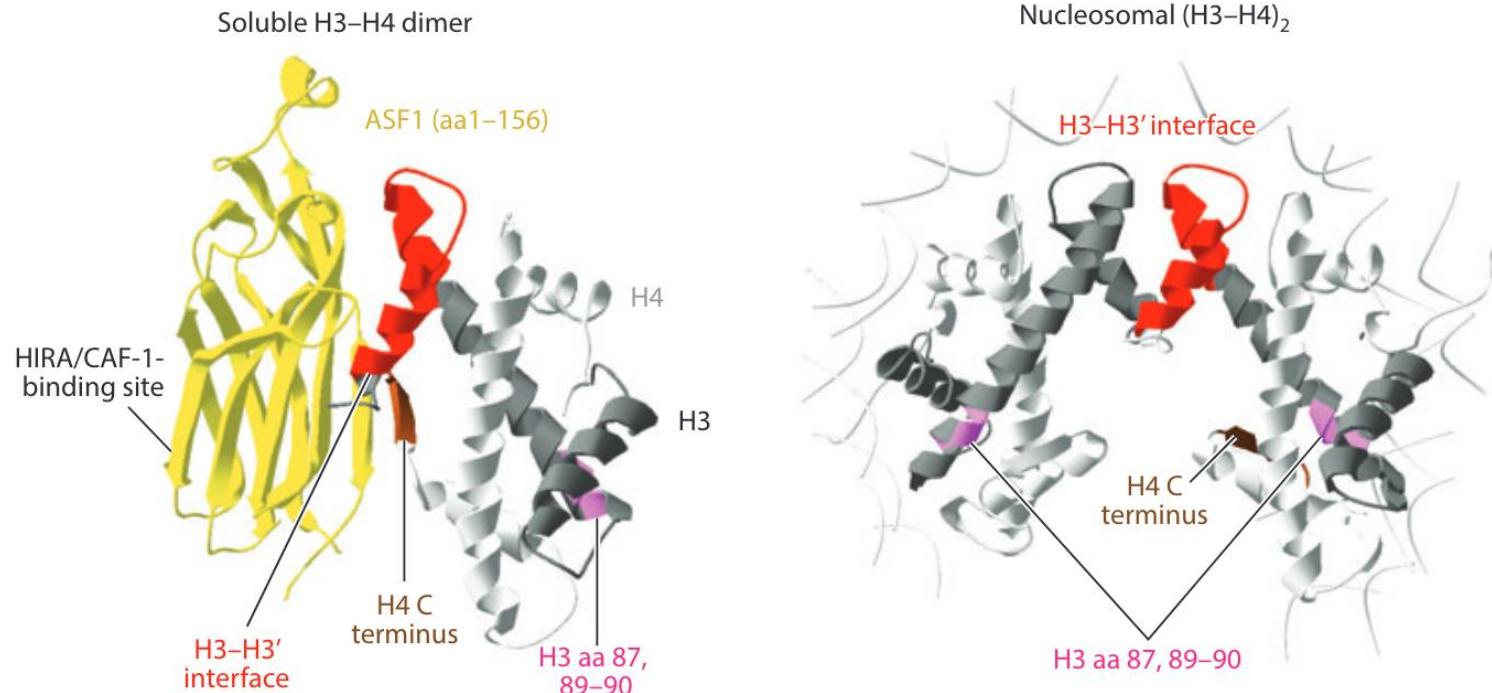


**Fig. 2.3** Replication-dependent chromatin disassembly and assembly. Schematic showing chromatin disassembly ahead of the replication fork and stepwise chromatin reassembly behind



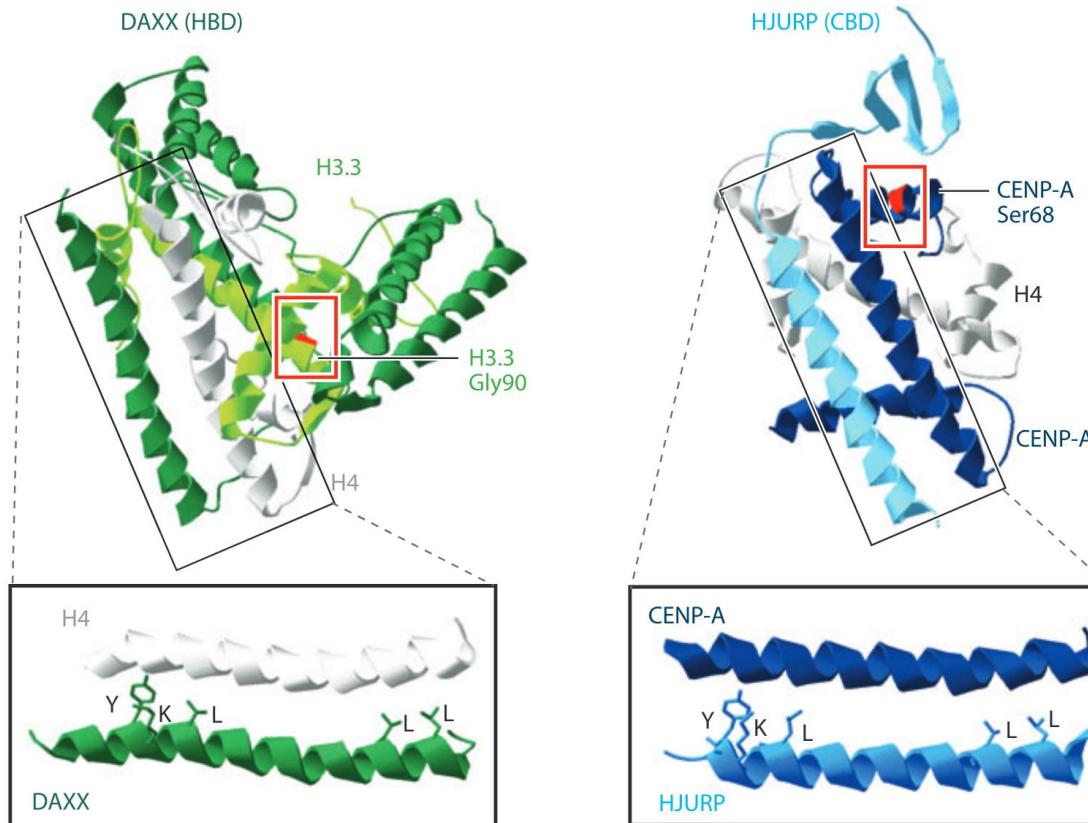
**Fig. 2.5** Replication-independent chromatin disassembly and assembly. Some histone chaper-

**a** ASF1 binds a dimer of H3–H4



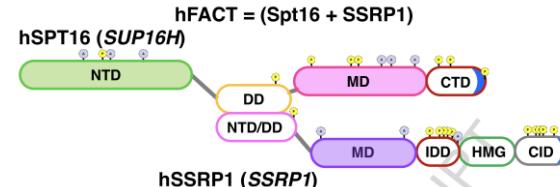
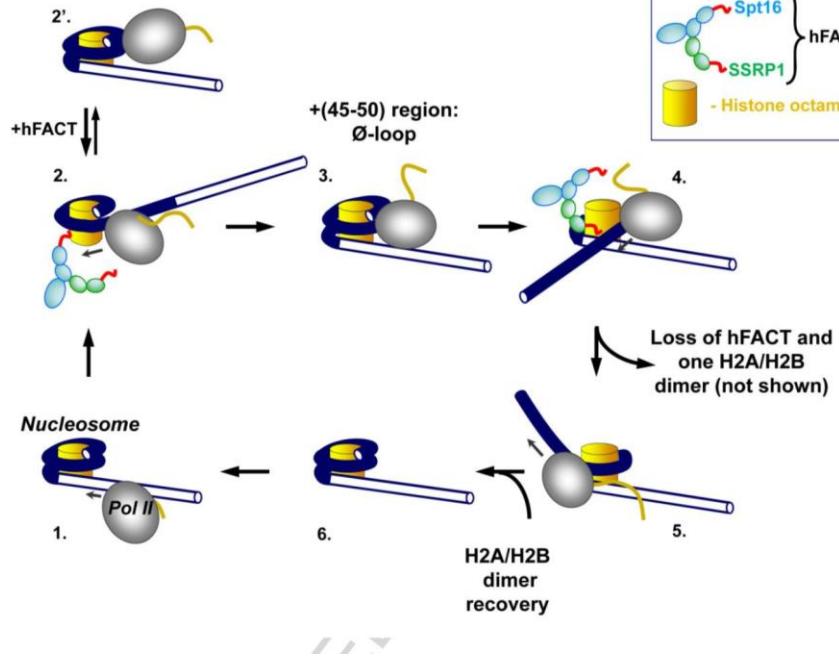
Gurard-Levin, Z. A., Quivy, J.-P. & Almouzni, G. Histone Chaperones: Assisting Histone Traffic and Nucleosome Dynamics. *Annual Review of Biochemistry* **83**, 487–517 (2014).

**b** Similar binding motifs: DAXX with H3.3–H4 and HJURP with CENP-A–H4

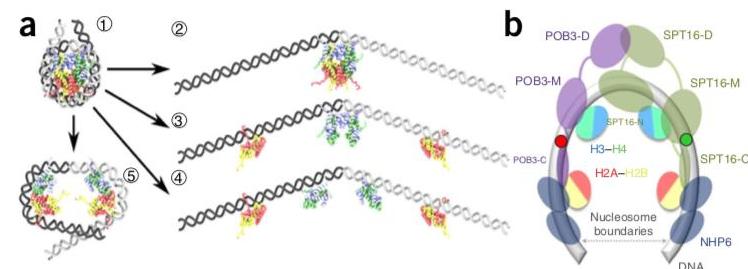


Gurard-Levin, Z. A., Quivy, J.-P. & Almouzni, G. Histone Chaperones: Assisting Histone Traffic and Nucleosome Dynamics. *Annual Review of Biochemistry* **83**, 487–517 (2014).

# Транскрипция через нуклеосомы

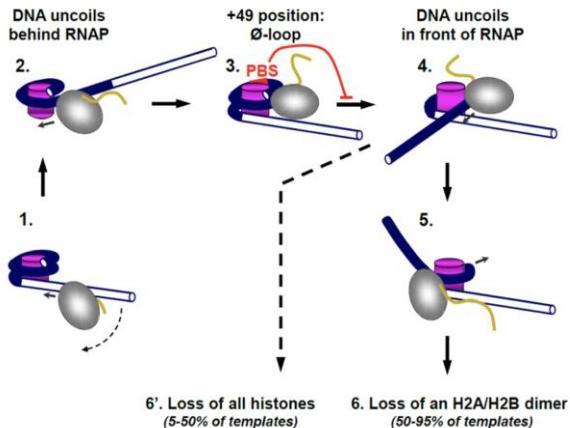
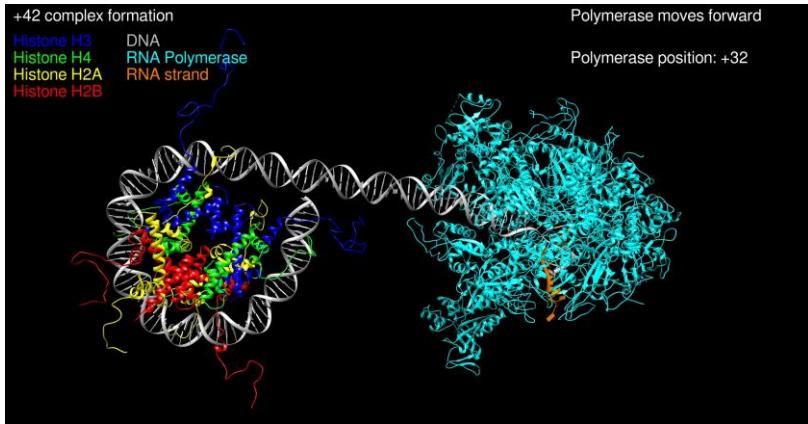


FACT chaperone



Valieva, M. E.; Armeev, G. A.; Kudryashova, K. S.; Gerasimova, N. S.; Shaytan, A. K.; Kulaeva, O. I.; McCullough, L. L.; Formosa, T.; Georgiev, P. G.; Kirpichnikov, M. P.; et al. Large-Scale ATP-Independent Nucleosome Unfolding by a Histone Chaperone. *Nature Structural & Molecular Biology* **2016**, *23*(12), 1111–1116. <https://doi.org/10.1038/nsmb.3321>.  
Gurova, K., Chang, H.-W., Valieva, M. E., Sandlesh, P., & Studitsky, V. M. (2018). Structure and function of the histone chaperone FACT – Resolving FACTual issues. *Biochimica et Biophysica Acta (BBA) - Gene Regulatory Mechanisms*: doi:10.1016/j.bbagr.2018.07.008

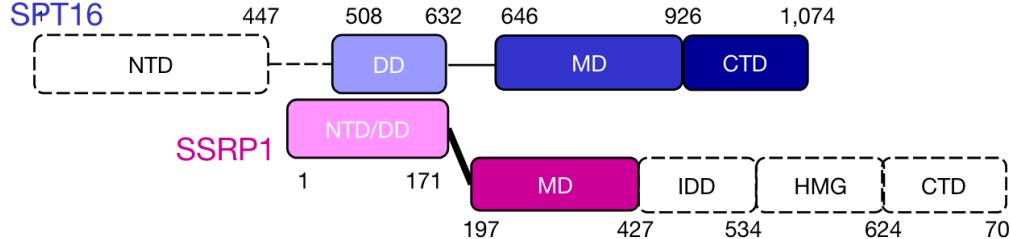
# Transcription through nucleosomes



Biochim Biophys Acta. 2013 January ; 1829(1): 76–83. doi:10.1016/j.bbapm.2012.08.015.

Mechanism of Transcription through a Nucleosome by RNA polymerase II

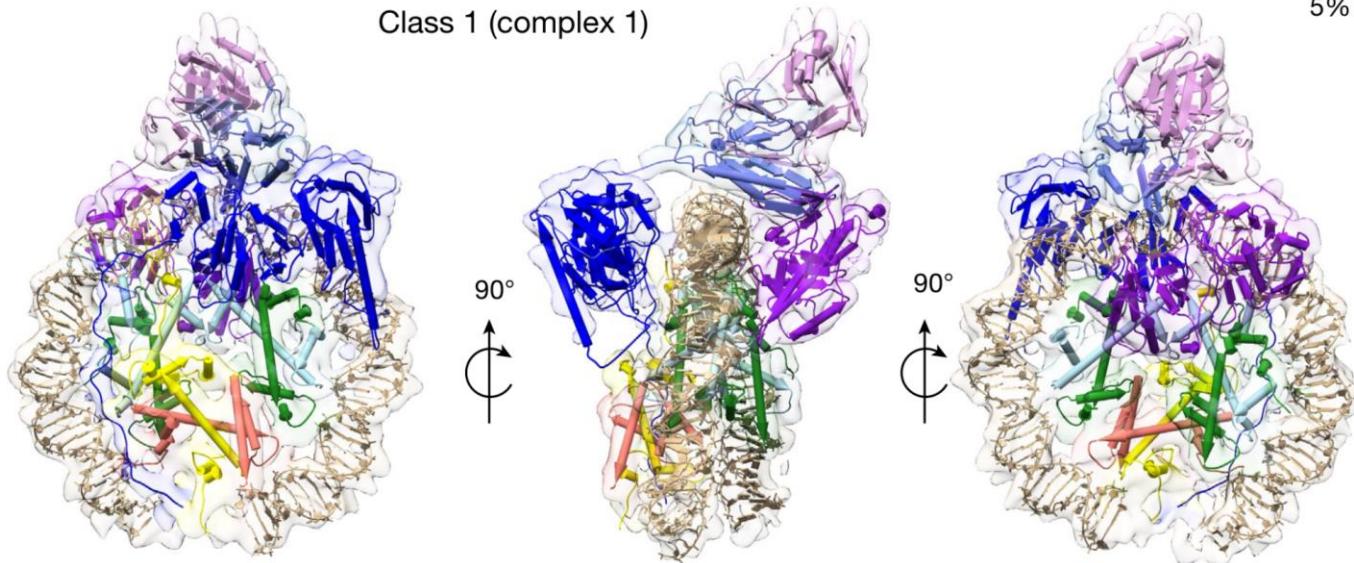
Olga I. Kulæva<sup>1,2</sup>, Fu-Kai Hsieh<sup>1</sup>, Han-Wen Chang<sup>1</sup>, Donald S. Luse<sup>3</sup>, and Vasily M. Studitsky<sup>1,2,4</sup>

**a****c**

DNA H2A H2B H3 H4 SSRP1 (MD/DD) SPT16 (MD/DD) 50 bp

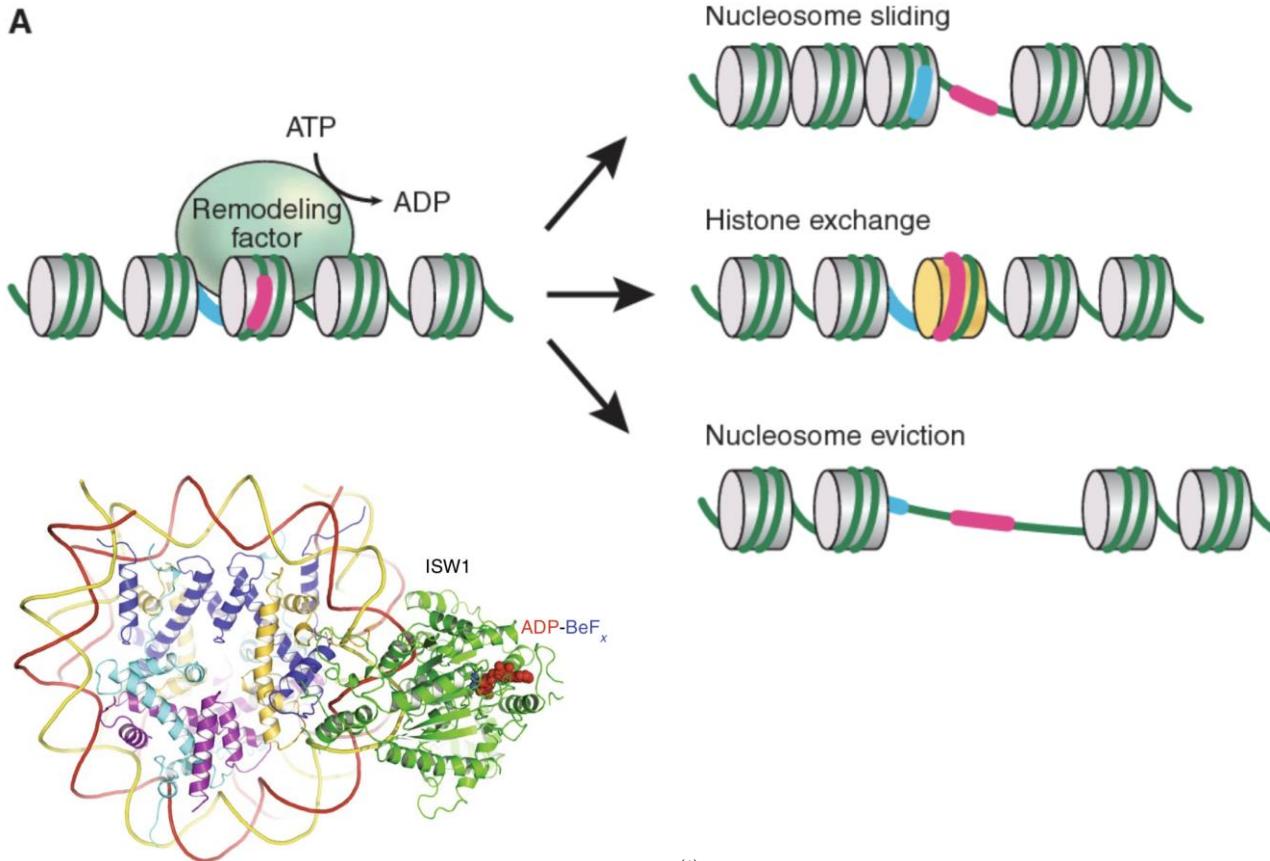
Class 1 (complex 1)

5% n.s.



# ATP-dependent nucleosome remodeling

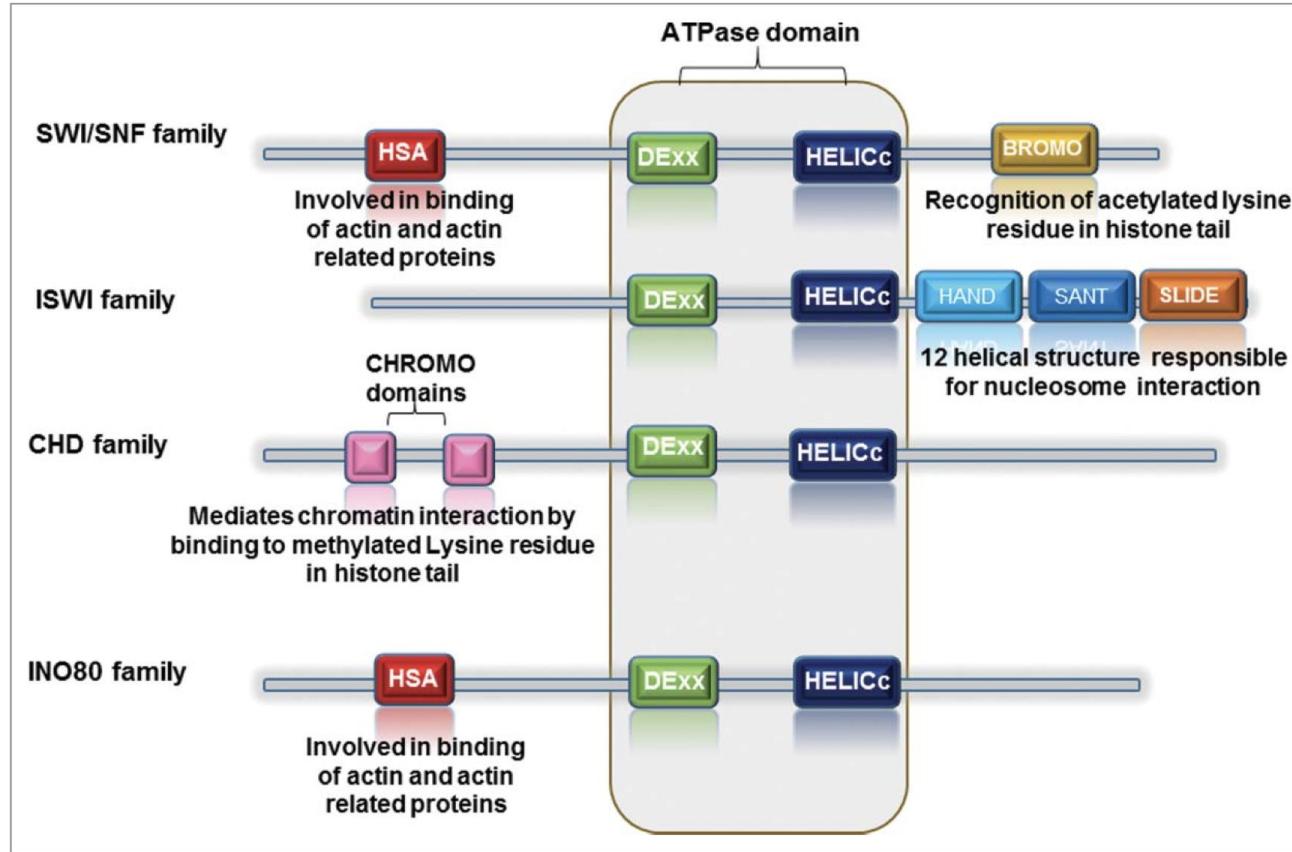
A



(1)

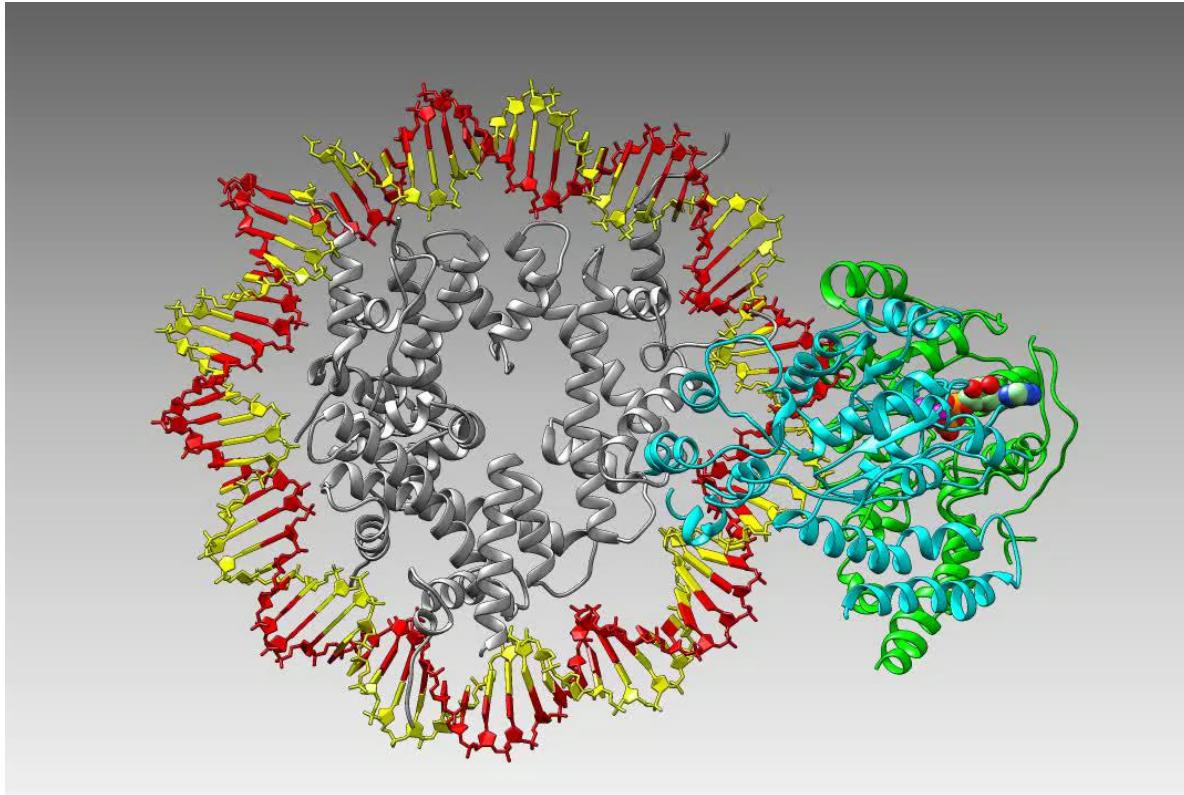
Yan, L.; Wu, H.; Li, X.; Gao, N.; Chen, Z. Structures of the ISWI–Nucleosome Complex Reveal a Conserved Mechanism of Chromatin Remodeling. *Nature Structural & Molecular Biology* **2019**, *26* (4), 258. <https://doi.org/10.1038/s41594-019-0199-9>

Nucleosome remodeling and epigenetics. Peter B. Becker, Jerry L. Workman Published in Cold Spring Harbor perspectives in biology 2013 DOI:10.1101/cshperspect.a017905



**Figure 1.** Diagrammatic representation of chromatin remodeler family highlighting the conserved domain with each family member. The DEX and HELICc domains are conserved throughout the family. However, HAND, SANT and SLIDE domains are specific to ISWI family, whereas BROMO domain distinguishes the SWI/SNF family. The presence of CHROMO domains is characteristic of CHD family.

# ATP-dependent nucleosome remodeling

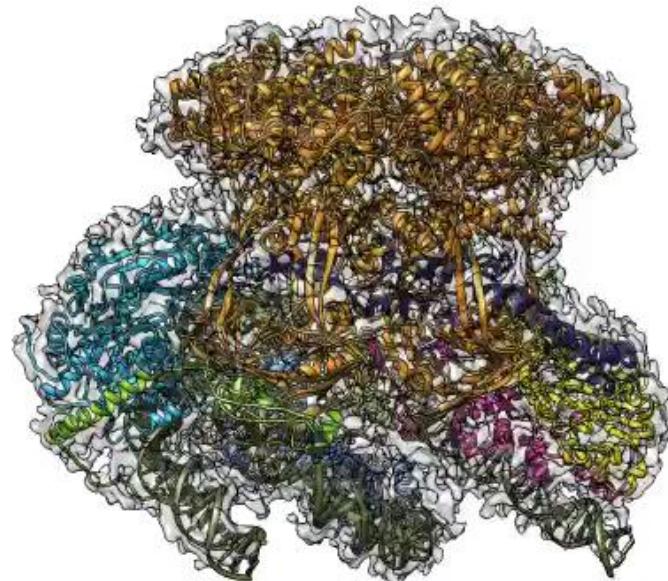
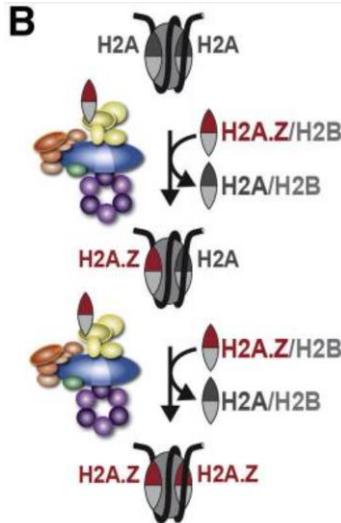


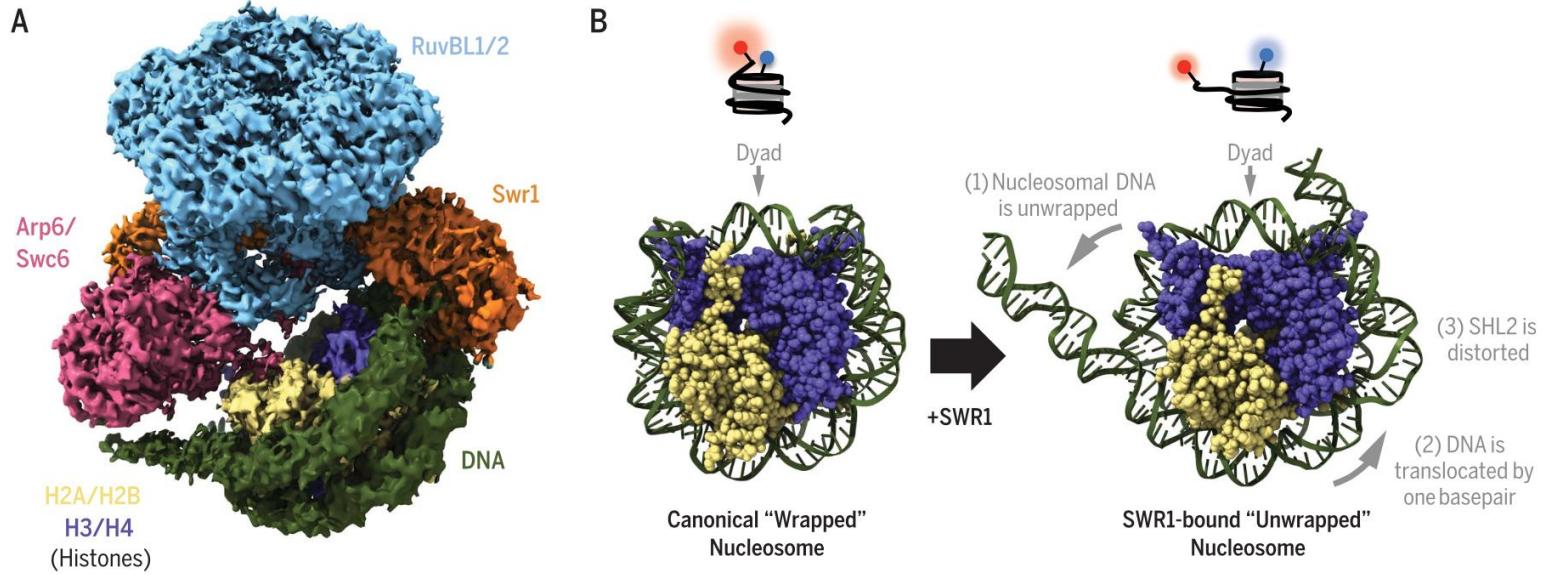
(1)

Li, M.; Xia, X.; Tian, Y.; Jia, Q.; Liu, X.; Lu, Y.; Li, M.; Li, X.; Chen, Z. Mechanism of DNA Translocation Underlying Chromatin Remodelling by Snf2. *Nature* **2019**, *567* (7748), 409–413.  
<https://doi.org/10.1038/s41586-019-1029-2>.

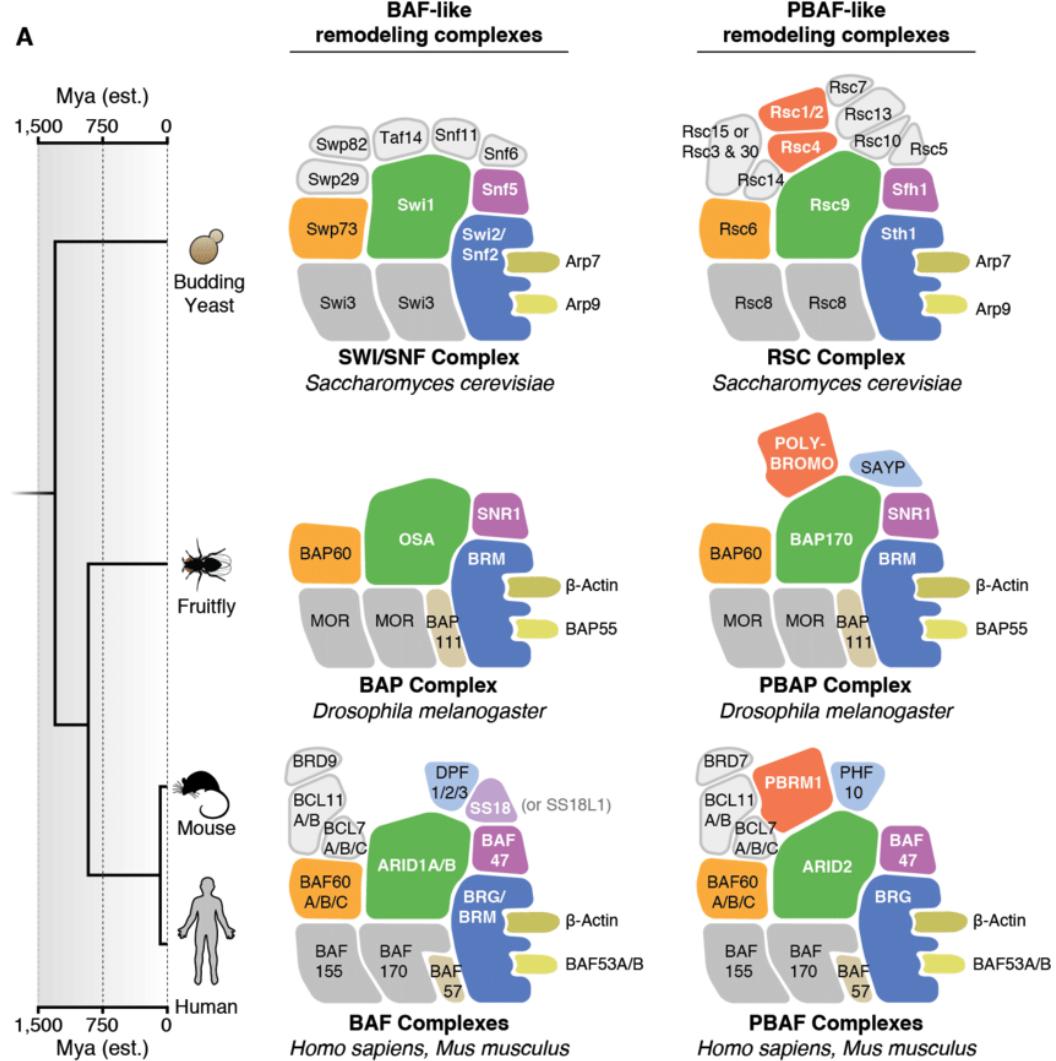
# ATP-dependent nucleosome remodeling

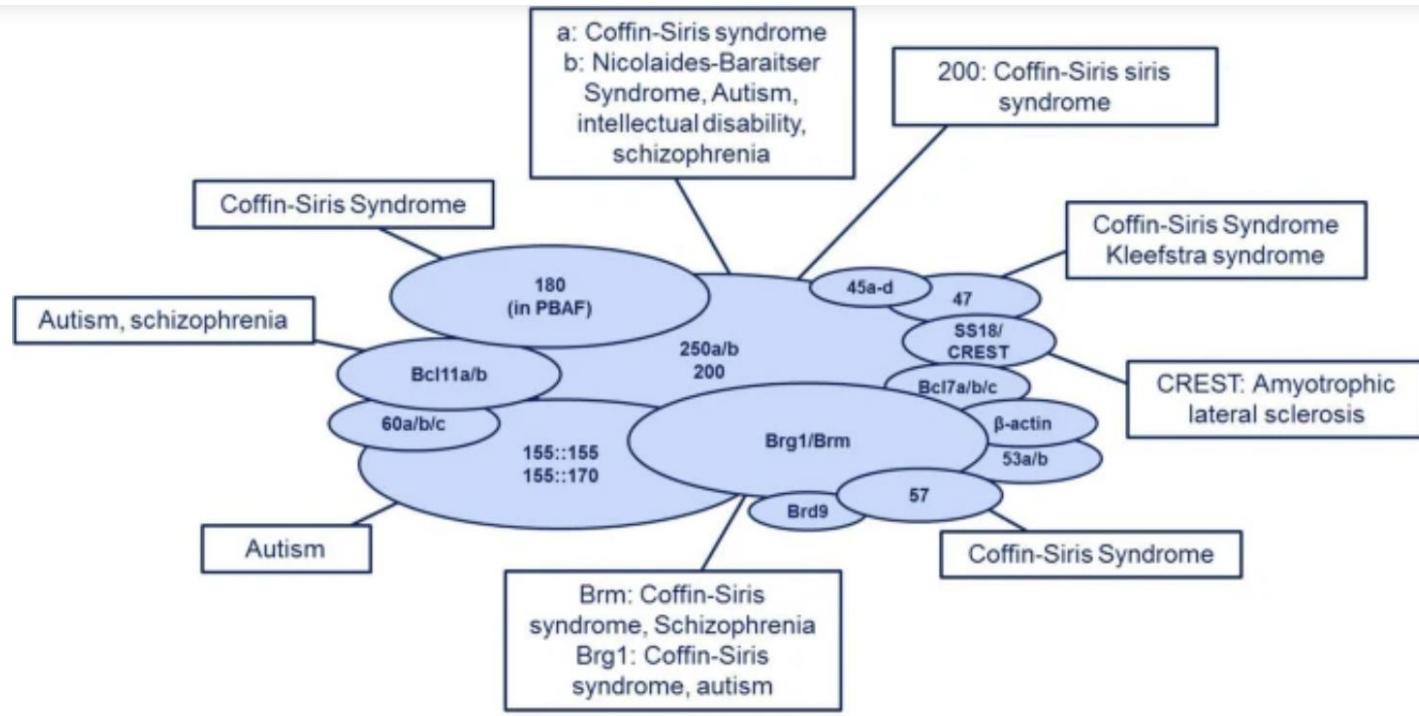
SWR1 remodeler  
replaces H2A with  
H2A.Z





Willhoft O, Ghoneim M, Lin CL, Chua EYD, Wilkinson M, Chaban Y, Ayala R, McCormack EA, Ocloo L, Rueda DS, Wigley DB. Structure and dynamics of the yeast SWR1-nucleosome complex. *Science*. 2018 Oct 12;362(6411):eaat7716.

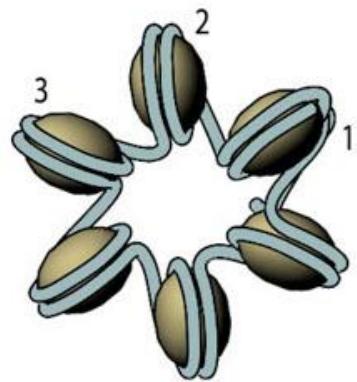
**A**



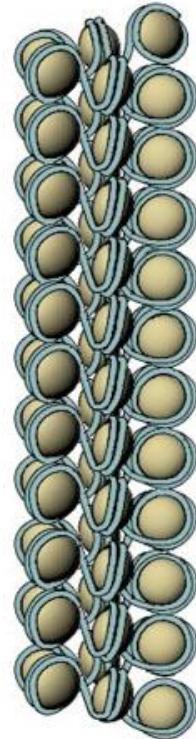
The role of subunit mutations in developmental disorders. BAF subunit mutations have a high implication in human developmental disorders. The most frequent mutations and associations with human disease are summarised in this figure. Subunits being involved most frequently include the ATPase subunit BRM as well as the subunit BAF250b

# Супрануклеосомная структура хроматина

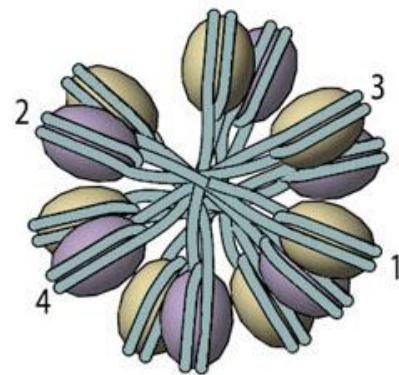
A. Solenoid



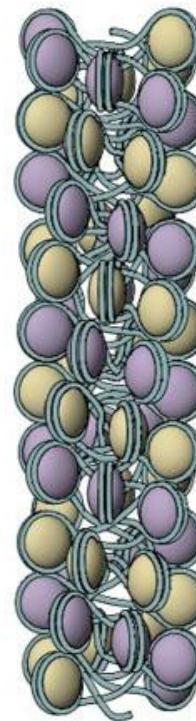
↔ ~30 nm



B. Zigzag



↔ ~30 nm



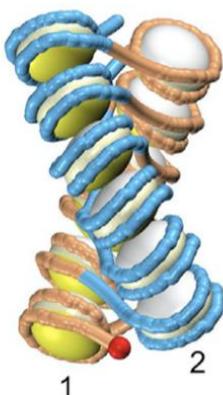


Edward N. Trifonov (2015): Nucleosome repeat lengths and columnar chromatin structure.,  
Journal of Biomolecular Structure and  
Dynamics, DOI:  
[10.1080/07391102.2015.1075158](https://doi.org/10.1080/07391102.2015.1075158)

# Супрануклеосомная структура хроматина

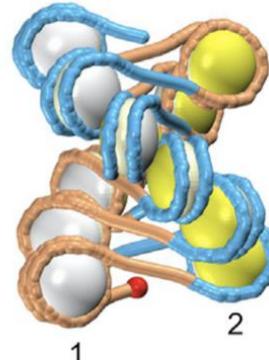
Low  
expressed  
genes

A



T2: L = 20 bp ( $\Delta Lk \approx -1.5$ )

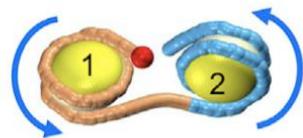
B



T1: L = 25 bp ( $\Delta Lk \approx -1.0$ )

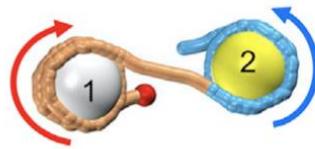
Highly  
expressed  
genes

C



L = {10n} cis

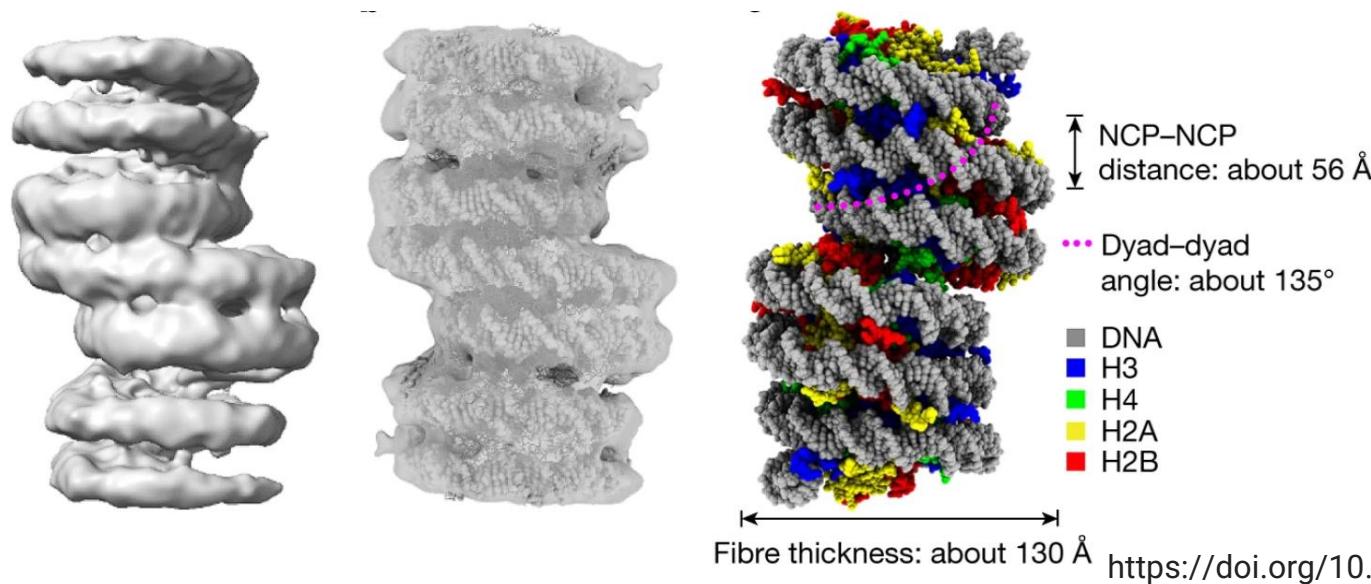
D



L = {10n+5} trans

# Теломеры

- Mammalian telomeres consist of the conserved and tandemly arranged DNA sequence repeat TTAGGG
- the telomeric NCP was less stable and markedly more dynamic than NCPs that contained DNA-positioning sequences. The explanation for this difference is based on the physical properties of the G-rich telomeric TTAGGG 6-bp repeat, which disfavours nucleosome positioning and renders telomeric nucleosomes more mobile



# Супрануклеосомная структура хроматина

Регулярного расположения нуклеосом и 30-нм фибриллы не существует.  
Могут быть нуклеосомные кластеры, клатчи, определенной структуры.

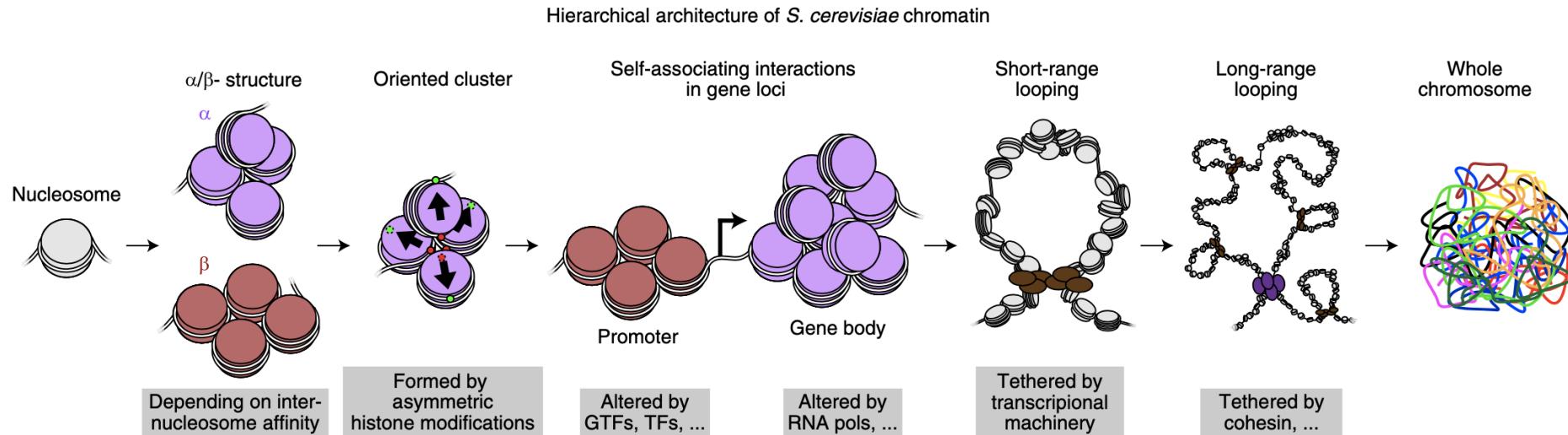
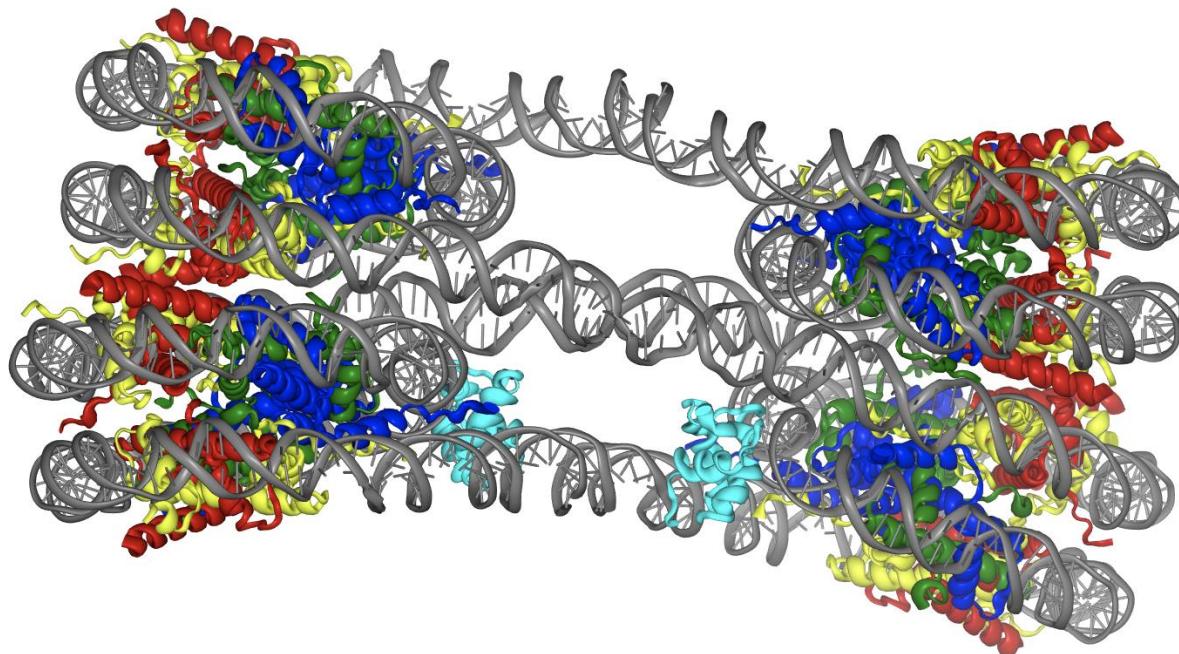


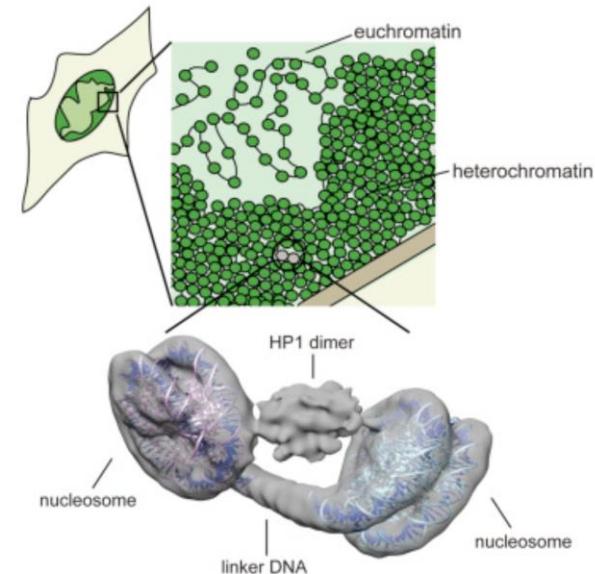
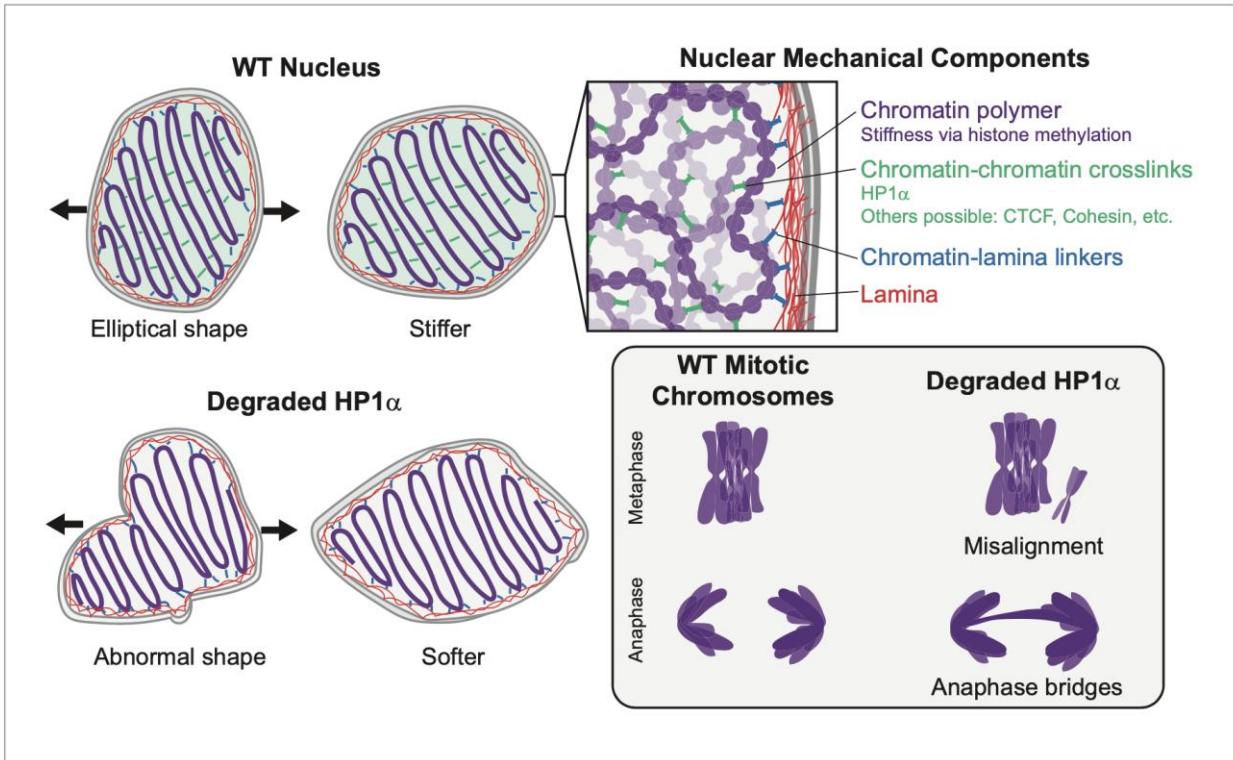
Figure 7. Model of Hierarchical Architecture of *S. cerevisiae* Chromatin from the Nucleosome Level to Whole Chromosomes

# Супрануклеосомная структура хроматина

<https://nucldb.intbio.org>



# Супрануклеосомная структура хроматина

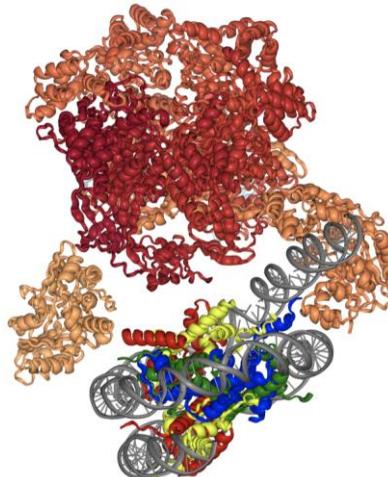
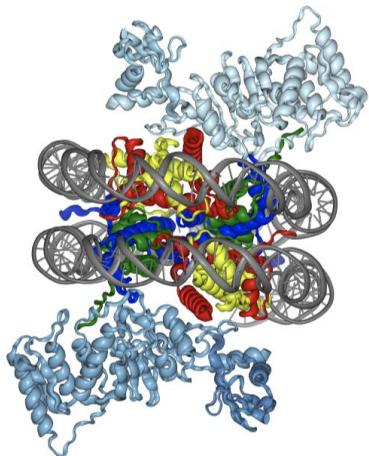
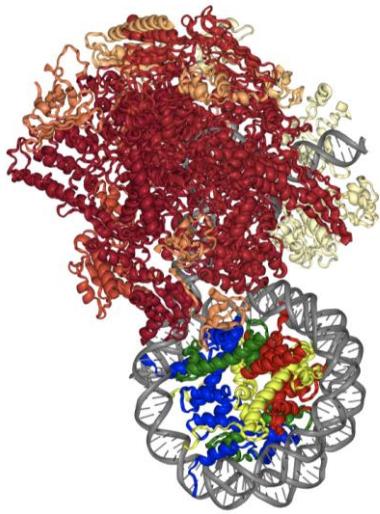


**Figure 6.** HP1 $\alpha$  is a mechanical element of interphase nuclei and mitotic chromosomes. In wild-type (WT) nuclei, HP1 $\alpha$  acts as a chromatin-chromatin

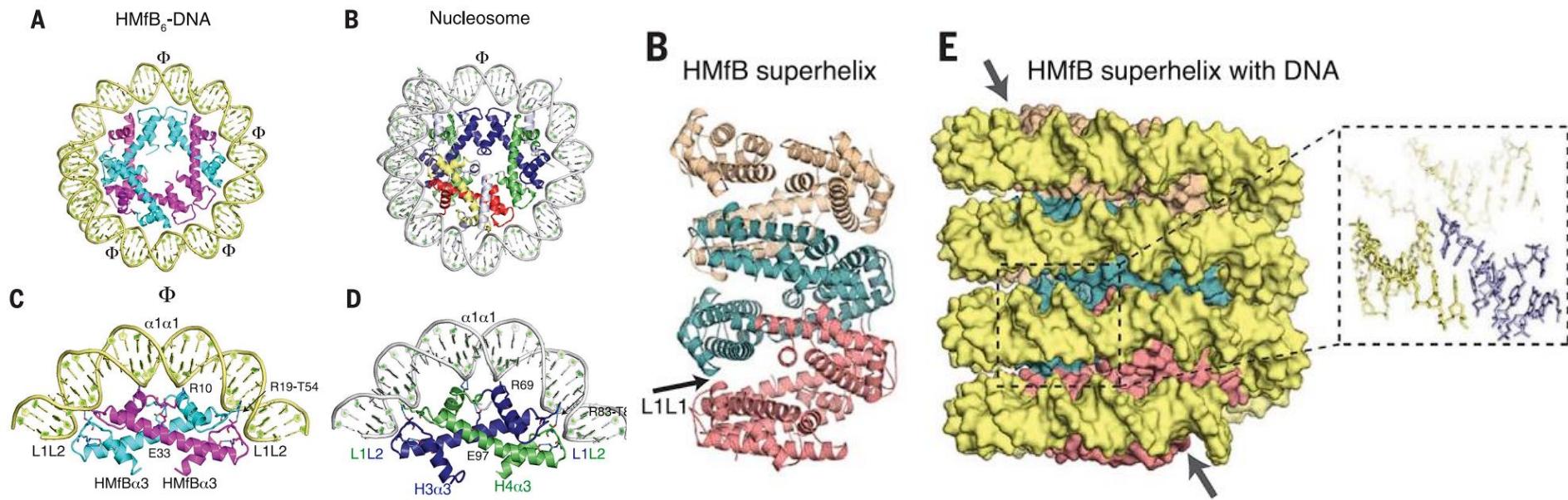
Strom, A. R.; Biggs, R. J.; Banigan, E. J.; Wang, X.; Chiu, K.; Herman, C.; Collado, J.; Yue, F.; Ritland Politz, J. C.; Tait, L. J.; Scalzo, D.; Telling, A.; Groudine, M.; Brangwynne, C. P.; Marko, J. F.; Stephens, A. D. HP1 $\alpha$  Is a Chromatin Crosslinker That Controls Nuclear and Mitotic Chromosome Mechanics. *eLife* 2021, 10, e63972. <https://doi.org/10.7554/eLife.63972>.

# Супрануклеосомная структура хроматина

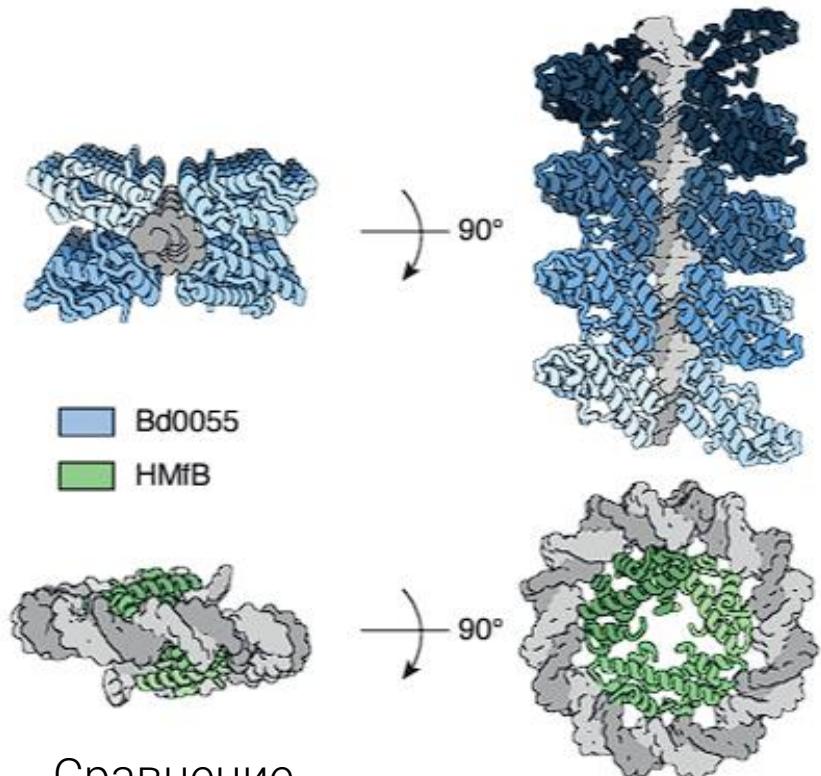
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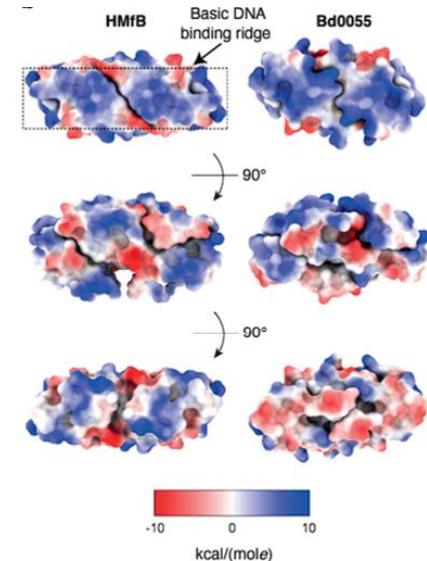
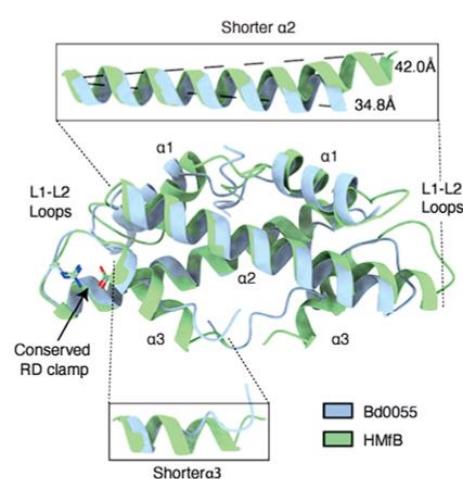
# Гистоны архей



# Бактериальные гистоны



Сравнение  
с  
архейными



### Marseilleviruses



### Insect iridoviruses



### Medusavirus



### Medusavirus stheno



### Clandestinovirus



### Klosneuviruses



### Nudiviruses



### Marine iridoviruses



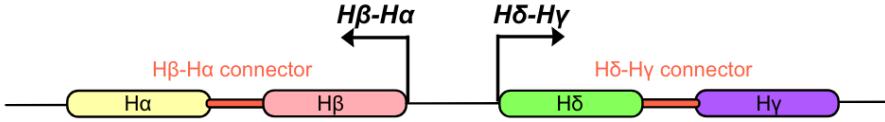
### Loki's Castle viruses



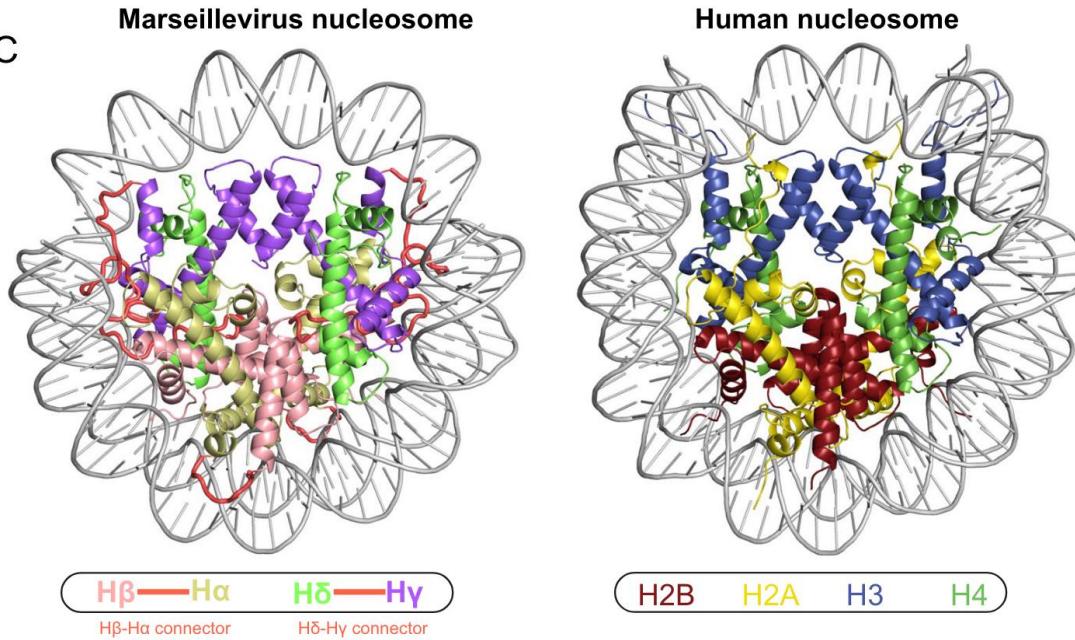
# Вирусные

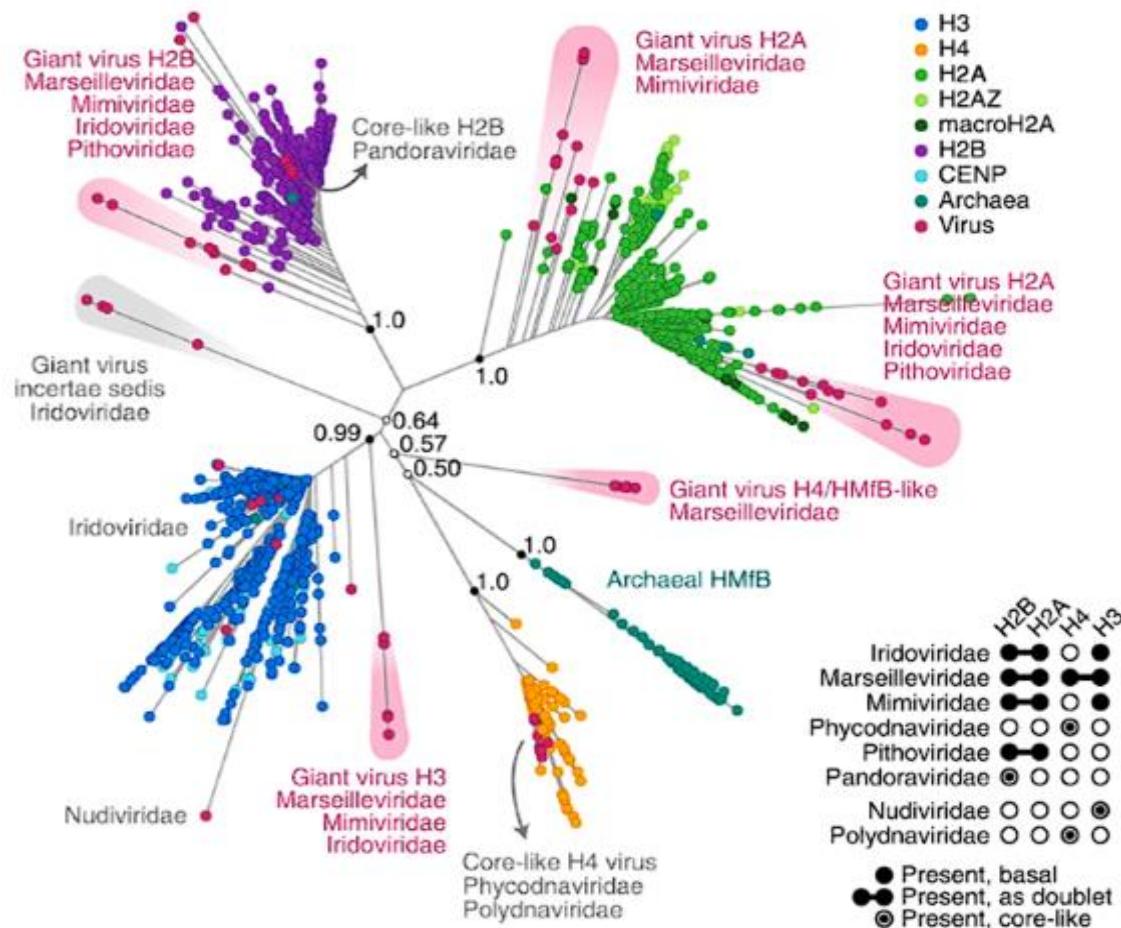
## Marseillevirus histone “doublet” genes

A



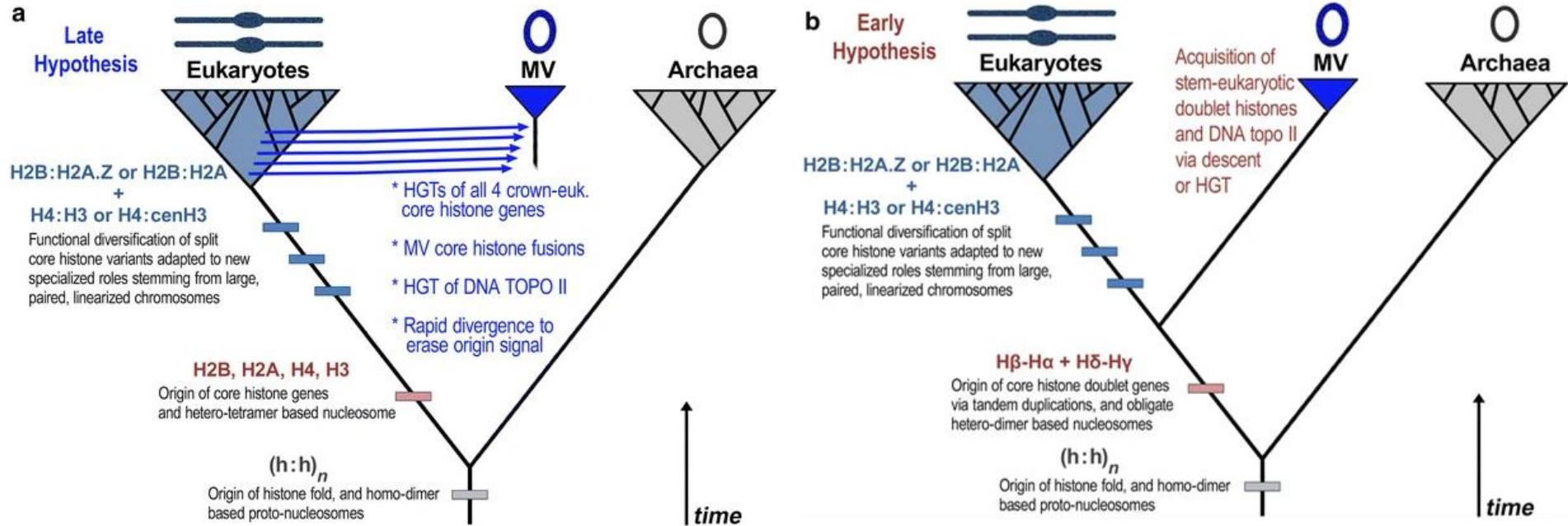
C



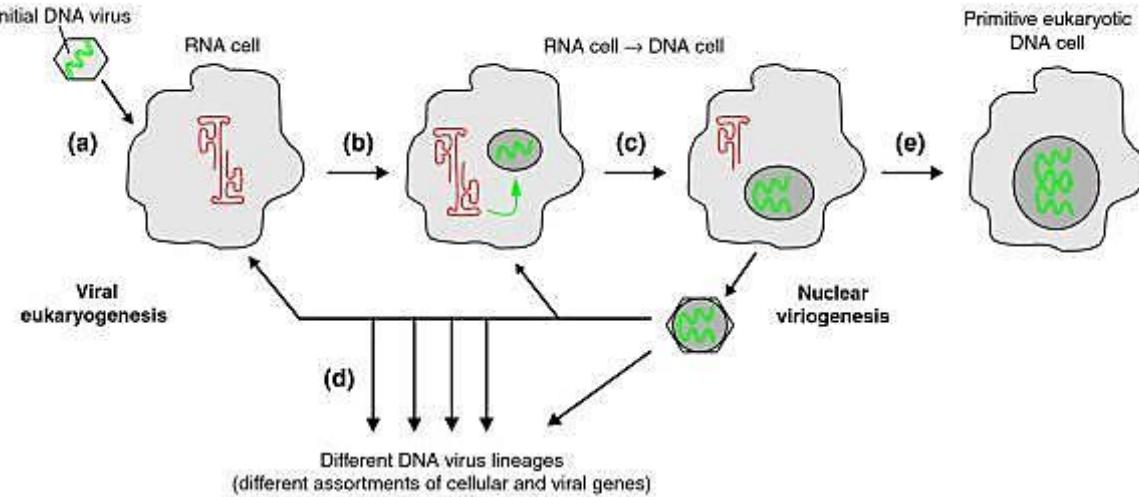


Phylogenetic analysis of histone domains, with a focus on viral homologues. Statistical supports (approximate Bayes posterior probabilities) are shown for the deepest node of each canonical eukaryotic or archaeal histone clade. The inset table summarizes the presence of doublet histone genes per lineage

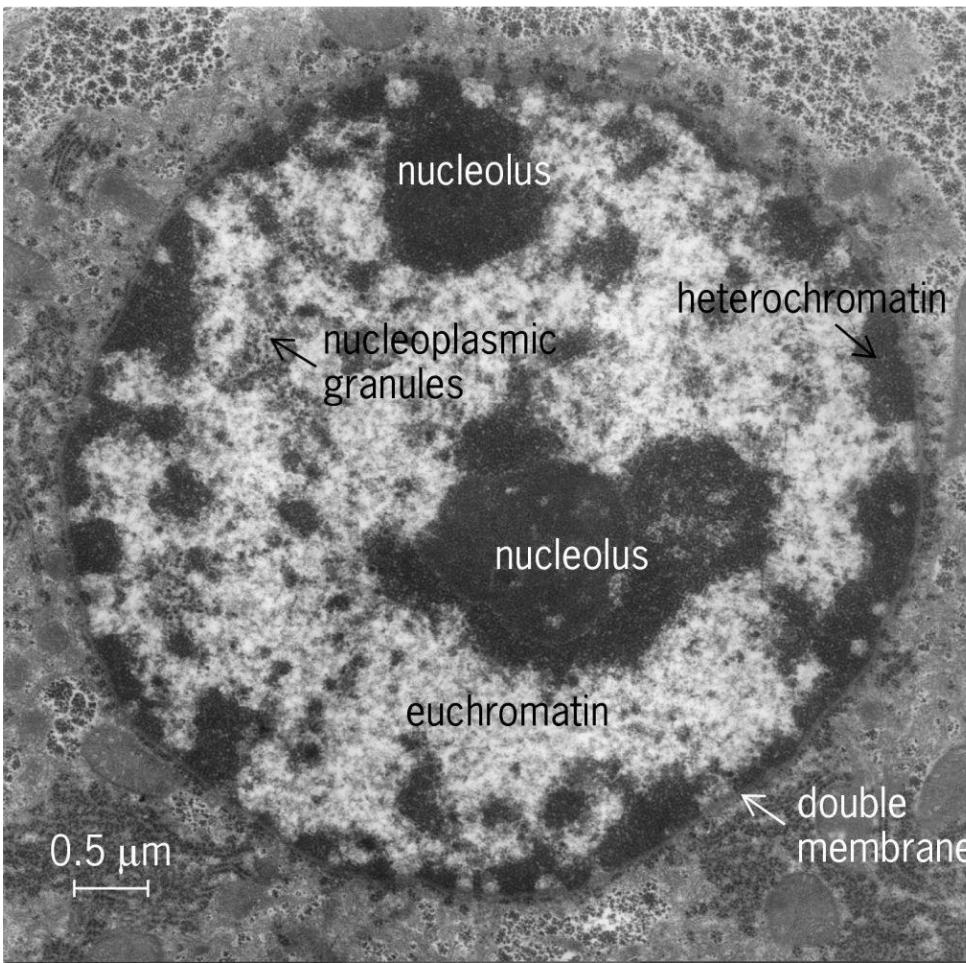
# Эволюция гистонов вирусов



# viral karyogenesis (?)



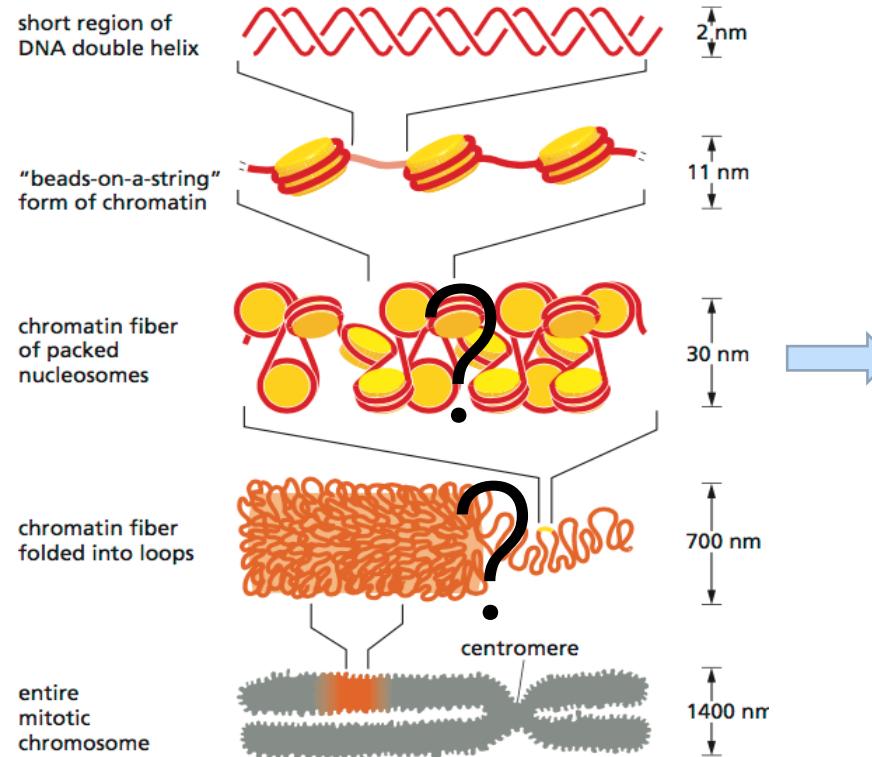
Далее поговорим про устройство  
интерфазного хроматина на более больших  
масштабах



McGraw-Hill Concise Encyclopedia of Bioscience. © 2002 by The McGraw-Hill Companies, Inc.

# Представления о структуре хроматина

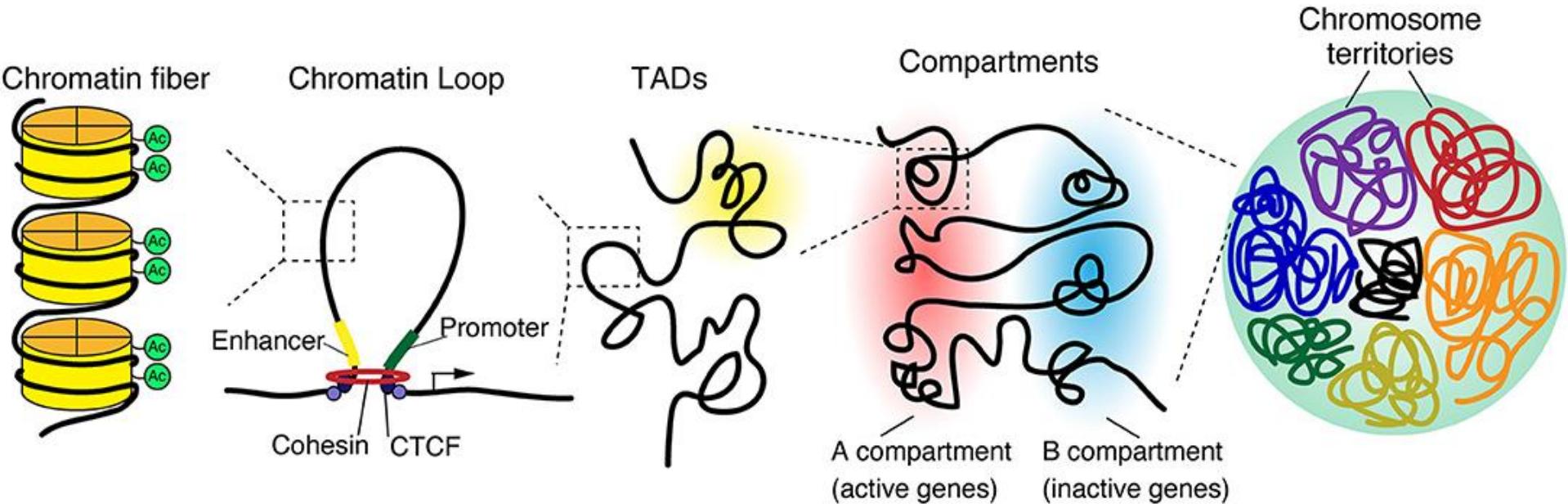
## Устаревшее иерархическое представление



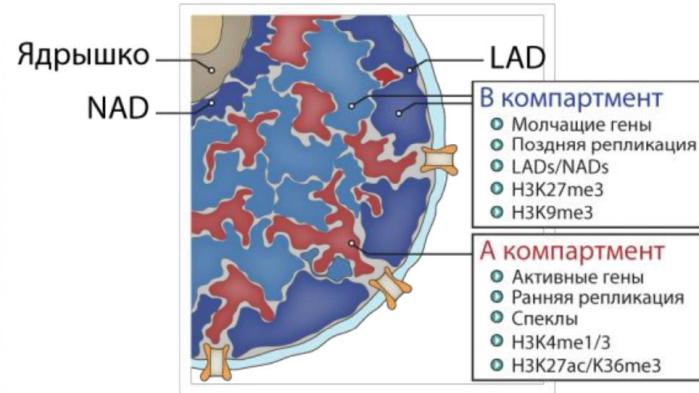
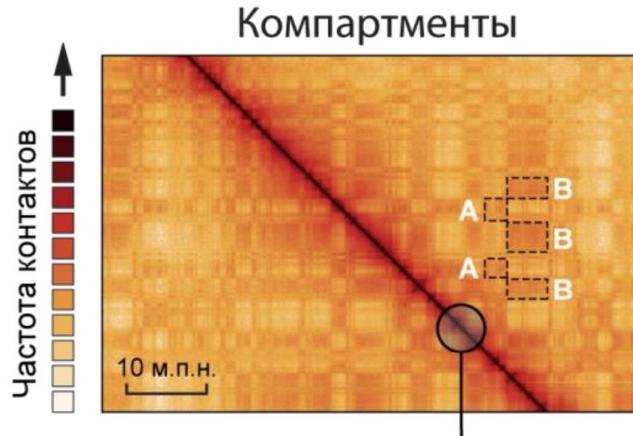
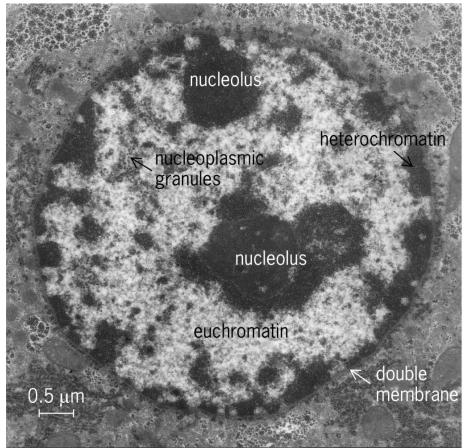
В естественных  
условиях не  
существует

## Представления о структуре хроматина

Более современное представление



# Концепция 1: Эу/гетерохроматин, А/В – компартменты

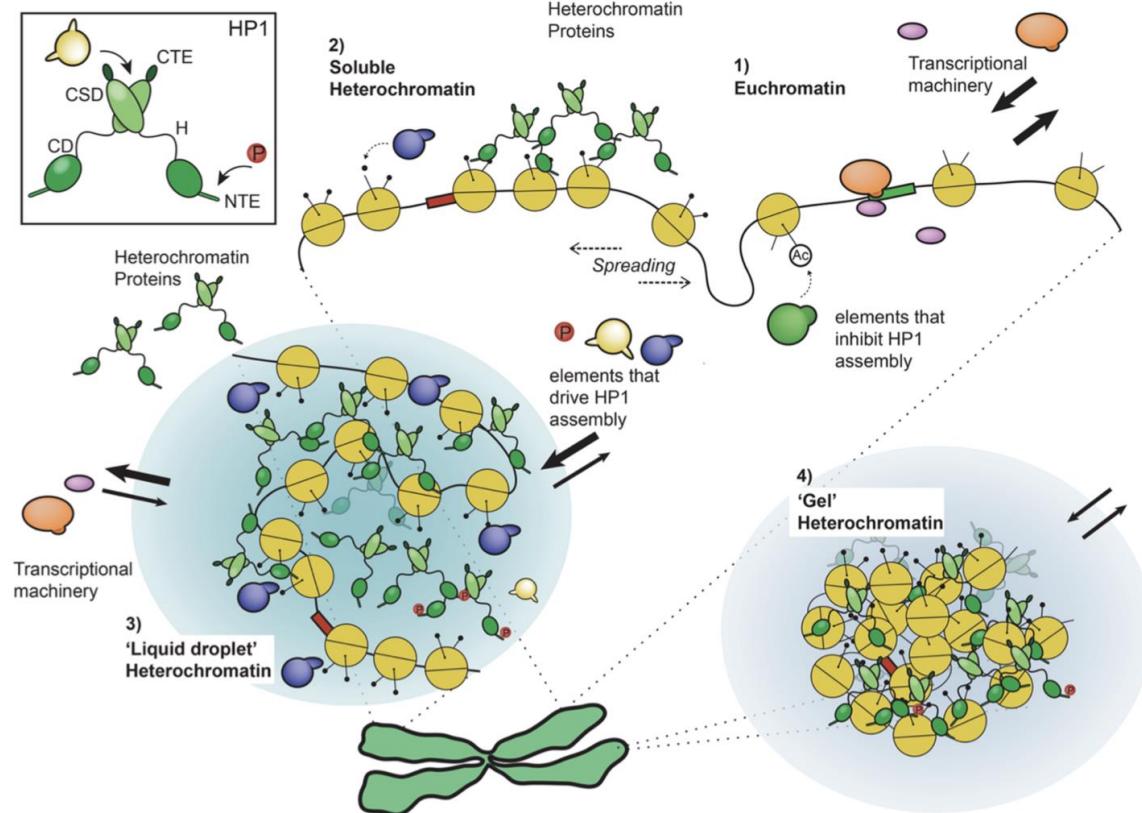


С.В. Ульянов –  
докторская  
диссертация 2023 г.

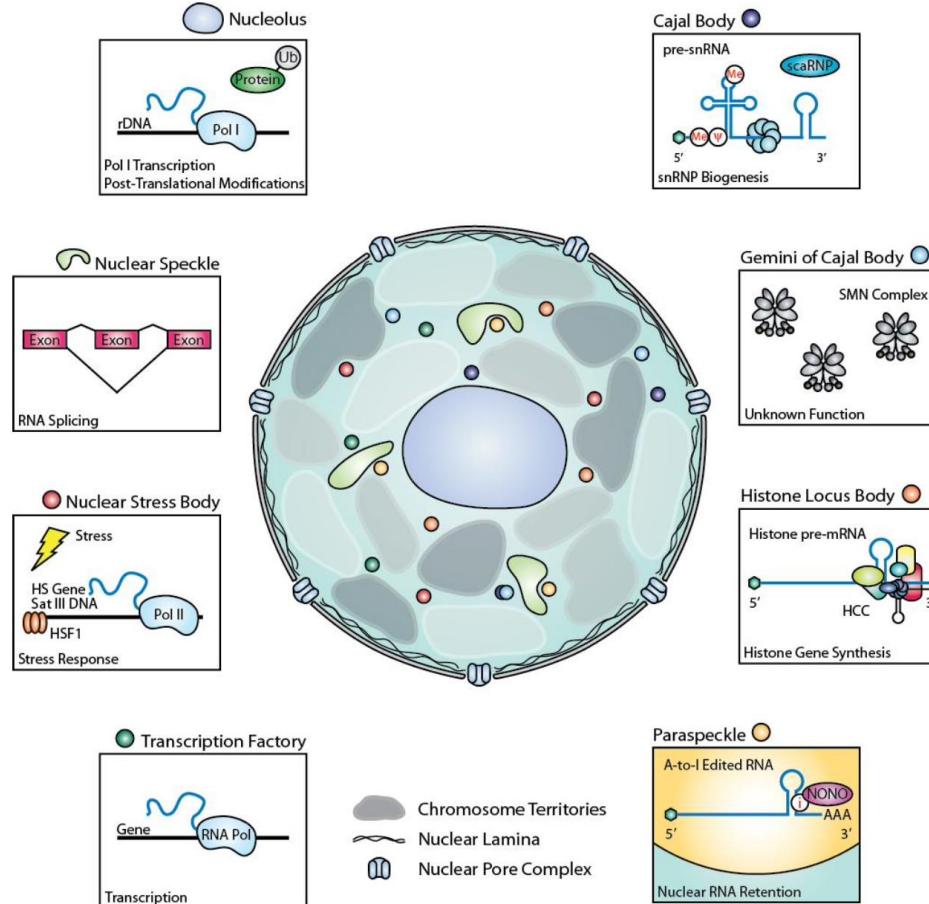
## Концепция 2: "Жидкие капли"

### разделение фаз жидкость-жидкость

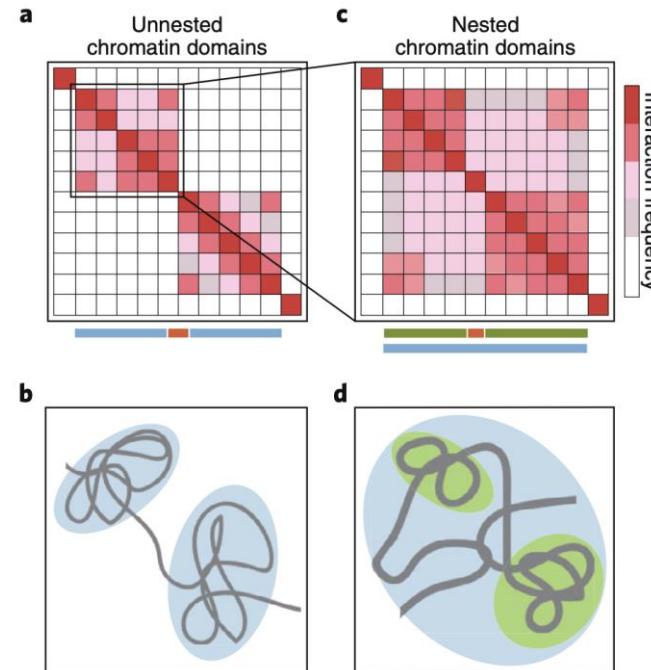
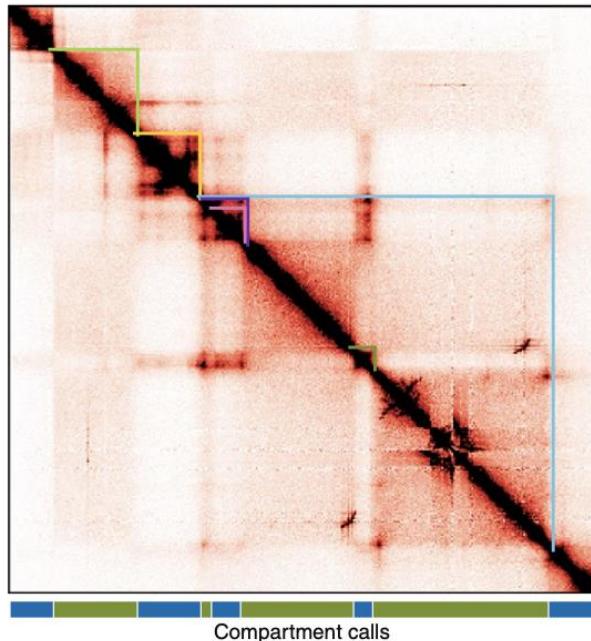
a.



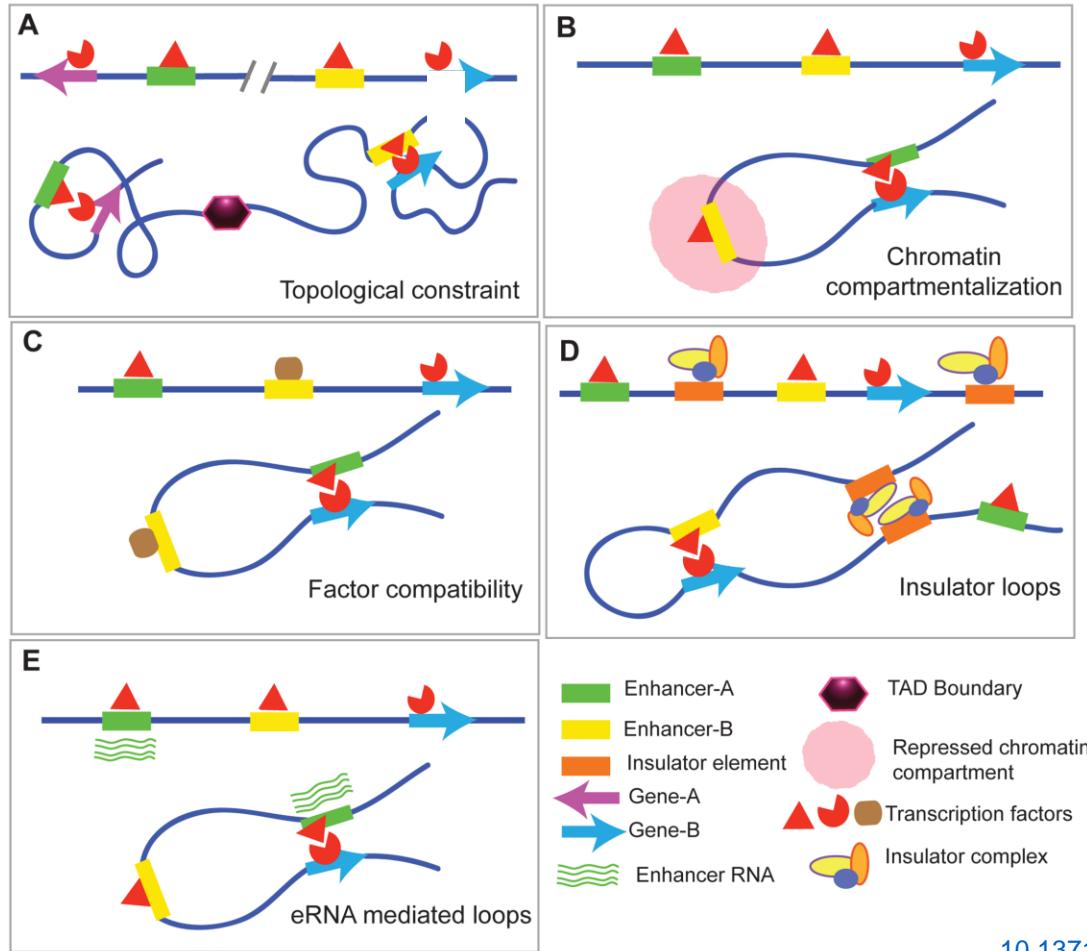
# В формировании немембранных органелл важную роль играют статистические физические взаимодействия (разделение фаз)



## Концепция 3: ТАДы – топологически ассоциирующие домены

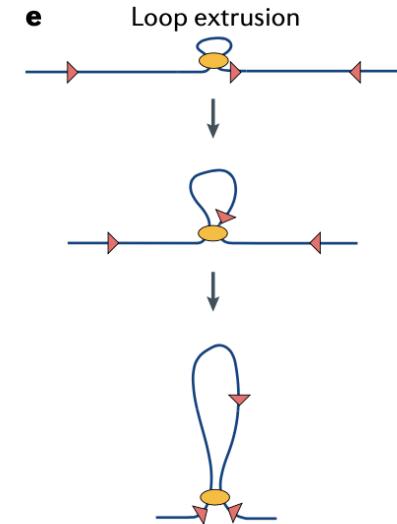
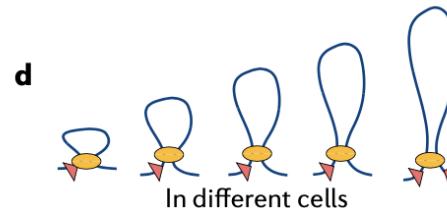
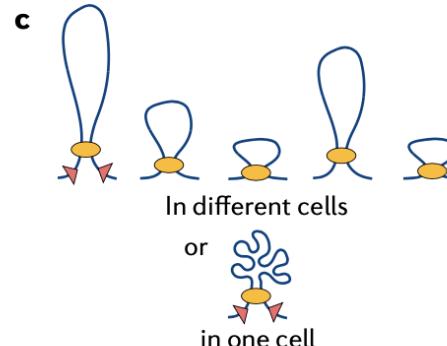
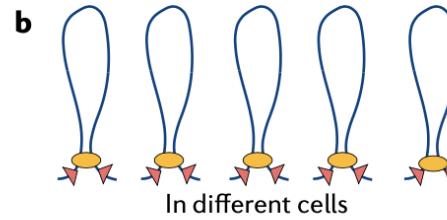
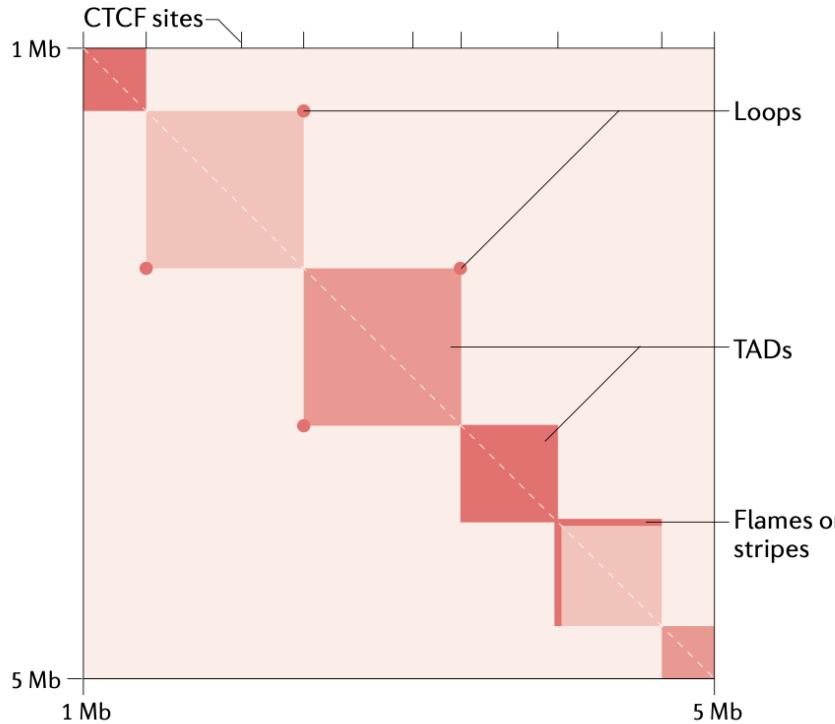


## Концепция 4: "Петли", топология и взаимодействия элементов вдоль ДНК



## Концепция 5: Loop extrusion – экструзия петель

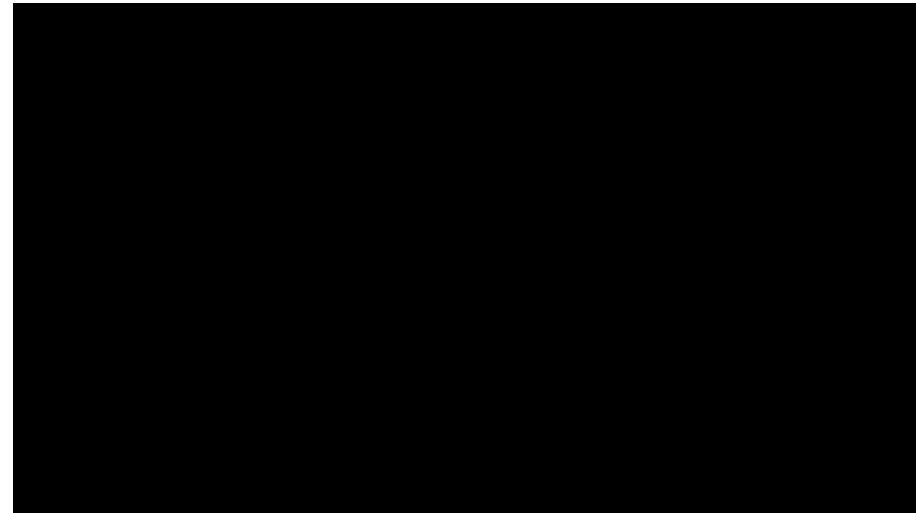
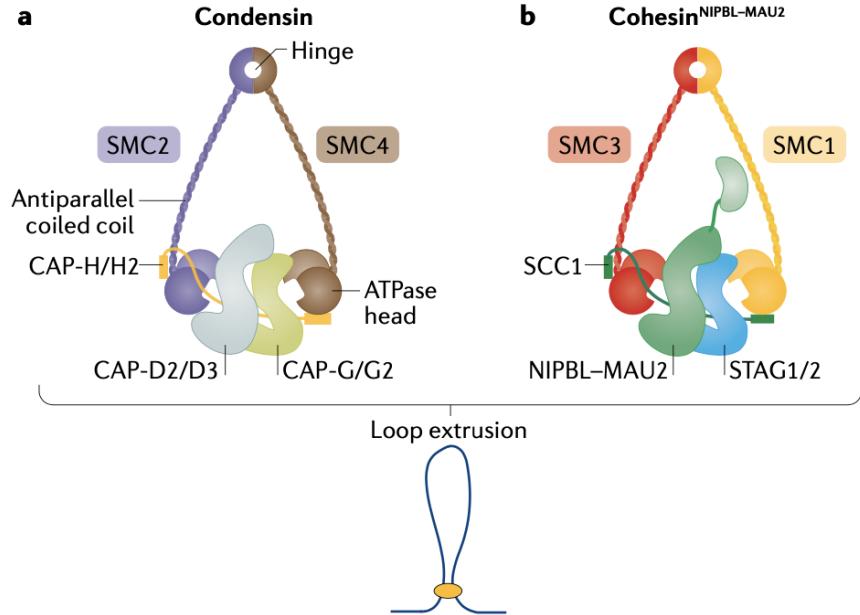
### a Cell population

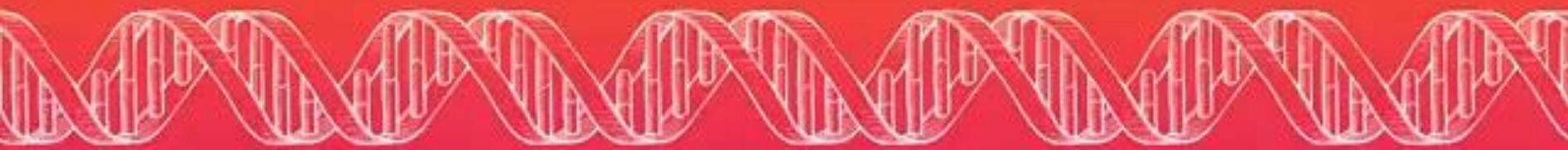


● Cohesin complex  
● CTCF

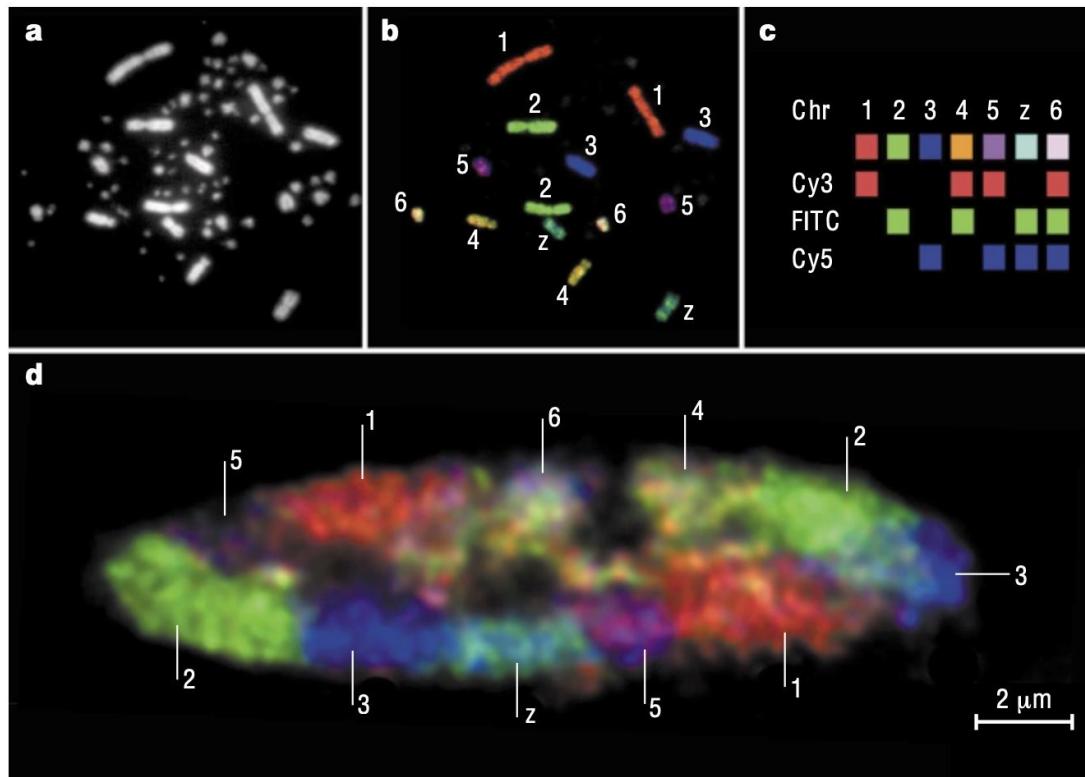
Fig. 1 | Interphase genome organization. a | Schematic representation of a Hi-C map depicting the organization, across

## Концепция 5: Loop extrusion – экструзия петель





## Концепция 6: Хромосомные территории

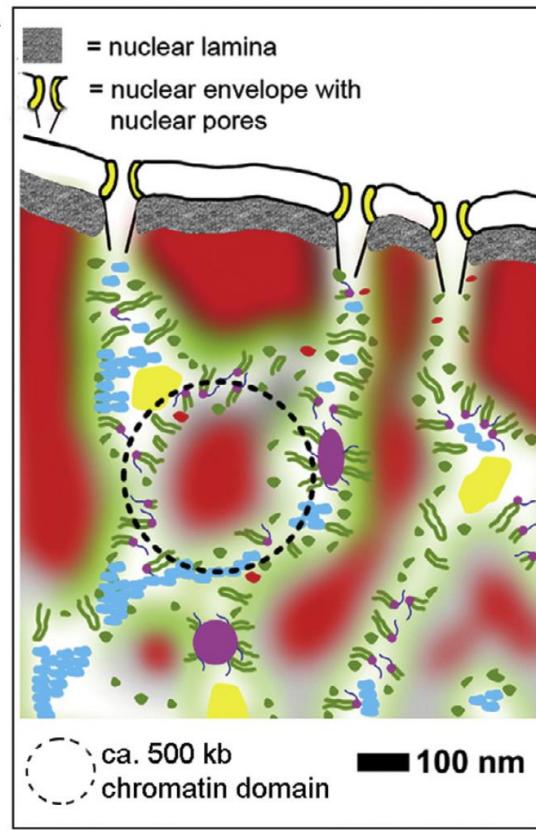


**Figure 2 | Chromosome territories in the chicken.** **a** | 4,6-diamidino-2-phenylindole (DAPI)-stained, diploid, chicken metaphase spread with macro- and microchromosomes. **b** | The same metaphase spread after multicolour fluorescence *in situ* hybridization with pseudocoloured chromosome paint probes (image courtesy of Johannes Wienberg) were labelled by a combinatorial scheme with oestradiol (1, 4, 5, 6),

Cremer, T.; Cremer, C. (2001). . Nature Reviews Genetics, 2(4), 292–301. doi:10.1038/35066075

## Концепция 7: active compartment/inactive compartment/interchromatin compartment

A



### active nuclear compartment **ANC**

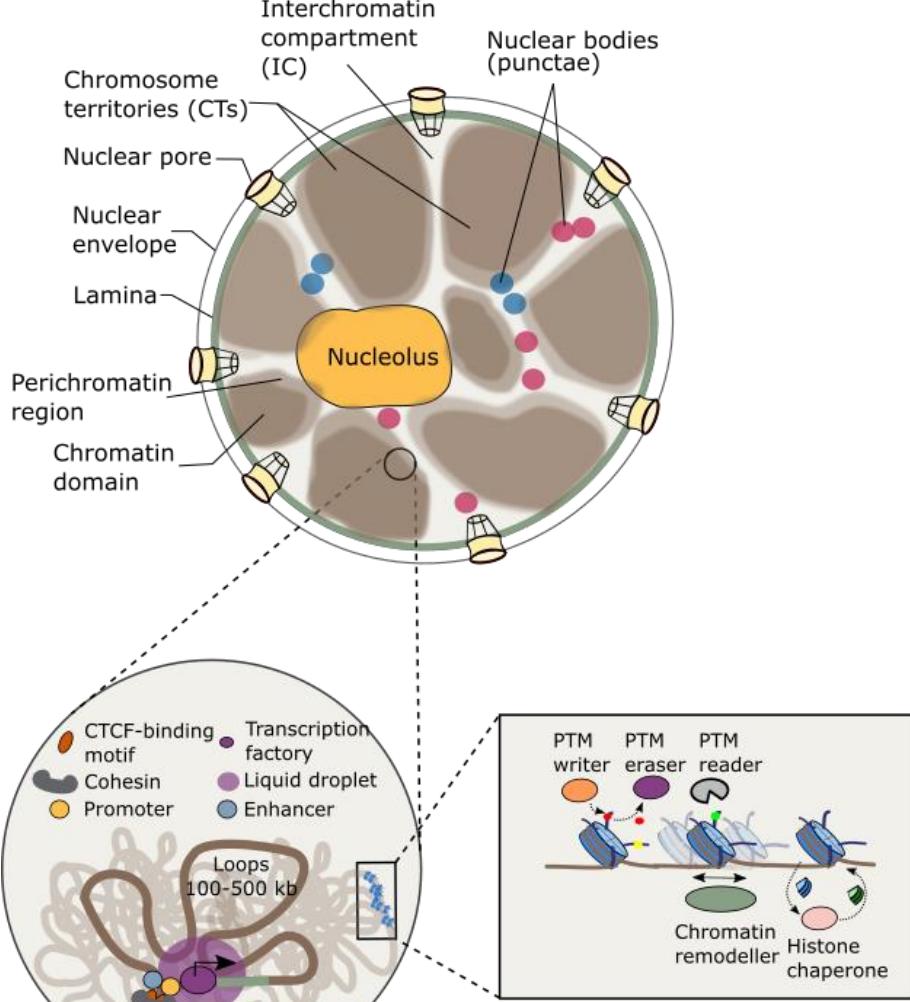
- Transcriptionally competent decondensed chromatin marked by „active“ histone marks
- transcriptionally competent chromatin loops,
- transcriptionally active chromatin loops
- Interchromatin compartment, harboring
  - Transcription factories,
  - splicing speckles,
  - architectural proteins, e.g. CTCF, SAF-A, Matrin

B

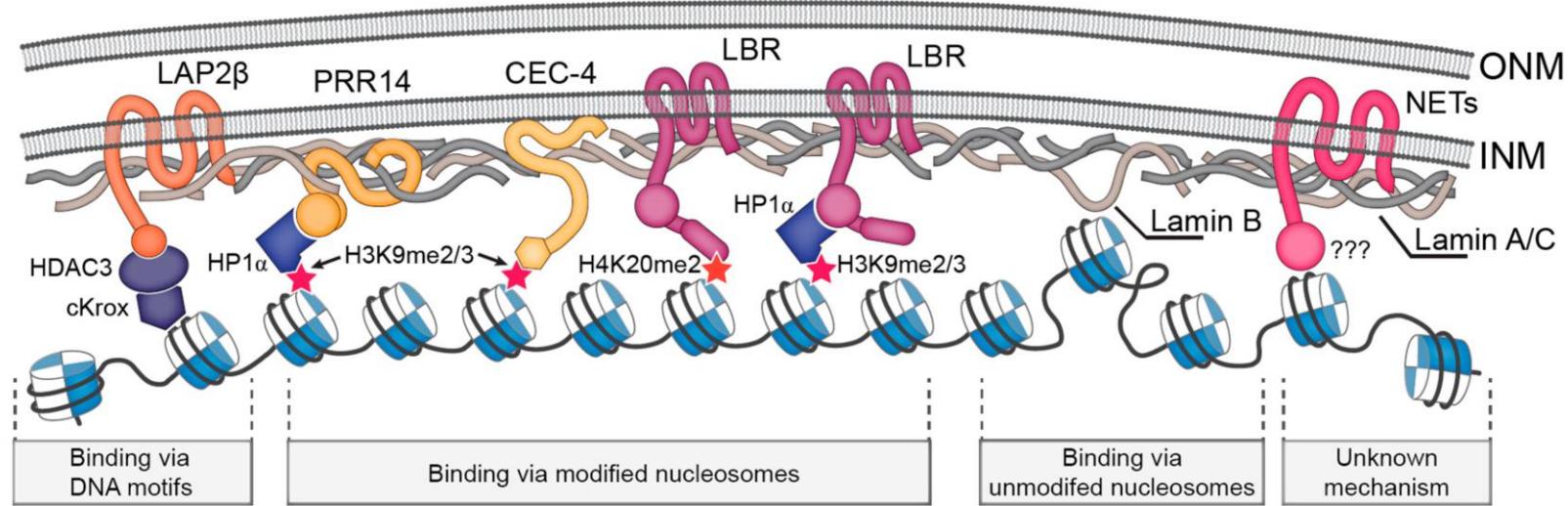


### inactive nuclear compartment **INC**

- Compacted part of chromatin domain clusters (CDCs) marked by repressive histone marks



## Концепция 8: ядерная ламина и lamina-associated domains



The Nuclear Lamina as an Organizer of Chromosome Architecture

by Yuri Y. Shevelyov 1,\* and Sergey V. Ulianov 2

Спасибо за внимание!