Name Surname :_____ Group Nº _____2023

Androgen Nuclear Receptor **Proteins** with **Lipid** gene expression trigger.

A. Task studies for the use of Interactive Molecule viewers:

ChemScape MDLi **RasMol** (RasMac); MAGE FireFox application.

B. RSU Aris Kaksis 2023 studies about **androgens** look at address:

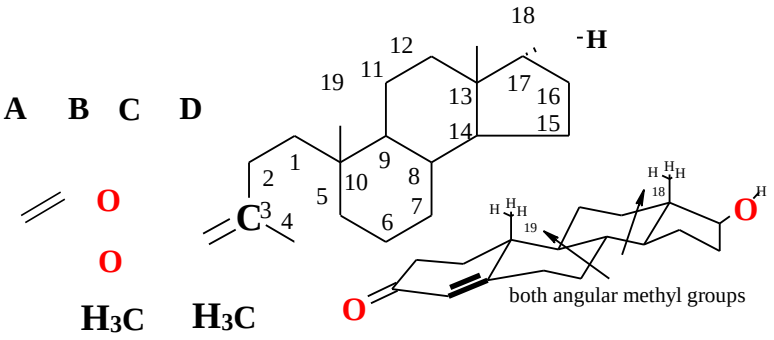
htdocsLocal http://aris.gusc.lv/ChemFiles/BilipidCholine/Membrane/AndrogenReceptor/Androgen1.htm

1) 2AM9 TES, 2AMA DHT, 2AMBMarz 17H THG, 1XQ3 R1881; human androgen receptor ligand-binding domain (hARLBD) with testosterone (TES), dihydrotestosterone (DHT), androgenic steroid used in sport doping, tetrahydrogestrinone (THG (17H)) and synthetic androgen (R1881)

2) 3DZYMarz DNA binding **Zn** finger motifs REA_model.pdb;

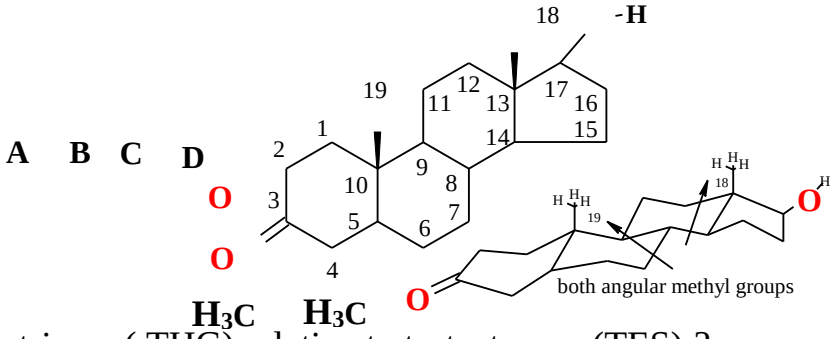
peroxisome proliferator-activated receptors (PPARs) form heterodimers with the retinoid X receptor (RXR)

3. Put in Testosterone (TES) hydrocarbon chain ring symbols:
establishing double bond from C4 to C5 >**C=C**<
and oxygen atoms in alcohol **HO**- at C17 and carbonyl at C3 and methyl groups at C10, C13!



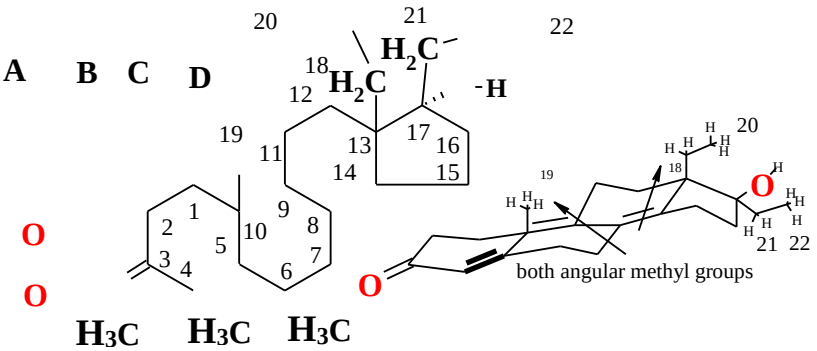
4. What difference has 5-ALPHA-DIHYDROTESTOSTERONE (DHT) relative to ..... double bond between C4=C5 in testosterone (TES)?

5. Put in 5α-dihydro-testosterone (DHT)
5α-dihidro-testosteron ring symbols:
and oxygen atoms in alcohol **HO**- at C17 and carbonyl at C3 and methyl groups at C10, C13!



6. What difference has 17H tetrahydrogestrinone(THG) relative to testosterone (TES) ?
TES. double bond between C4=C5 have additional at C.....=C..... and at C.....=C....?

7. Put in 17Htetrahydrogestrinone (THG) testosterone ring symbols:
double bonds C4-5, C10-9, C8-14 >**C=C**<
and oxygen atoms in alcohol **HO**- at C17 and carbonyl at C3 and methyl groups at C10, C18, C21!!



8. Nuclear Receptor three short cut names of domains protein subunits which are involved in gene expression regulation to bind response-element on DNA?

1. Highly conserved DNA-binding domain ..... **Zn** finger motifs.
2. Second complementar molecule receptor conserved ligand-binding domain .....;
3. **N-terminal** domen ..... variable receptor **activations domen** ... DNA binding;

9a. **N-terminus 2AM9.pdb** amino acid is Gln... and **C-terminal** Gln…..? What is number of amino acids on androgen ..... (see 5th p.) and **2AM9.pdb** 919-670=249+1=.....

9aa. What is total number of amino acids on androgen receptor liganda binding domain hARLBD **2AM9.pdb** primary structure? 919-670=249+1=.....

9b. Using **Backbone** Display **N-terminus** domain **2AMA.pdb** starting amino acid is Pro.....and finishing **C-terminal** amino acid is Thr .....

What is total number of amino acids on androgen receptor liganda binding domain hARLBD **2AMA.pdb** primary structure? 919-671=248+1=.....

9c. Using **Backbone** Display **N-terminus** domain **2AMB.pdb** starting amino acid is Pro..... and finishing **C-terminal** amino acid is Thr.....

What is total number of amino acids on androgen receptor liganda binding domain hARLBD **2AMB.pdb** primary structure 919-671=248+1=.....

9d. Using **Backbone** Display **N-terminus** domain **1XQ3.pdb** starting amino acid is Gln..... and finishing **C-terminal** amino acid is Gln.....

What is total number of amino acids on androgen receptor liganda binding domain hARLBD **1XQ3.pdb** primary structure.. 919-671=248+1=...

10. What type secondary structures dose contains the **LBD** androgen receptor **AR 2AM9.pdb**?

.....**Alpha-helixes** and .....**strands and** .....**β-sheets**

11. What number of **Alpha-helixes** constitute **LBD** polypeptide molecule?.....

12. What type of **beta structure** and **sheets** and how many **beta strands** constitute **LBD** ?

..... **β -strands,** ..... **β-sheets**.

13. What three water molecules with hydrogen bonds stabilize testosterone binding in **LBD**?

HOH....., HOH....., HOH.....

14. What two amino acids bind with hydrogen bonds carbonyl group **O=C<** of testosterone?

Arg.....—**N**—**H**···**O=C<TES**, Gln.....—(**O=C**)**N**—**H**···**O=C<TES**.....

15. What two amino acids bind with hydrogen bonds hydroxyl group –**O**–**H** of testosterone?

Thr.....**H-O**···**H**–**O**–**TES**, Asn.....—(**N-H**)-**C=O**··· **H**–**O**–**TES**;

16. 45 nonpolar amino acids pocket of H2, H4, H5 and β1, β2 for steroid binding **LBD** protein?

H2:Phe.....,Ala.....,Leu.....,Leu.....,Leu.....,Leu.....,Gly.....,Leu.....,

Val.....,Val.....,Val.....,Ala.....,Ala.....;

H4:Val.....,Met.....,Ala.....,Val.....,Ile.....,Trp.....,Met.....,Gly.....,

Leu....., Met.....,Val.....,Phe.....,Ala.....,Met.....,Gly.....,Trp.....,

Phe.....,Val.....;

beta1:Leu.....,Phe.....,Ala.....,Pro.....;beta2 Leu.....,Val.....,Phe.....;

H5:Met.....; H9:Pro.....,Cys.....,Phe.....,Leu.....,Leu.....,Leu.....,

Val.....,Pro.....,Ile.....,Ala.....,Leu.....,Phe.....,Phe.....,Leu.....,

Leu.....,Ile.....; What binding energy have TES ; DHT; THG doping?

TES ..... $^{kJ}/_{mol}$; DHT .....$^{kJ}/_{mol}$; THG .....$^{kJ}/_{mol}$; dopings

17. What two amino acids make disulfide bond in **LBD** protein unit structure 1E3G.pdb? .....

..... disulfide bond between Cys.....- **S** - **S** -Cys.....

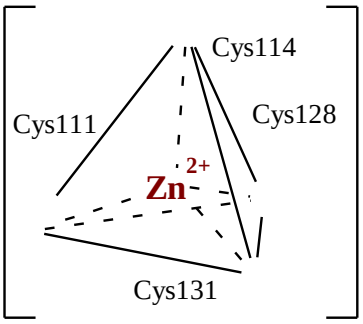
18a. What four amino acids in zinc **Zn** finger coordination sphere 1? ...

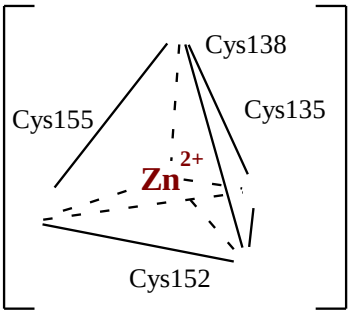
3DZY.pdb coordination sphere are **Nr1** Cys.....,Cys.....,Cys.....,Cys.....

18b. What four amino acids in zinc finger coordination sphere 2? **3DZY.pdb** coordination sphere are**Nr2** Cys.....,Cys.....,Cys.....,Cys.....

19a. Put in **Zn** coordinative bonds Nr1 with sulfide S^- atoms from four amino acids and coordinated ionic charge! !

S^- S^- S^- S^- **2-**





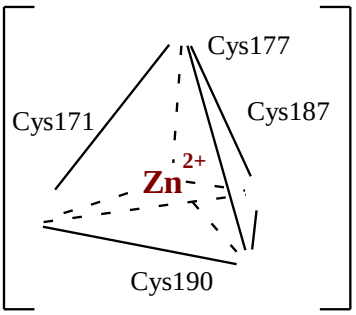
S^- S^- S^- S^- **2-**

19b. . Put in **Zn** coordinative bonds Nr2 with sulfide S^- atoms from four amino acids and coordinated ionic charge! !

18c. What four amino acids in zinc finger coordination sphere Nr3? **3DZY.pdb** coordination sphere Nr3 are C171.....,C177.....,C187.....,C190.....

19c. Put in **Zn** coordinative bonds Nr3 with sulfide S^- atoms from four amino acids and coordinated ionic charge!

S^- S^- S^- S^- **2-**



20. What of two symmetric DNA six base pair repeats bind to hetero dimer the peroxi some proliferators activated receptors (**PPARs**) with complementary retinoid X receptor (**RXR**) using one letter symbols :

adenin A, thimin T, guanin G, cytosin C and order number on DNA chain? **PPARs+RXR:**

A.....G.....G.....T....C....A....; A....G....G....T....C....A....

T....C....C....A....G.....; T.....C.....C.....A.....G.....T...

21. What six amino acids of the **LBD PPARs** from their ß-strand S1, S2, S3 and S4 with linchpin (DNA slīdass spraudnis šplinte) interact with what nine amino acids on **RXR-a DBD** in strand S4 form hydrophobic also as well hydrogen Bond interactions (needed for receptor activation)?

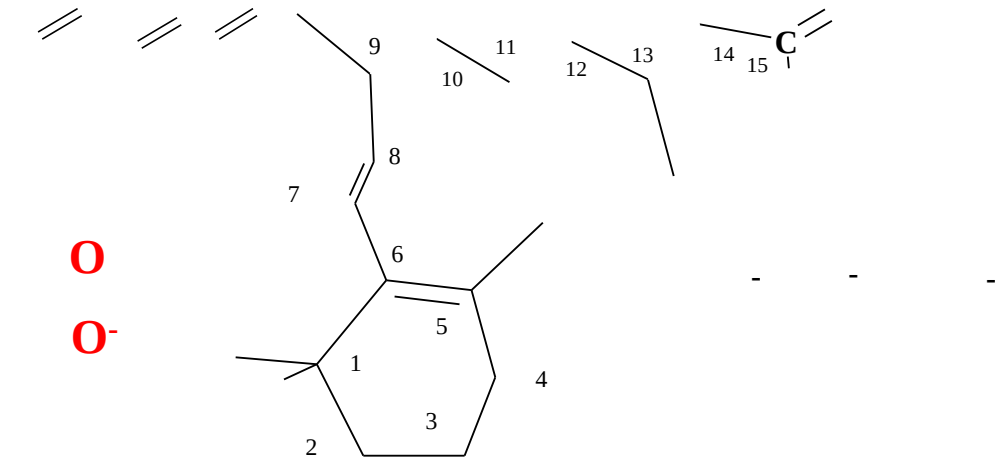
LBD PPARs six 6: Phe.....,Val.....,Asn.....,Lys.....,Asp.....,Glu.....and

9 nine **DBD RXR-a** : Leu.....,Ala.....,Asp.....,Tyr.....,Tyr.....,

Gln.....,Lys.....,Arg.....,Glu.....

22. Put in Cis-Retinoate **PPAR**-gamma ligand agonist hydrocarbon chains C20 double bonds of C9-10, C11-12, C13-14 >**C=C**< and two oxygen atoms ,wich is agonist **PPAR**-gamma!

REA_model.pdb



23.1-23.5 Analyses human AR TES isoelectric point IEP=pH=pK_{mean} at physiologic pH=7,36 . Determine at solution pH with AR TES concentration $C=10^{-6,96947}$ M ($^{mol}/_{Liter}$)!

http://aris.gusc.lv/ChemFiles/BilipidCholine/Membrane/AndrogenReceptor/2AM9pIStudS.doc ;
http://aris.gusc.lv/ChemFiles/BilipidCholine/Membrane/AndrogenReceptor/2AM9pI.xls

SQ SEQUENCE 920 >2AM9:A|PDBID|CHAIN|SEQUENCE AR_TES_Human

MEVQLGLGRVYPRPPSKTYRGAFQNLFQSVREVIQNPGPRHPEAASAAPPGASLLLLQQQQQQQQQQQQQQQQQQQQQQQ
ETSPRQQQQQQGEDGSPQAHRRGPTGYLVLDEEQQPSQPQSALECHPERGCVPEPGAAVAASKGLPQQLPAPPDEDDSAA
PSTLSLLGPTFPGLSSCSADLKDILSEASTMQLLQQQQQEAVSEGSSSGRAREASGAPTSSKDNYLGGTSTISDNAKELC
KAVSVSMGLGVEALEHLSPGEQLRGDCMYAPLLGVPPAVRPTPCAPLAECKGSLLDDSAGKSTEDTAEYSPFKGGYTKGL
EGESLGCSGSAAAGSSGTLELPSTLSLYKSGALDEAAAYQSRDYYNFPLALAGPPPPPPPPHPHARIKLENPLDYGSAWA
AAAAQCRYGDLASLHGAGAAGPGSGSPSAAASSSWHTLFTAEEGQLYGPCGGGGGGGGGGGGGGGGGGGGGGEAGAVAP
YGYTRPPQGLAGQESDFTAPDVWYPGGMVSRVPYPSPTCVKSEMGPWMDSYSGPYGDMRLETARDHVLPIDYYFPPQKTC
LICGDEASGCHYGALTCGSCKVFFKRAAEGKQKYLCASRNDCTIDKFRRKNCPSCRLRKCYEAGMTLGARKLKKLGNLKL
QEEGEASSTTSPTEETTQKLTVSHIEGYECQPIFLNVLEAIEPGVVCAGHDNNQPDSFAALLSSLNELGERQLVHVVKWA
KALPGFRNLHVDDQMAVIQYSWMGLMVFAMGWRSFTNVNSRMLYFAPDLVFNEYRMHKSRMYSQCVRMRHLSQEFGWLQI
TPQEFLCMKALLLFSIIPVDGLKNQKFFDELRMNYIKELDRIIACKRKNPTSCSRRFYQLTKLLDSVQPIARELHQFTFD
LLIKSHMVSVDFPEMMAEIISVQVPKILSGKVKPIYFHTQ 2AM9

AA	pKa$_{COO-}$	pKa$_{NH3+}$	pK$_{RR}$	Nr	AA	pKa$_{COO-}$	pKa$_{NH3+}$	pK$_{RR}$	Nr	AA	pKa$_{COO-}$	pKa$_{NH3+}$	pK$_{RR}$	Nr	AA	pKa$_{COO-}$	pKa$_{NH3+}$	pK$_{RR}$	Nr
M	1	9,21		1	E	39	4,25		200	E	77	4,25		355	E	115	4,25		541	E	153	4,25		645	E	191	4,25		794
E	2	4,25		2	E	40	4,25		204	Y	78	10,07		359	R	116	12,48		544	E	154	4,25		654	E	192	4,25		804
R	3	12,48		9	R	41	12,48		210	R	79	12,48		362	D	117	3,65		545	E	155	4,25		655	K	193	10,53		809
Y	4	10,07		11	R	42	12,48		212	D	80	3,65		363	H	118	6		546	K	156	10,53		659	D	194	3,65		820
R	5	12,48		13	E	43	4,25		213	Y	81	10,07		364	D	119	3,65		551	H	157	6		664	K	195	10,53		823
K	6	10,53		17	K	44	10,53		222	Y	82	10,07		365	Y	120	10,07		552	E	158	4,25		666	K	196	10,53		826
Y	7	10,07		19	D	45	3,65		223	H	83	6		382	Y	121	10,07		553	Y	159	10,07		668	D	197	3,65		829
R	8	12,48		20	Y	46	10,07		225	H	84	6		384	K	122	10,53		558	E	160	4,25		669	E	198	4,25		830
R	9	12,48		31	D	47	3,65		234	R	85	12,48		386	D	123	3,65		565	E	161	4,25		679	R	199	12,48		832
E	10	4,25		32	K	48	10,53		237	K	86	10,53		388	E	124	4,25		566	E	162	4,25		682	Y	200	10,07		835
R	11	12,48		40	E	49	4,25		238	E	87	4,25		390	H	125	6		571	H	163	6		690	K	201	10,53		837
H	12	6		41	K	50	10,53		241	D	88	3,65		394	Y	126	10,07		572	D	164	3,65		691	E	202	4,25		838
E	13	4,25		43	E	51	4,25		252	Y	89	10,07		395	K	127	10,53		581	D	165	3,65		696	D	203	3,65		840
E	14	4,25		81	E	52	4,25		255	R	90	12,48		407	K	128	10,53		585	E	166	4,25		707	R	204	12,48		841
R	15	12,48		85	H	53	6		256	Y	91	10,07		408	R	129	12,48		586	E	167	4,25		710	K	205	10,53		846
E	16	4,25		93	E	54	4,25		261	D	92	3,65		410	E	130	4,25		589	R	168	12,48		711	R	206	12,48		847
D	17	3,65		94	R	55	12,48		264	H	93	6		415	K	131	10,53		591	H	169	6		715	K	207	10,53		848
H	18	6		100	D	56	3,65		266	H	94	6		436	K	132	10,53		593	K	170	10,53		718	R	208	12,48		855
R	19	12,48		101	Y	57	10,07		269	E	95	4,25		442	Y	133	10,07		594	K	171	10,53		721	R	209	12,48		856
R	20	12,48		102	R	58	12,48		280	E	96	4,25		443	R	134	12,48		599	R	172	12,48		727	Y	210	10,07		858
Y	21	10,07		107	E	59	4,25		289	Y	97	10,07		447	D	135	3,65		601	H	173	6		730	K	211	10,53		862
D	22	3,65		111	K	60	10,53		291	E	98	4,25		474	D	136	3,65		605	D	174	3,65		732	D	212	3,65		865
E	23	4,25		112	D	61	3,65		296	Y	99	10,07		481	K	137	10,53		606	D	175	3,65		733	R	213	12,48		872
E	24	4,25		113	D	62	3,65		297	Y	100	10,07		483	R	138	12,48		608	Y	176	10,07		740	E	214	4,25		873
E	25	4,25		124	K	63	10,53		301	R	101	12,48		485	R	139	12,48		609	R	177	12,48		753	H	215	6		875
H	26	6		126	E	64	4,25		304	E	102	4,25		494	K	140	10,53		610	R	178	12,48		761	D	216	3,65		880
E	27	4,25		128	D	65	3,65		305	D	103	3,65		496	R	141	12,48		616	Y	179	10,07		764	K	217	10,53		884
R	28	12,48		129	E	66	4,25		308	D	104	3,65		501	R	142	12,48		618	D	180	3,65		768	H	218	6		886
E	29	4,25		134	Y	67	10,07		309	Y	105	10,07		504	K	143	10,53		619	E	181	4,25		773	D	219	3,65		891
K	30	10,53		143	K	68	10,53		313	R	106	12,48		511	Y	144	10,07		621	Y	182	10,07		774	E	220	4,25		894
D	31	3,65		154	Y	69	10,07		316	Y	107	10,07		514	E	145	4,25		622	R	183	12,48		775	E	221	4,25		898
E	32	4,25		155	K	70	10,53		318	K	108	10,53		521	R	146	12,48		630	H	184	6		777	K	222	10,53		906
D	33	3,65		156	E	71	4,25		321	E	109	4,25		523	K	147	10,53		631	K	185	10,53		778	K	223	10,53		911
D	34	3,65		157	E	72	4,25		323	D	110	3,65		529	K	148	10,53		633	R	186	12,48		780	K	224	10,53		913
D	35	3,65		180	E	73	4,25		340	Y	111	10,07		531	K	149	10,53		634	Y	187	10,07		782	Y	225	10,07		916
K	36	10,53		182	Y	74	10,07		348	Y	112	10,07		535	K	150	10,53		639	R	188	12,48		787	H	226	6		918
D	37	3,65		183	K	75	10,53		349	D	113	3,65		537	E	151	4,25		642	R	189	12,48		789	Q	2,17	227		920
E	38	4,25		187	D	76	3,65		354	R	114	12,48		539	E	152	4,25		643	H	190	6		790		7,7505286; 227; 1757,2			

2AM9:A|PDBID acid constants number account 227 pKa summa 1757,2 dod vidējo vērtību pK_{avid}=7,7505286;

Protolytic average constant isoelectric point IEP=pK_{mean} calculate of side chains $\Sigma pK_{aRside\ group}$.. $pK_{aNterminal}NH_3$

and

$pK_{aCterminal}COO^-$ constants sum divide with number of acid groups NpK_a:

$IEP=pK_{amean}=(\Sigma pKa_{Rside\ group}+pKa_{Nterminal}+pKa_{Cterminal})/NpKa$

Calculate human AR TES nucleara receptor 99,342-kDa molecule

23.1 Acid groups number in sum NpKa=Sum of 225 + 2 = ... pKa values sum in table: .....

920 amino acids of them protolytic constants pK_a for side groups 225+2 ,

N-terminal methionine M $pK_{aNterminal}$=9.21 and C-terminal glutamate Q $pK_{aCterminal}$=2.17 .

Sum are calculate as $\Sigma pKa_{Rside\ group}+pK_{aNterminal}+pKa_{Cterminal}$ = ...

23.2 Average acid group constant **ISOELEKTRIC POINT** pK_{mean}= IEP = 1757,2 / 227 =.....

At pH value of amino acid and protein on isoelectric point pH=**IEP total charge** is zero „**0**”

0——— plus (+) acidic————————zero charge „**0**” **IEP**=pH———————— minus (-) basic———→ 14 pH scale

-COOH & **-NH_3^+** positive charge .....**-COO^-** & **-NH_3^+**.....charge is negative **-COO^-** & **-NH_2**.

Underline existing and to cut incorrect given answer charge:

23.3 Determine human AR TES molecule charge sign (+). zero „**0**” or (-) at physiologic pH=7.36

Underline existing and to cut incorrect given answer charge:

-COOH & **-NH_3^+** positive (+) charge ……. pH=7.36 < IEP=**7.75** ..... charge negative(-) **-COO^-** & **-NH_2**.

23.4 Determine human AR TES molecule charge sign (+). zero „**0**” or (-) at **electrophoresis** pH **8.8**

Underline existing and to cut incorrect given answer charge:

-COOH & **-NH_3^+** positive (+) charge ……. IEP=**7.75**< pH=8.8 ..... charge negative(-) **-COO^-** & **-NH_2**.

23.5 Calculate $C=10^{-6,96947\ mol\ /\ Liter}$ M human AR TES solution pH by *Ostwald dilution law* in logarithm of C:

$$pH=\frac{pK_a-\log C}{2}=\frac{7,7505286-\log 10^{-6,96947}}{2}=\frac{7,7505286+6,96947}{2}$$ = **14,72** / 2 = ...

7,36 Attractor human AR TES concentration is C=.....M .

24.1-24.5 Analyse human RXRD 1XQ3.pdb isoelectric point IEP=pH=pK_{mean} at physiologic pH=7,36 .
Determine at solution pH with human RXRD concentration C=$10^{-6,99476}$ M ($^{mol}/_{Liter}$)!

http://aris.gusc.lv/ChemFiles/BilipidCholine/Membrane/AandrogenReceptor/3DZYpI.doc ;
http://aris.gusc.lv/ChemFiles/BilipidCholine/Membrane/AndrogenReceptor/3DZYpI.xls

```
SQ SEQUENCE   462 >1XQ3.pdb:A|PDBID|CHAIN|SEQUENCE                    RXRA_HUMAN
 MDTKHFLPLDFSTQVNSSLTSPTGRGSMAAPSLHPSLGPGIGSPGQLHSPISTLSSPINGMGPPFSVISSPMGPHSMSVP
 TTPTLGFSTGSPQLSSPMNPVSSSEDIKPPLGLNGVLKVPAHPSGNMASFTKHICAICGDRSSGKHYGVYSCEGCKGFFK
 RTVRKDLTYTCRDNKDCLIDKRQRNRCQYCRYQKCLAMGMKREAVQEERQRGKDRNENEVESTSSANEDMPVERILEAEL
 AVEPKTETYVEANMGLNPSSPNDPVTNICQAADKQLFTLVEWAKRIPHFSELPLDDQVILLRAGWNELLIASFSHRSIAV
 KDGILLATGLHVHRNSAHSAGVGAIFDRVLTELVSKMRDMQMDKTELGCLRAIVLFNPDSKGLSNPAEVEALREKVYASL
 EAYCKHKYPEQPGRFAKLLLRLPALRSIGLKCLEHLFFFKLIGDTPIDTFLMEMLEAPHQMT          RXRA_Human
```

AA	pKa$_{COO-}$	pKa$_{NH3+}$	pK$_{RR}$	Nr	AA	pKa$_{COO-}$	pKa$_{NH3+}$	pK$_{RR}$	Nr	AA	pKa$_{COO-}$	pKa$_{NH3+}$	pK$_{RR}$	Nr	AA	pKa$_{COO-}$	pKa$_{NH3+}$	pK$_{RR}$	Nr
M	1	9,21		1	E	23	4,25		153	R	45		12,48	202	E	67	4,25		251	R	89		12,48	348	H		109	6	406
D	2		3,65	2	K	24	10,53		156	E	46		4,25	203	D	68	3,65		263	E	90		4,25	352	K		110	10,53	407
K	3		10,53	4	K	25	10,53		160	E	47		4,25	207	D	69	3,65		273	K	91		10,53	356	Y		111	10,07	408
H	4		6	5	R	26	12,48		161	E	48		4,25	208	K	70	10,53		274	R	92		12,48	358	E		112	4,25	410
D	5		3,65	10	R	27	12,48		164	R	49		12,48	209	E	71	4,25		281	D	93		3,65	359	R		113	12,48	414
R	6		12,48	25	K	28	10,53		165	R	50		12,48	211	K	72	10,53		284	D	94		3,65	363	K		114	10,53	417
H	7		6	34	D	29	3,65		166	K	51		10,53	213	R	73	12,48		285	K	95		10,53	364	R		115	12,48	421
H	8		6	48	Y	30	10,07		169	D	52		3,65	214	H	74	6		288	E	96		4,25	366	R		116	12,48	426
H	9		6	75	R	31	12,48		172	R	53		12,48	215	E	75	4,25		291	R	97		12,48	371	K		117	10,53	431
E	10		4,25	105	D	32	3,65		173	E	54		4,25	217	D	76	3,65		295	D	98		3,65	379	E		118	4,25	434
D	11		3,65	106	K	33	10,53		175	E	55		4,25	219	D	77	3,65		296	K	99		10,53	381	H		119	6	435
K	12		10,53	108	D	34	3,65		176	E	56		4,25	221	R	78	12,48		302	E	100		4,25	388	K		120	10,53	440
K	13		10,53	118	D	35	3,65		180	E	57		4,25	228	E	79	4,25		307	E	101		4,25	390	D		121	3,65	444
H	14		6	122	K	36	10,53		181	D	58		3,65	229	H	80	6		315	R	102		12,48	393	D		122	3,65	448
K	15		10,53	132	R	37	12,48		182	E	59		4,25	233	R	81	12,48		316	E	103		4,25	394	E		123	4,25	453
H	16		6	133	R	38	12,48		184	R	60		12,48	234	K	82	10,53		321	K	104		10,53	395	E		124	4,25	456
D	17		3,65	140	R	39	12,48		186	E	61		4,25	237	D	83	3,65		322	Y	105		10,07	397	H		125	6	459
R	18		12,48	141	Y	40	10,07		189	E	62		4,25	239	H	84	6		331	E	106		4,25	401	T	2,11	126		462
K	19		10,53	145	R	41	12,48		191	E	63		4,25	243	H	85	6		333	Y	107		10,07	403					
H	20		6	146	Y	42	10,07		192	K	64		10,53	245	R	86	12,48		334	K	108		10,53	405					
Y	21		10,07	147	K	43	10,53		194	E	65		4,25	247	H	87	6		338										
Y	22		10,07	150	K	44	10,53		201	Y	66		10,07	249	D	88	3,65		347										

pK_{a_mean}=7.725; of pK_a nuber 126 sum 973,38

Protolytic average constant isoelectric point IEP=pK_{mean} calculate of side chains $\Sigma pK_{aRside\ group}$.. $pK_{aNterminal}NH_3$ and $pK_{aCterminal}COO^-$ constants sum divide with number of acid groups NpK_a:
$IEP=pK_{amean}=(\Sigma pKa_{Rside\ group}+pKa_{Nterminal}+pKa_{Cterminal})/NpKa$

Calculate human RXRD 1XQ3.pdb nuclear receptor 50,829 kDa molecule bound retnoate

24.1 Acid groups number in sum NpKa=Sum of 124 + 2 = ... pKa values sum in table: .....
462 amino acids of them protolytic constants pK_a for side groups 124+2 ,
N-terminal methionine M $pK_{aNterminal}$=9.21 and C-terminal Threonine T $pK_{aCterminal}$=2.11 .
Sum are calculate as $\Sigma pKa_{Rside\ group}+pK_{aNterminal}+pKa_{Cterminal}$ = ...

24.2 Average acid group constant **ISOELEKTRIC POINT** pK_{mean}= IEP = 973,38 / 126 =.....
At pH value of amino acid and protein on isoelectric point pH=**IEP total charge** is zero „**0**”
0——— plus (+) acidic————zero charge „**0**” **IEP**=pH———— minus (-) basic———→ 14 pH scale
-COOH & **-NH_3^+** positive charge .....**-COO^-** & **-NH_3^+**.....charge is negative **-COO^-** & **-NH_2**
Underline existing and to cut incorrect given answer charge:

24.3 Determine human AR TES molecule charge sign (+). zero „**0**” or (-) at physiologic pH=7.36
Underline existing and to cut incorrect given answer charge:
-COOH & **-NH_3^+** positive (+) charge ……. pH=7.36 < IEP=**7.725** ..... charge negative(-) **-COO^-** & **-NH_2**.

24.4 Determine human AR TES molecule charge sign (+). zero „**0**” or (-) at **electrophoresis** pH **8.8**
Underline existing and to cut incorrect given answer charge:
-COOH & **-NH_3^+** positive (+) charge ……. IEP=**7.725**< pH=8.8 ..... charge negative(-) **-COO^-** & **-NH_2**.

24.5 Calculate C=$10^{-6,96947\ mol\ /\ Liter}$ M human AR TES solution pH by *Ostwald dilution law* in logarithm of C:

$$pH=\frac{pK_a-\log C}{2}=\frac{7,725238-\log 10^{-6,99476}}{2}=\frac{7,725238+6,99476}{2}=\mathbf{14,72}\ /\ 2=.....$$

7,36 Attractor human AR TES concentration is C=.....M .