Name Surname :_____ Teacher _____ Group Nº __ Teacher ___2025

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

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

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

B. RSU Aris Kaksis 2025 studies about **androgens** look at address:

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

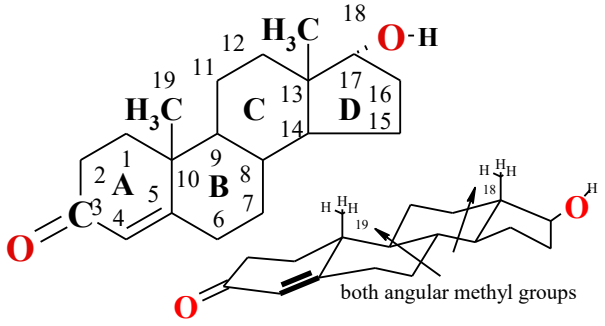
1) 2AM9 TES, 2AMA DHT, 2AMBMarz 17H THG, 1XQ3 R1881; human androgen receptor ligand-binding domain (hARLBD) with testosterone (TES), dihydrotestosterone (DHT), androgenic steroid used in sport doping, tetrahydrogestrinone (THG (17H)) and synthetic androgen (R1881)

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: stabilizing 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!

A B C D



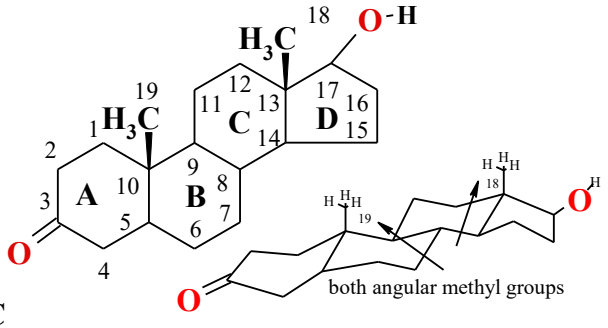
4. What difference has 5-ALPHA-DIHYDROTESTOSTERONE (DHT) relative to .....

.....absent double bond between C4=C5 in testosterone (TES)?

5. Put in 5α-dihydro-testosterone DHT 5α-dihidro-testosteron ring symbols:

A B C D

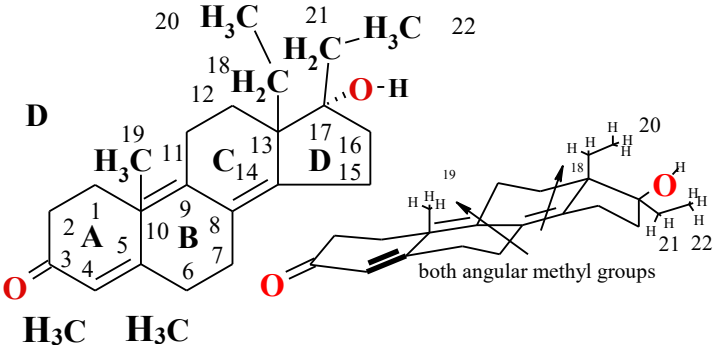
and oxygen atoms in alcohol **HO**- at C17 and carbonyl at C3 and methyl groups at C10, C13!



6. What difference has 17H tetrahydrogestrinone(THG) relative to testosterone (TES) ?

TES. double bond between C4=C5 have additional C9.....=C10..... and C8.....=C14....?

7. Put in 17H tetrahydrogestrinone(THG) testosteron ring symbols: **A B C D** 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 domains protein subunits in heterodimer are involved in gene expression regulation to bind response-element on DNA?

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

9a. N-terminus 2AM9.pdb amino acid is Gln670... and **C-terminal** Gln919…..? What is number of amino acids on androgen 920..... (see 5th p.) and **2AM9.pdb** 919-670=249+1=250.....

9b. Using **Backbone** Display **N-terminus** domain **2AMA.pdb** starting amino acid is .....Pro671... and finishing **C-terminal** amino acid is .....Thr919.
What is total number of amino acids on androgen receptor liganda binding domain hARLBD **2AMA.pdb** primary structure?.. 919-671=248+1=249.....

9c. Using **Backbone** Display **N-terminus** domain **2AMB.pdb** starting amino acid is .....Pro671...and finishing **C-terminal** amino acid is? .....Thr919.
What is total number of amino acids on androgen receptor liganda binding domain hARLBD **2AMB.pdb** primary structure. 919-671=248+1=249...

9d. Using **Backbone** Display **N-terminus** domain **1XQ3.pdb** starting amino acid is .....Gln671...and finishing **C-terminal** amino acid is? .....Gln919.
What is total number of amino acids on androgen receptor liganda binding domain hARLBD **1XQ3.pdb** primary structure.. 919-671=248+1=249...

10. What type secondary structures dose contains the **LBD** androgen receptor **AR 2AM9.pdb**?
.....**11 eleven Alpha-helixes**.....**4 four-strands and** .....**two two β-sheets**

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

12. What type of **beta structure** and **sheets** and how many **beta strands** constitute **LBD** ?
.....**4 four strands and** .....**2 two β-sheets**.....

13. What three water molecules with hydrogen bonds stabilize testosterone binding in **LBD**?
..... HOH46, HOH3, HOH14 .....

14. What two amino acids bind with hydrogen bonds carbonyl group **O=C<** of testosterone?
Arg752.....—**N**—**H**···**O=C<TES**, Gln711.....—(**O=C**)**N**—**H**···**O=C<TES**.....

15. What two amino acids bind with hydrogen bonds hydroxyl group **–O–H** of testosterone?
Thr877.....**H-O**···**H**–**O**–**TES**, Asn705.....—(**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:Phe697.....,Ala698.....,Leu700.....,Leu701.....,Leu704.....,Leu707.....,Gly708.....,Leu712.....,
Val713.....,Val715.....,Val716.....,Ala719.....,Ala721.....;
H4:Val730.....,Met734.....,Ala735.....,Val736.....,Ile737.....,Trp741.....,Met742.....,Gly743.....,
Leu744....., Met745.....,Val746.....,Phe747.....,Ala748.....,Met749.....,Gly750.....,Trp751.....,
Phe754.....,Val757.....;
beta1:Leu762.....,Phe764.....,Ala765.....,Pro766.....;beta2 Leu768.....,Val769.....,Phe770.....;
H5:Met775.....; H9:Pro849.....,Cys852.....,Phe856.....,Leu859.....,Leu862.....,Leu863.....,
Val866.....,Pro868.....,Ile869.....,Ala870.....,Leu873.....,Phe876.....,Phe878.....,Leu880.....,
Leu881.....,Ile882.....; What binding energy have TES ; DHT; THG doping?

TES -129,88..... $^{kJ}/_{mol}$; DHT -140,53 ..... $^{kJ}/_{mol}$; THG -173,36 ..... $^{kJ}/_{mol}$; dopings

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

..... disulfide bond between Cys669.....- **S** - **S** -Cys844.....

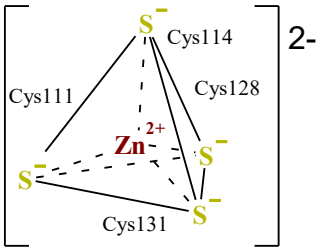
18a. What four amino acids in zinc **Zn** finger coordination sphere Nr 1? .....

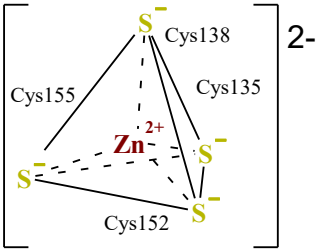
3DZY.pdb coordination sphere are **Nr1** C111.....,C114.....,C128.....,C131.....

18b. What four amino acids in zinc **Zn** finger coordination sphere Nr 2? .....

3DZY.pdb coordination sphere are **Nr2** C135.....,C138.....,C152.....,C155.....

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



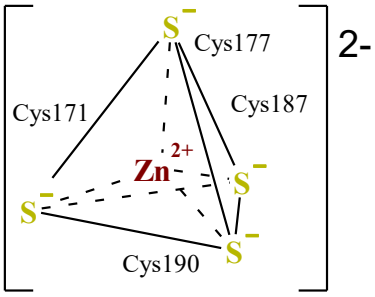


19b. . Put in **Zn** coordinative bonds Nr2 with sulfide S^- atoms from four amino acids and coordinated ionic charge! !

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

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

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



20. What of two symmetric DNA six base pair repeats bind to hetero dimmer 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**:

A7.....G8.....G9.....T10....C11....A12....; A14....G15....G16....T17....C18....A19....

T14....C13....C12....A11....G10....T9.....; T7.....C6.....C5.....A4.....G3.....T2...

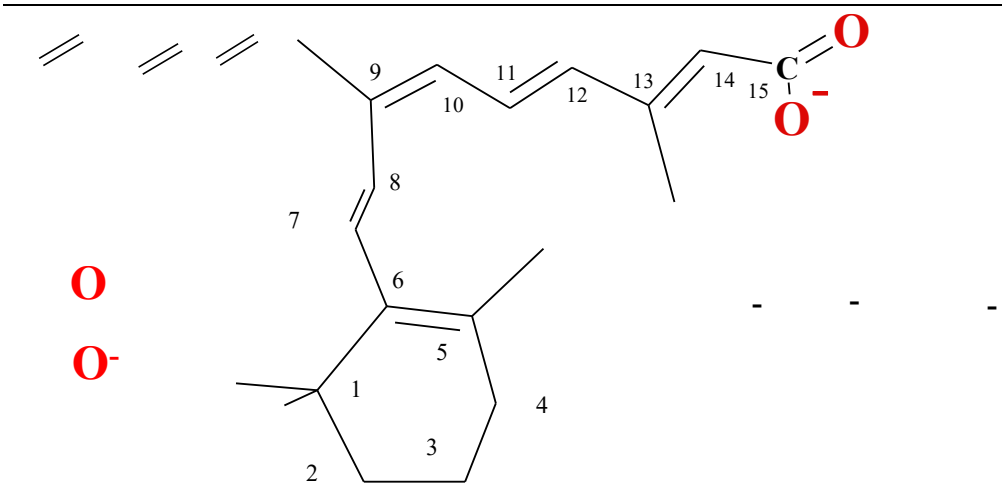
21. What six amino acids of the **LBD PPARs** from their ß-strand S1, S2, S3 and S4 with linchpin (DNA slīdass spraudnis šplinte) interact with what nine amino acids on **RXR-a DBD** in strand S4 form hydrophobic also as well hydrogen Bond interactions (needed for receptor activation)?

LBD PPARs six 6: Phe347.....,Val248.....,Asn335.....,Lys336.....,Asp337.....,Glu351.....and

9 nine **DBD RXR-a** : Leu196.....,Ala197.....,Asp166.....,Tyr189.....,Tyr192.....,

Gln193.....,Lys201.....,Arg202.....,Glu203.....

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

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

MEVQLGLGRVYPRPPSKTYRGAFQNLFQSVREVIQNPGPRHPEAASAAPPGASLLLLQQQQQQQQQQQQQQQQQQQQQQQQ
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	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;

23.1 Acid groups number in sum NpKa=Sum of 225 + 2 = 227..... pKa values sum in table: 1757,2.....

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 $\Sigma pKa_{Rside\ group}+pK_{aNterminal}+pKa_{Cterminal}$ = 1757,2.....

23.2 Average acid group constant **ISOELEKTRIC POINT** pK_{mean}= IEP = 1757,2 / 227 =**7,75053**.....

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:

(-).....is negative 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.....

7,36 Attractor human AR TES concentration is $C=10^{-6,96947}$.....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/AndrogenReceptor/3DZYpI.pdf ;
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
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AA	pKa$_{COO-}$	pKa$_{NH3+}$	pK$_{RR}$	Nr
M	1	9,21		1
D	2		3,65	2
K	3		10,53	4
H	4		6	5
D	5		3,65	10
R	6		12,48	25
H	7		6	34
H	8		6	48
H	9		6	75
E	10		4,25	105
D	11		3,65	106
K	12		10,53	108
K	13		10,53	118
H	14		6	122
K	15		10,53	132
H	16		6	133
D	17		3,65	140
R	18		12,48	141
K	19		10,53	145
H	20		6	146
Y	21		10,07	147
Y	22		10,07	150
E	23	4,25		153
K	24	10,53		156
E	25	10,53		160
R	26	12,48		161
R	27	12,48		164
K	28	10,53		165
D	29	3,65		166
Y	30	10,07		169
R	31	12,48		172
D	32	3,65		173
K	33	10,53		175
D	34	3,65		176
D	35	3,65		180
K	36	10,53		181
R	37	12,48		182
R	38	12,48		184
R	39	12,48		186
Y	40	10,07		189
R	41	12,48		191
Y	42	10,07		192
K	43	10,53		194
K	44	10,53		201
R	45	12,48		202
E	46	4,25		203
E	47	4,25		207
R	48	4,25		208
R	49	12,48		209
R	50	12,48		211
K	51	10,53		213
D	52	3,65		214
R	53	12,48		215
E	54	4,25		217
E	55	4,25		219
E	56	4,25		221
E	57	4,25		228
D	58	3,65		229
E	59	4,25		233
R	60	12,48		234
E	61	4,25		237
E	62	4,25		239
E	63	4,25		243
K	64	10,53		245
E	65	4,25		247
Y	66	10,07		249
E	67	4,25		251
D	68	3,65		263
D	69	3,65		273
K	70	10,53		274
E	71	4,25		281
K	72	10,53		284
R	73	12,48		285
H	74	6		288
E	75	4,25		291
D	76	3,65		295
D	77	3,65		296
R	78	12,48		302
E	79	4,25		307
H	80	6		315
R	81	12,48		316
K	82	10,53		321
D	83	3,65		322
H	84	6		331
H	85	6		333
R	86	12,48		334
H	87	6		338
D	88	3,65		347
R	89	12,48		348
E	90	4,25		352
K	91	10,53		356
R	92	12,48		358
D	93	3,65		359
D	94	3,65		363
K	95	10,53		364
E	96	4,25		366
R	97	12,48		371
D	98	3,65		379
K	99	10,53		381
E	100	4,25		388
E	101	4,25		390
R	102	12,48		393
E	103	4,25		394
K	104	10,53		395
Y	105	10,07		397
E	106	4,25		401
Y	107	10,07		403
K	108	10,53		405
H			109	406
K			110	407
Y			111	408
E			112	410
R			113	414
K			114	417
R			115	421
R			116	426
K			117	431
E			118	434
H			119	435
K			120	440
D			121	444
D			122	448
E			123	453
E			124	456
H			125	459
T	2,11		126	462

$pK_{a\ mean}$=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:
$IEP=pK_{amean}=(\Sigma pK_{aRside\ group}+pK_{aNterminal}+pK_{aCterminal})/NpKa$
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 = 126..... pKa values sum in table: 973,38.....
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 $\Sigma pK_{aRside\ group}+pK_{aNterminal}+pK_{aCterminal}$ = 973,38.....

24.2 Average acid group constant **ISOELEKTRIC POINT** pK_{mean}= IEP = 973,38 / 126 =**7,725238**.....
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:

$$pH=\frac{pK_a-\log C}{2}=\frac{7,725238-\log 10^{-6,99476}}{2}=\frac{7,725238+6,99476}{2}=\mathbf{14,72}/2=7,36.....$$

7,36 Attractor human AR TES concentration is $C=10^{-6,96947}$.....M .