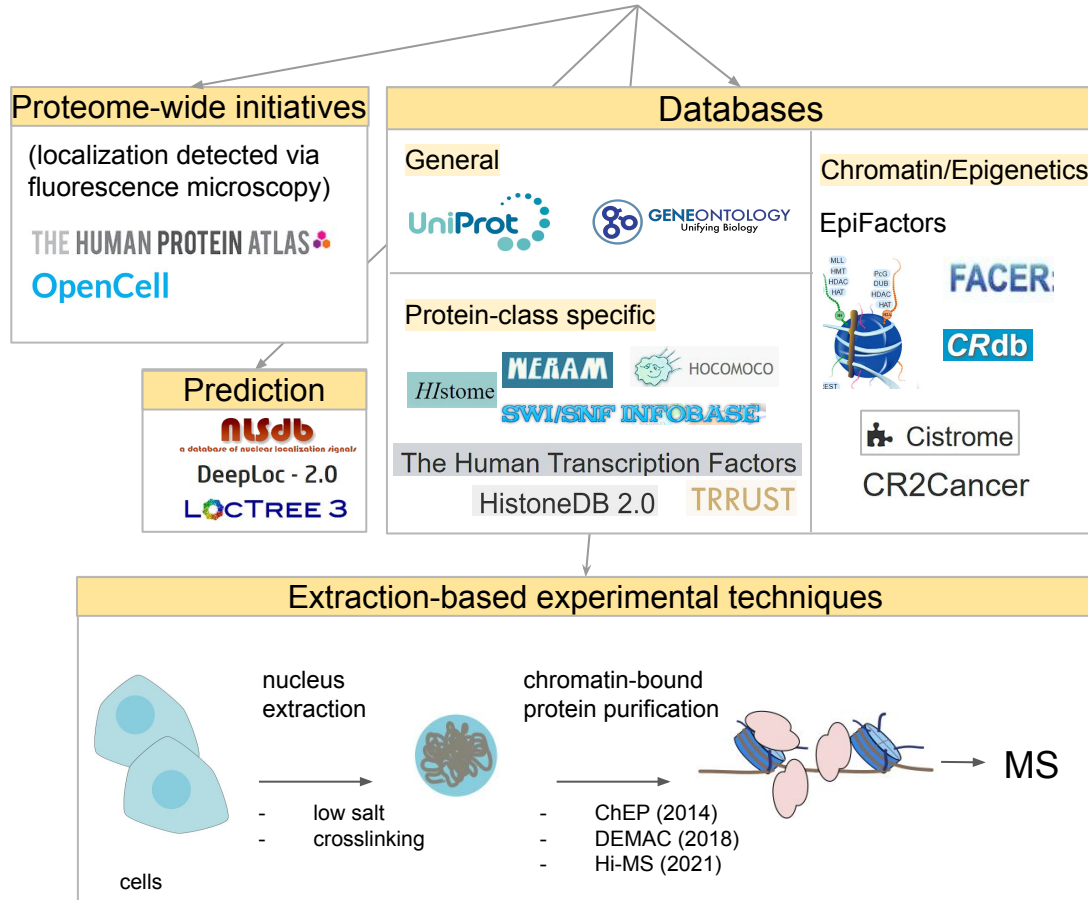


Строение хроматина и ядра клетки

семинар 2

Sources of information about nuclear proteome, protein localization and functional annotation

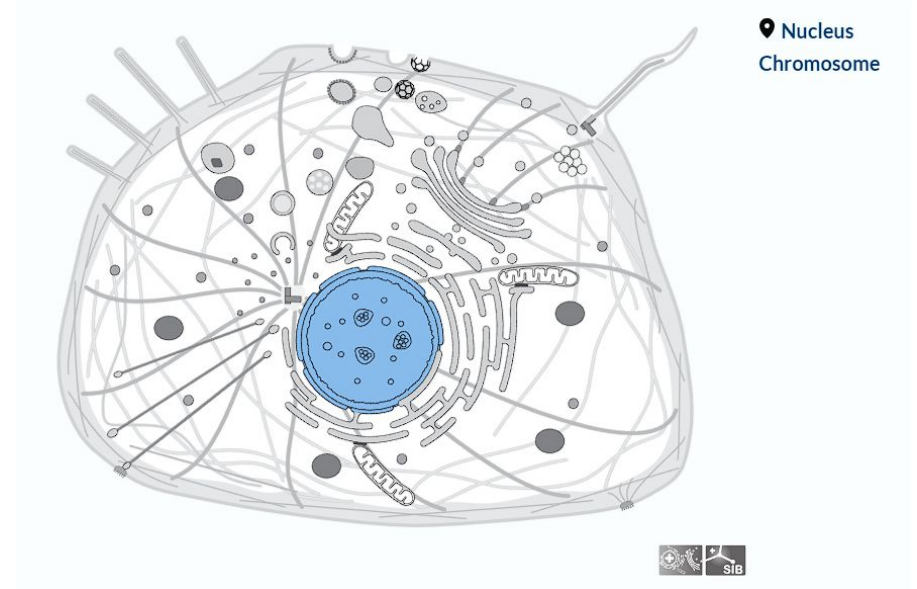


UniProt Subcellular location

Controlled vocabulary: 561 terms

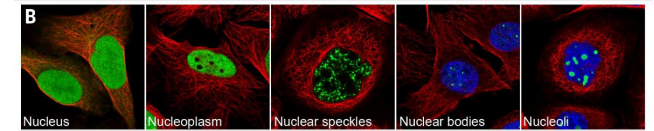
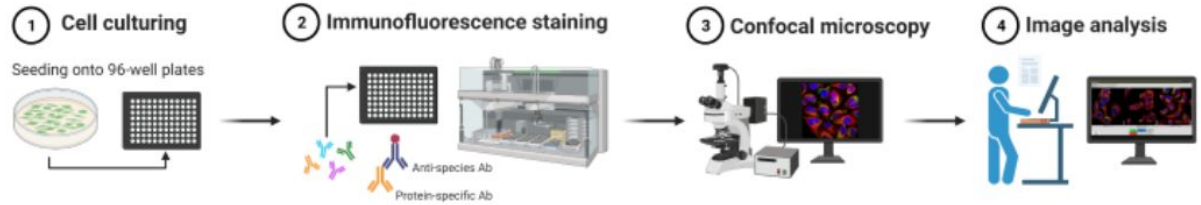
Evidences:

- ECO:[0000269](#): Experimental evidence
- ECO:[0000250](#): Sequence similarity evidence
- ECO:[0000305](#): Curator inference evidence
- ECO:[0000255](#): match to sequence model evidence used in manual assertion
- ECO:[0000303](#): author statement without traceable support used in manual assertion

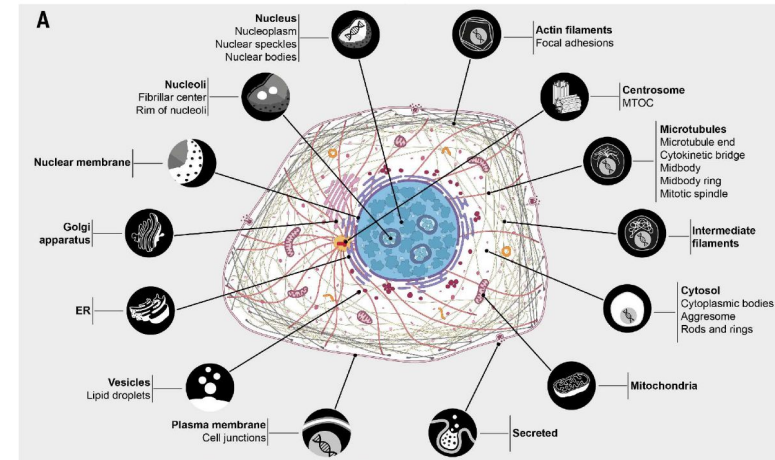


Human Protein Atlas

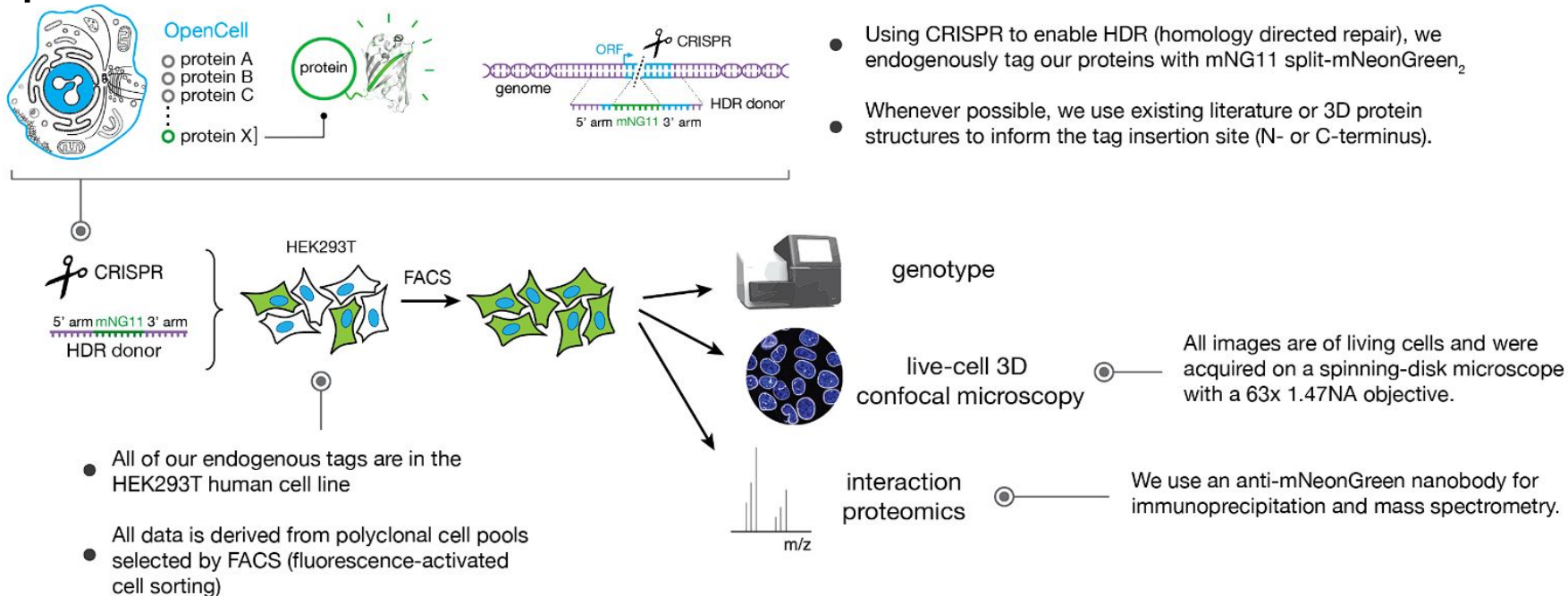
13 major organelles,
30 subcellular structures,
13k human proteins
4 level of evidences:



- **Enhanced** - One or more antibodies are enhanced validated and there is no contradicting data, such as literature describing experimental evidence for a different location.
- **Supported** - There is no enhanced validation of the used antibody, but the annotated localization is reported in external literature.
- **Approved** - The localization of the protein is partially in agreement with external data, or has not been previously described.
- **Uncertain** - The antibody-staining pattern contradicts experimental data or expression is not detected at RNA level.

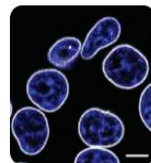


OpenCell

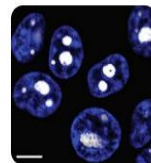


Levels of evidences:

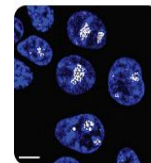
- grade 3 identifies prominent localization compartment(s),
- grade 2 represents less pronounced localizations,
- grade 1 annotates weak localization patterns nearing our limit of detection



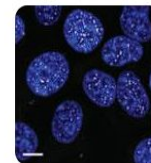
Nuclear membrane
48 proteins



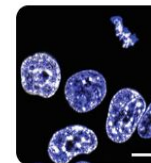
Nucleolus (GC)
100 proteins



Nucleolus (FC/DFC)
37 proteins

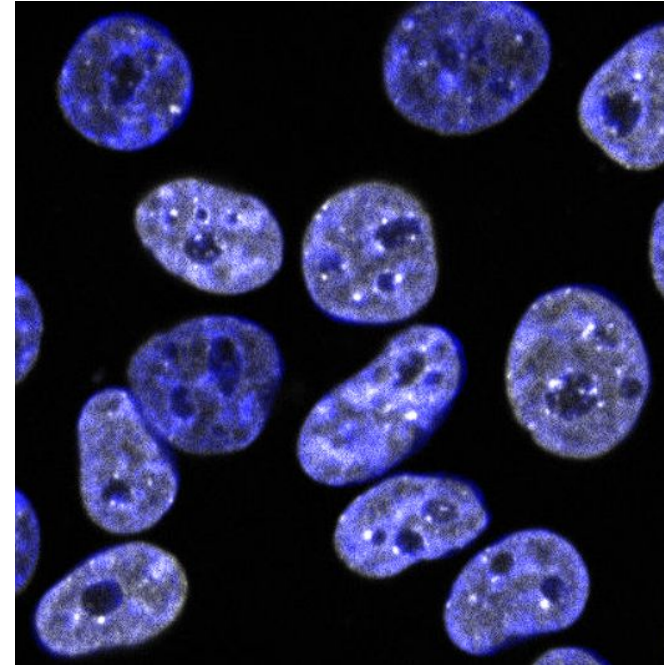
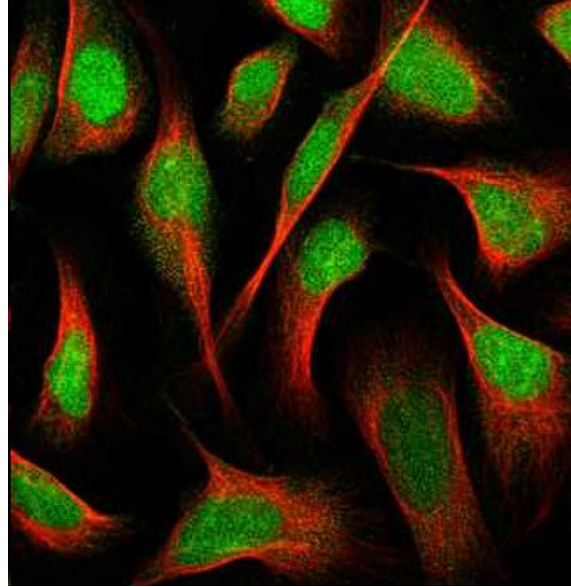
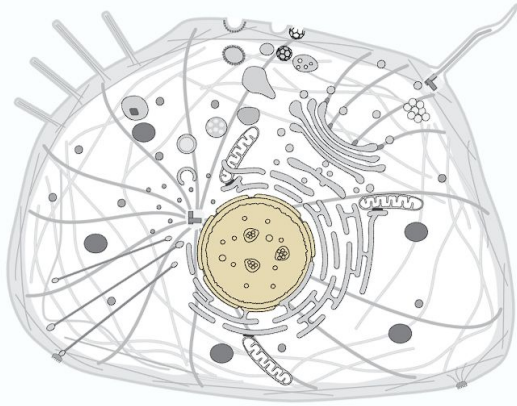


Nuclear punctae
152 proteins



Chromatin
145 proteins

Задача: найти клеточную локализацию CBX5 (HP1alpha) или CBX1 в UniProt, Human Protein Atlas, OpenCell




Знакомство с HistoneDB 2.0

<https://histonedb.bioeng.ru/>

HistoneDB 2.0

Browse

Analyze Your Sequence

 Basket **5**

Human Histones

Help

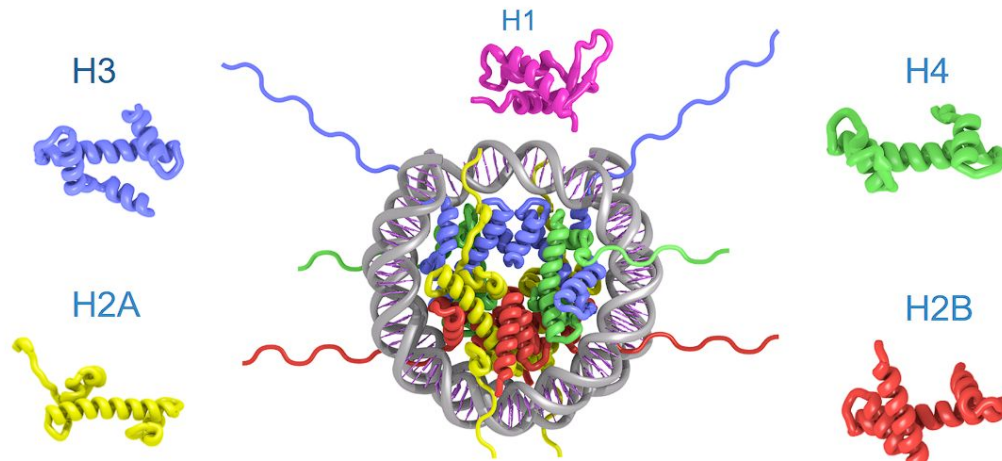
Search (H2A.Z.2.s1)

Search

Advanced

HistoneDB 2.0 – with variants

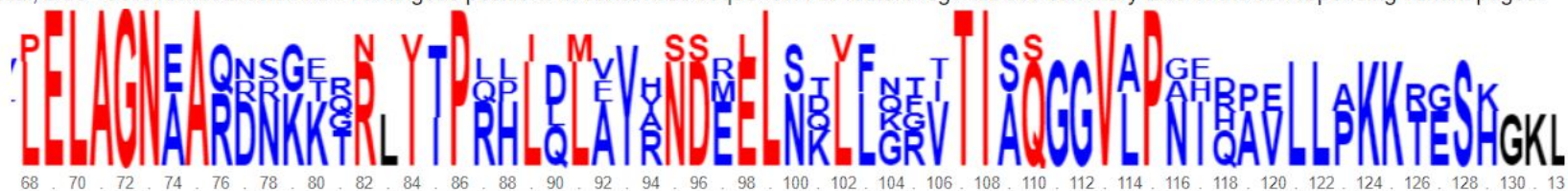
This histone database can be used to explore the diversity of histone proteins and their sequence variants in many organisms. The resource was established to better understand how sequence variation may affect functional and structural features of nucleosomes. To get started, select a histone type to explore its variants.



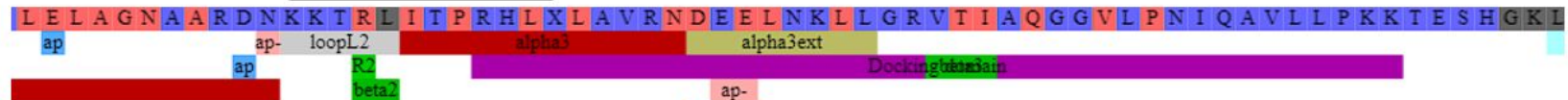
Задача: сделать множественное выравнивание гистонов H2A

1. Выбрать из Curated sequence нужные гистоновые варианты (например, канонический, macro, short H2A.B) для человека и мыши - положить последовательности в корзину
2. Сделать MSA

Keys: red - 80% identical, blue - 50% identical columns. X-ambiguous positions in consensus sequence. For feature legends see summary tabs of the corresponding variant pages.



Consensus



NP...1|homo..|ca_H2A
NP...1|mus..|ca_H2A
XP...1|homo..|macroH2A
NP...1|mus..|H2A.B
NP...1|homo..|H2A.B



Знакомство с NuclDB

<https://nucldb.intbio.org/>



Browse Statistics Help  Collection: 3

Search (e.g. DOT1L)

Search

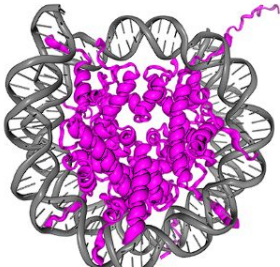
Advanced

NucleosomeDB - a database of nucleosome structures

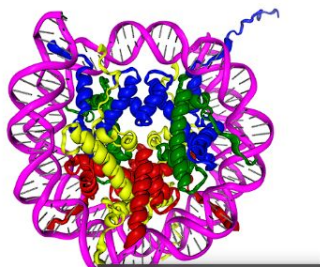
The database allows the exploration of nucleosome structures' diversity and searches them by histone and DNA sequence types, interaction partners, and multi-nucleosomal organization. NucleosomeDB provides tools for a comparative analysis of histone and DNA geometry and their contacts in an aligned reference frame. To get started explore nucleosome collections below.

Last update 01.02.2023

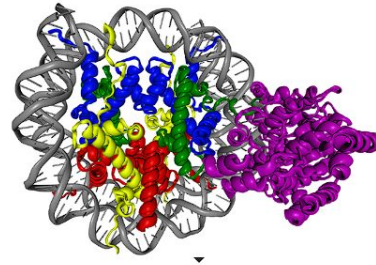
Core Histone Variants



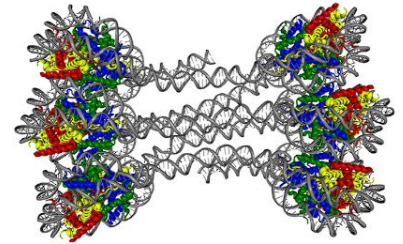
Dna Sequence Variants



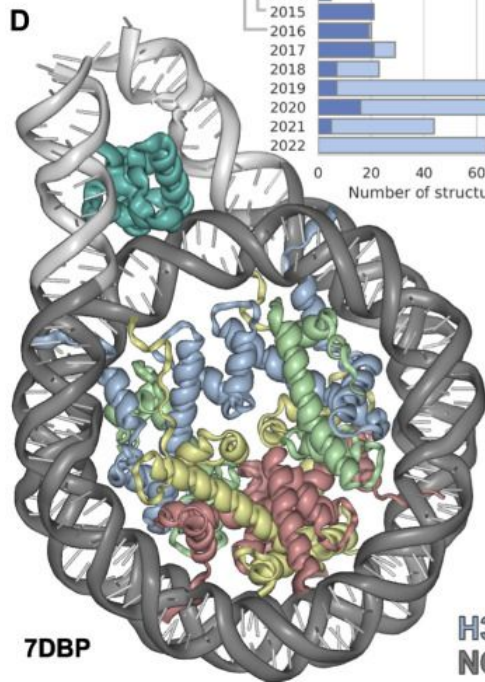
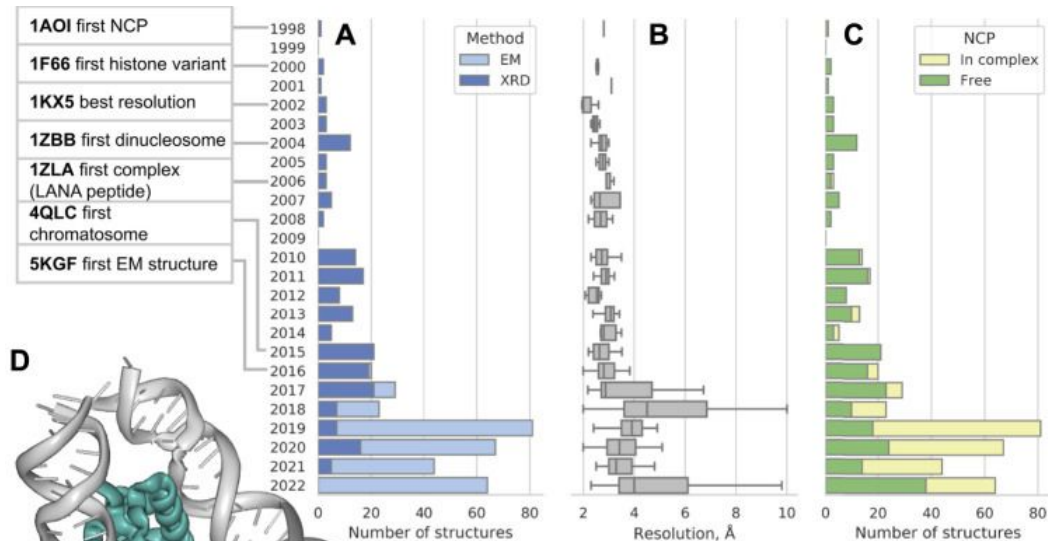
Nucleosome Complexes



Supranucleosomal Complexes



NuclDB



E

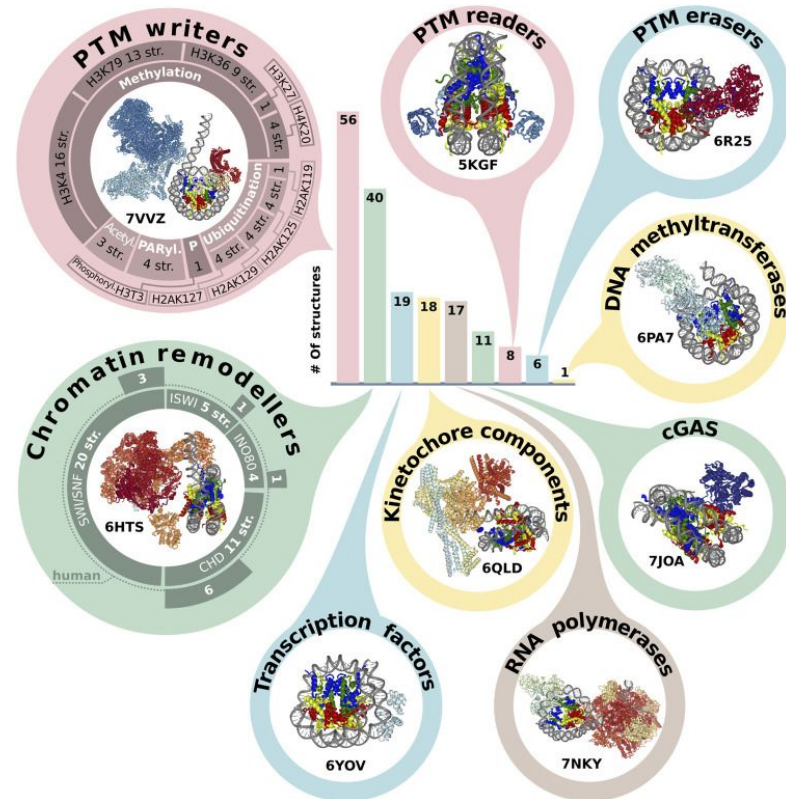
H3		H2B	
canonical	386	canonical	436
H3.3	31	H2B.1	5
cenH3	27		
TS_H3.4	1		
H3.5	1		
H3.Y	1		
H3.6	1		

Linker histone	
Human H1.4	20
Human H1.0	7
H5	2
Human H1.10	2
H1.8	1
H1.0-B	1

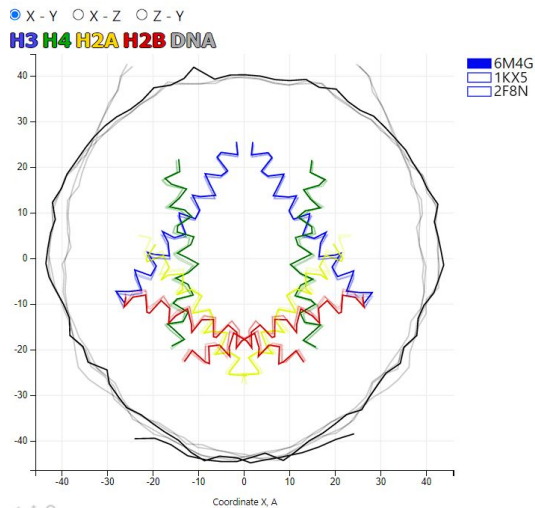
H2A	
canonical	407
H2A.X	19
H2A.Z	10
H2A.1	4
macroH2A	2
H2A.B	2

Positioning DNA sequence	
Widom 601 based	246
α -satellite based	166
telomeric	10
MMTV	3
other	16

H3H4H2AH2BH1
NCP DNA Linker DNA



Задача: сравнение структур нуклеосом с canonical H2A, H2A.B, macroH2A

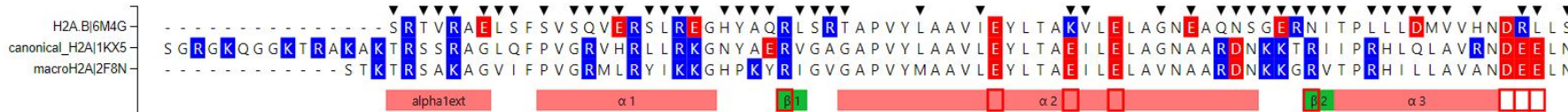


1. менее стабильные нуклеосомы с H2A.B
2. другие заряды в H2A.B в acidic patch
3. Макро-домен H2A не разрешен, так что разница структур с каноническим не велика

Comparative analysis of selected structures

H3 H4 H2A H2B DNA

Proximal Distal



A) H3 Histones H4 Histones H2A Histones H2B Histones

Canonical isoforms:
- H3.1 (*H3C1*, *H3C2*,
H3C3, *H3C4*,
H3C6, *H3C7*,
H3C8, *H3C10*,
H3C11, *H3C12*)
- H3.2 (*H3C13*,
H3C14, *H3C15*)

Variants:
- cenH3 (*CENPA*)
- H3.5 (*H3-5*)
- H3.3 (*H3-3A*, *H3-3B*)
- TS H3.4 (*H3-4*)
- H3.Y.1 (*H3Y1*)
- H3.Y.2 (*H3Y2*)

Canonical isoforms:
- H4C1, H4C2, H4C3,
H4C4, H4C5,
H4C6, H4C8,
H4C9, H4C11,
H4C12, H4C13,
H4C14, H4C15,
H4-16
- H4C7

Canonical isoforms:
- H2AC11, H2AC13,
H2AC15, H2AC16,
H2AC17
- H2AC4, H2AC8
- H2AC18, H2AC19
- H2AC6
- H2AC7
- H2AC12
- H2AC14
- H2AC20
- H2AC21
- H2AW

Variants:
- H2A.P (*H2AP*)
- H2A.Z.1 (*H2AZ1*)
- H2AZ.2 (*H2AZ2*)
- H2A.X (*H2AX*)
- TS H2A.1 (*H2AC1*)
- H2A.J (*H2AJ*)
- macroH2A.1 (*MACROH2A1*)
- macroH2A.2 (*MACROH2A2*)
- H2A.B.1 (*H2AB1*)
- H2A.B.2 (*H2AB2*)

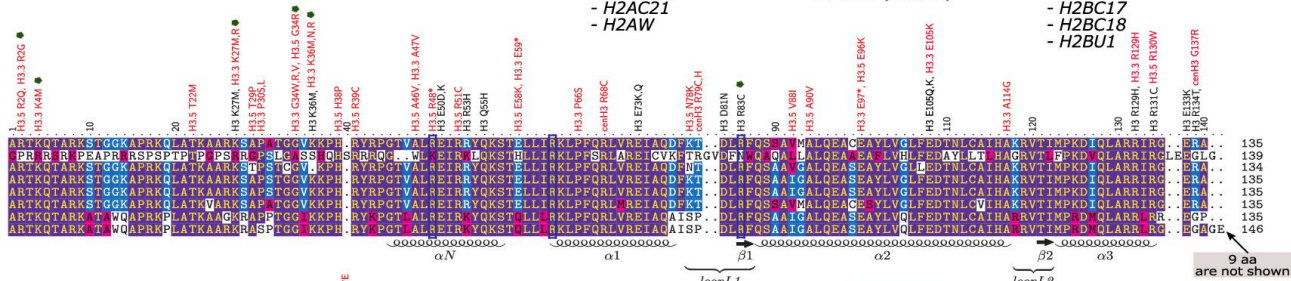
Canonical isoforms:
- H2BC4, H2BC6, H2BC7,
H2BC8, H2BC10
- H2BC3
- H2BC5
- H2BC9
- H2BC11
- H2BC12
- H2BC13
- H2BC14
- H2BC15
- H2BC17
- H2BC18
- H2BU1

Variants:
- TS H2B.1 (*H2BC1*)
- H2B.W (*H2BW1*,
H2BW2)
- H2B.S (*H2BS1*)
- H2B.E (*H2BE1*)

B)

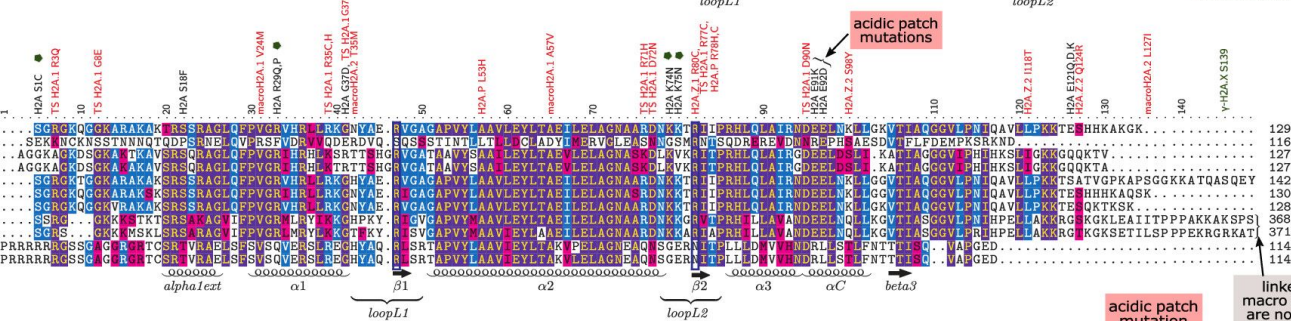
H3

canonical H3.1
cenH3
H3.5
H3.3.1
H3.3.2
TS H3.4
H3.Y.1
H3.Y.2



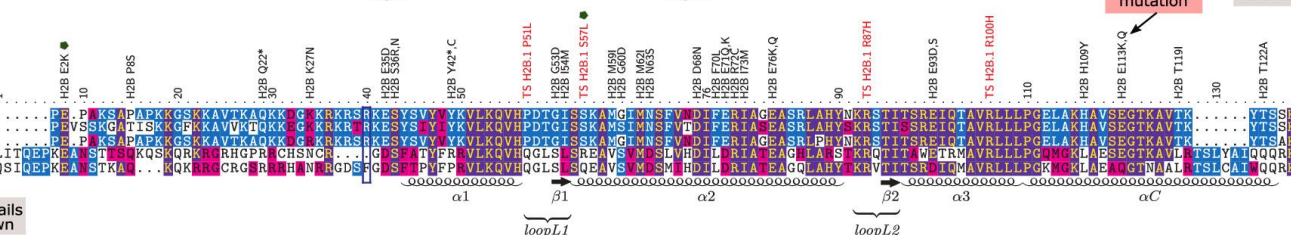
H2A

canonical H2A
H2A.P
H2A.Z.1
H2A.Z.2
H2A.X
TS-H2A.1
H2A.J
macroH2A.1
macroH2A.2
H2A.B.1
H2A.B.2



H2B

canonical H2B
TS H2B.1
H2B.S
H2B.W.1
H2B.W.2



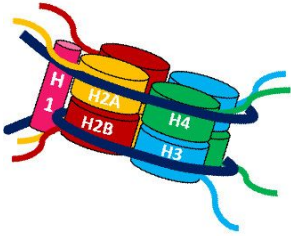
(Espirito, Gribkova, 2021)

PTM sites

Mutation: ★ ★

Interaction: — — —

Chromatosome



DNA: —

Histone H1: ●

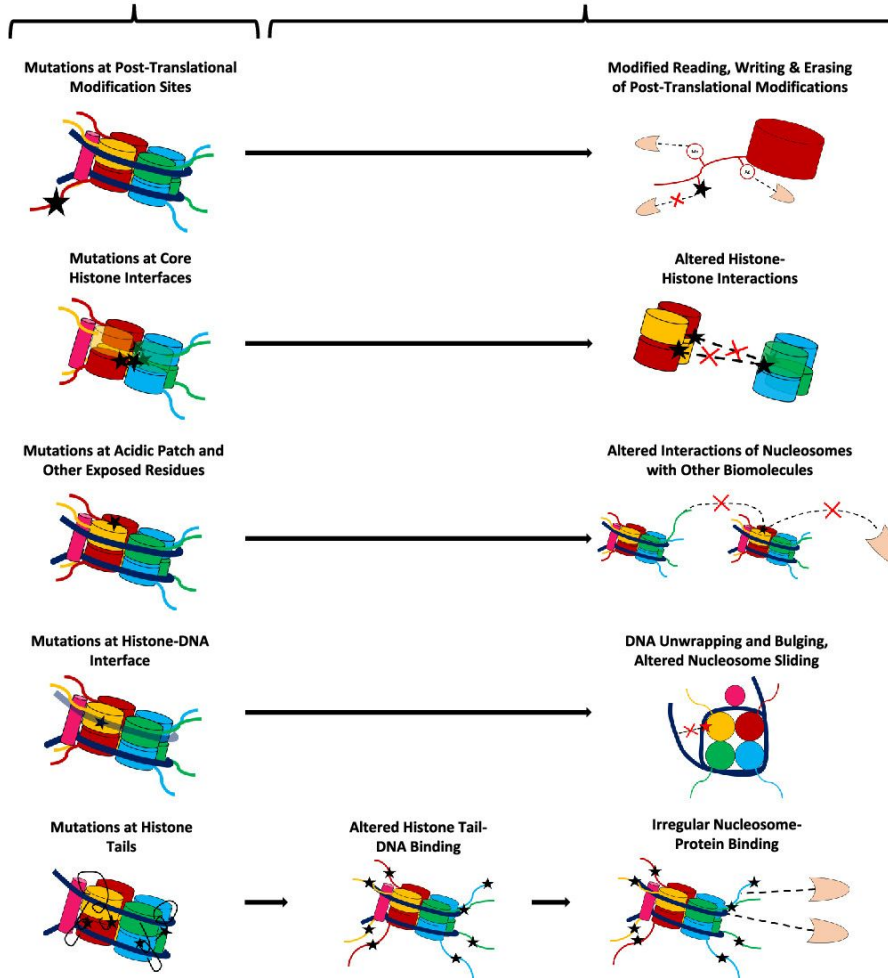
Histone H2A: ●

Histone H2B: ●

Histone H3: ●

Histone H4: ●

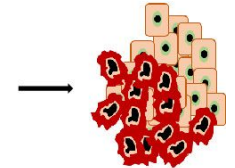
Histone Mutations



Global Effects

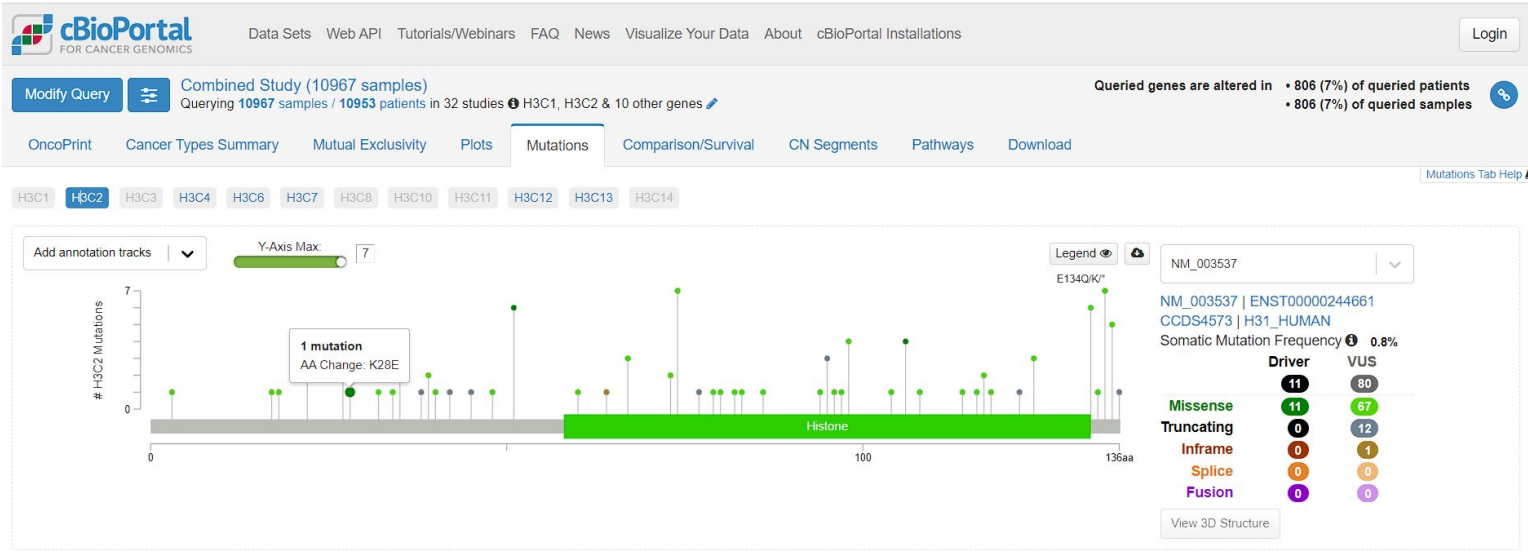
- Perturbed Regulation of:**
- DNA Accessibility
 - Chromatin Compaction
 - DNA Repair
 - DNA Replication
 - Gene Expression

Oncogenesis



Задача: поиск мутаций в генах гистонов

Гены каннического гистона H3: H3C1, H3C2, H3C3, H3C4, H3C6, H3C7, H3C8, H3C10, H3C11, H3C12, H3C13, H3C14



91 Mutations (page 1 of 4)

Study of Origin	Sample ID	Cancer Type Detailed	Protein Change	Annotation	Mutation Type	Copy #	COSMIC	Allele Freq (T)	# Mut in Sample
Ovarian Serous Cyst...	TCGA-04-1336...	Serous Ovarian Cancer	E51Q	ⓘ ⓘ ⓘ ⓘ ⓘ	Missense	Diploid		0.42	67
Bladder Urothelial Car...	TCGA-E7-A6M...	Bladder Urothelial Carcinoma	E51Q	ⓘ ⓘ ⓘ ⓘ ⓘ	Missense	Gain		0.39	120