

Supplementary Data

MSA of UniProt αV & PDB 1L5G αV

UniProt_1L5G_1 Chain	1	10	20	30	40	50	60
	MAFFPFRRLRLGPRGLPILLSGLLLPLCRAT			TNLOVDSPAEYSGPEGSTYFGAVDFFVPSA			
			TNLOVDSPAEYSGPEGSTYFGAVDFFVPSA			
UniProt_1L5G_1 Chain	70	80	90	100	110	120	
	SSRMFLVYGAPKANTTPQGVVEGGQVLKCDWSSTRRCQPIEFDATGNRDYAKDDPLEFKS						
	SSRMFLVYGAPKANTTPQGVVEGGQVLKCDWSSTRRCQPIEFDATGNRDYAKDDPLEFKS						
UniProt_1L5G_1 Chain	130	140	150	160	170	180	
	HQWFGASVRSKQDKILACAPLYHMRTEMKQREPVGTCTFLDQGTKEVYAPCRSQDIDAD						
	HQWFGASVRSKQDKILACAPLYHMRTEMKQREPVGTCTFLDQGTKEVYAPCRSQDIDAD						
UniProt_1L5G_1 Chain	190	200	210	220	230	240	
	CGGFCQGGFSTDPFERADRVLLGGPGSFYHQGGIIDDQVATIEVGRDIPNVTYSTIKYNQIAT						
	CGGFCQGGFSTDPFERADRVLLGGPGSFYHQGGIIDDQVATIEVGRDIPNVTYSTIKYNQIAT						
UniProt_1L5G_1 Chain	250	260	270	280	290	300	
	RTAQAIFFDDSYLGYSVAVGDFNGGIDDPFVSGVPRAARTLGMVYIYDGNMSSLYNFTGE						
	RTAQAIFFDDSYLGYSVAVGDFNGGIDDPFVSGVPRAARTLGMVYIYDGNMSSLYNFTGE						
UniProt_1L5G_1 Chain	310	320	330	340	350	360	
	QMAAYFGFSVAATDINGDDYADVFIGAPLFMDRGSQDKLQEVGQVSVLQRAAGDPQTTH						
	QMAAYFGFSVAATDINGDDYADVFIGAPLFMDRGSQDKLQEVGQVSVLQRAAGDPQTTH						
UniProt_1L5G_1 Chain	370	380	390	400	410	420	
	LHGFVFARFGSAIAPLDGLDQDGFNDIATAAPYGGEDKKGIYVIFNGRSTGLNAPVSGI						
	LHGFVFARFGSAIAPLDGLDQDGFNDIATAAPYGGEDKKGIYVIFNGRSTGLNAPVSGI						
UniProt_1L5G_1 Chain	430	440	450	460	470	480	
	LEGQNAARSMPSPFGYSMTGADIDRKNQYFDLIVGAFOVDRAILYRANFVITVHAGLIVV						
	LEGQNAARSMPSPFGYSMTGADIDRKNQYFDLIVGAFOVDRAILYRANFVITVHAGLIVV						
UniProt_1L5G_1 Chain	490	500	510	520	530	540	
	PSILNQDNKRCSLPGTALKVSCFNVRFLCADGKGVLPKRLNFQVELLDLKLKQKGAIRR						
	PSILNQDNKRCSLPGTALKVSCFNVRFLCADGKGVLPKRLNFQVELLDLKLKQKGAIRR						
UniProt_1L5G_1 Chain	550	560	570	580	590	600	
	ALFLYRSRPSHKNMTISRGGLMQCEELIAYLADSEFRDKLTPITIFMEYRLDYRTAAD						
	ALFLYRSRPSHKNMTISRGGLMQCEELIAYLADSEFRDKLTPITIFMEYRLDYRTAAD						
UniProt_1L5G_1 Chain	610	620	630	640	650	660	
	TTGLQPIINQFTPANISRQAAILLDGCGENVCKPKLEVSVDSQKKIYIGDDNRLSLIVK						
	TTGLQPIINQFTPANISRQAAILLDGCGENVCKPKLEVSVDSQKKIYIGDDNRLSLIVK						
UniProt_1L5G_1 Chain	670	680	690	700	710	720	
	AQNQGGAYEAEALIVSTPLEADFIGVVRNNEALARLSCAFKTENOTRQVVCGLGNPMKAG						
	AQNQGGAYEAEALIVSTPLEADFIGVVRNNEALARLSCAFKTENOTRQVVCGLGNPMKAG						
UniProt_1L5G_1 Chain	730	740	750	760	770	780	
	TQLLAGLRFVSRHQSEMDTSVKFDLQIQSSNLFDKVSPVVSRRKVDLAVLAAVEIRGVSSP						
	TQLLAGLRFVSRHQSEMDTSVKFDLQIQSSNLFDKVSPVVSRRKVDLAVLAAVEIRGVSSP						
UniProt_1L5G_1 Chain	790	800	810	820	830	840	
	DHVFLLPINWEHKKENPETEEDVGVVQRIYELRNNGPSSFSKAMHLQWPFYKYNNTLLY						
	DHVFLLPINWEHKKENPETEEDVGVVQRIYELRNNGPSSFSKAMHLQWPFYKYNNTLLY						
UniProt_1L5G_1 Chain	850	860	870	880	890	900	
	LHYDIDSGPMNCTSDMEINPLRKIKISLIQTEKNDTVAGQGERDHLTKKRDALSGQDII						
	LHYDIDSGPMNCTSDMEINPLRKIKISLIQTEKNDTVAGQGERDHLTKKRDALSGQDII						

MSA of UniProt β3 & PDB 1L5G β3

UniProt_1L5G_2 Chain	1	10	20	30	40	50	60
	MRARPRPRPLWATVLAALGALAGVGVG			GNICTTAGVSSCQQCLAVSPMCWCSDALPLG			
			GNICTTAGVSSCQQCLAVSPMCWCSDALPLG			
UniProt_1L5G_2 Chain	70	80	90	100	110	120	
	SPRCDLKENLLKDNCAPESTIEFPVSEARVLEDRPLSDKGGSDSQVTQVSPQRIALRLRP						
	SPRCDLKENLLKDNCAPESTIEFPVSEARVLEDRPLSDKGGSDSQVTQVSPQRIALRLRP						
UniProt_1L5G_2 Chain	130	140	150	160	170	180	
	DDSKNFSIQVRQVEDYFVDIYYLMDLSYSMKDDLWSIQNLGTKLATQMRKLTSLNLRIGFG						
	DDSKNFSIQVRQVEDYFVDIYYLMDLSYSMKDDLWSIQNLGTKLATQMRKLTSLNLRIGFG						
UniProt_1L5G_2 Chain	190	200	210	220	230	240	
	AFVDKPVSPYMYISPPALENFCYDMKTTCLMPGYKHVLTITDQVTFNSEEVEKKQSVSR						
	AFVDKPVSPYMYISPPALENFCYDMKTTCLMPGYKHVLTITDQVTFNSEEVEKKQSVSR						
UniProt_1L5G_2 Chain	250	260	270	280	290	300	
	NRCAPGGFDATMQATVCGDKIGWRNDASHLLVFTDARKTHALDGRAGIYQPNQGGCH						
	NRCAPGGFDATMQATVCGDKIGWRNDASHLLVFTDARKTHALDGRAGIYQPNQGGCH						
UniProt_1L5G_2 Chain	310	320	330	340	350	360	
	VGSDNHYASATTMDYPSLGLMTEKLSQNNINIFAVTENVVNLQNTSELIPGTTTGVLS						
	VGSDNHYASATTMDYPSLGLMTEKLSQNNINIFAVTENVVNLQNTSELIPGTTTGVLS						
UniProt_1L5G_2 Chain	370	380	390	400	410	420	
	MDSSNVQLIVDAYGRIRSKVELEVRDLPFELSLSFNATCLNNEVIPGLKSCMGLKIGDT						
	MDSSNVQLIVDAYGRIRSKVELEVRDLPFELSLSFNATCLNNEVIPGLKSCMGLKIGDT						
UniProt_1L5G_2 Chain	430	440	450	460	470	480	
	VSFSEAKVRGCPQKEKESFTIKFVGPDKSLIVQVTFDCCACQCAQAEFNSHRCNNGNGT						
	VSFSEAKVRGCPQKEKESFTIKFVGPDKSLIVQVTFDCCACQCAQAEFNSHRCNNGNGT						
UniProt_1L5G_2 Chain	490	500	510	520	530	540	
	FECGVRCRCPGWLGSQCCESEEDYRPSQQDECSPREGQPVCSQRGECGQCVCCHSSDFG						
	FECGVRCRCPGWLGSQCCESEEDYRPSQQDECSPREGQPVCSQRGECGQCVCCHSSDFG						
UniProt_1L5G_2 Chain	550	560	570	580	590	600	
	KITGKYCECDPFSCVRYKGMCSGHGQCRCGDCGLCDSDMHGYCNCCTATATDTCMSBNGLL						
	KITGKYCECDPFSCVRYKGMCSGHGQCRCGDCGLCDSDMHGYCNCCTATATDTCMSBNGLL						
UniProt_1L5G_2 Chain	610	620	630	640	650	660	
	CSGRGKCEGSCVCIQPGSYGDTCEKCPCTCPDACTFKKECVCCKKFD	GALHD	ENTCNRY				
	CSGRGKCEGSCVCIQPGSYGDTCEKCPCTCPDACTFKKECVCCKKFD	EPYHT	ENTCNRY				
UniProt_1L5G_2 Chain	670	680	690	700	710	720	
	CRDEIESVKELKDTGKDAVNCTYKNEDDCVVRFOYYEDSSGKSLVYVVEEPECCKPGD	IL					
	CRDEIESVKELKDTGKDAVNCTYKNEDDCVVRFOYYEDSSGKSLVYVVEEPECCKPGD	..					
UniProt_1L5G_2 Chain	730	740	750	760	770	780	
	VVLLSVMGAILLIGLAALLIWKLITIHDRKEFAKFEERARAKWDATTNNPLYKEATSTF						
						

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          910      920      930      940      950      960
Uniprot_  TLGGVAAQLKIVCQVGRIDRGESAILYVKSLLWETTFMKNENQNHSTSLKSSASPNVIE
1L5G_1|Chain TLGGVAAQLKIVCQVGRIDRGESAILYVKSLLWETTFMKNENQNHSTSLKSSASPNVIE

          970      980      990      1000     1010     1020
Uniprot_  PFYKNLPIDITNSTLVTNTVTWGIDPAPMFVFWVIIILAVLAGLLLVFVVMYRMGF
1L5G_1|Chain PFYKNLPIDITNSTLVTNTVTWGIDP.....

          1030     1040
Uniprot_  FRRVRPFQEEQEREQLQPHENGEGNSET
1L5G_1|Chain .....

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Figure 3. ClustalW multiple sequence alignment (MSA) of human integrin subunits αV (UniProt P06756) and $\beta 3$ (UniProt P05106) from UniProt (full-length sequences) and the corresponding αV and $\beta 3$ extracellular domains from the crystal structure PDB 1L5G. For αV (left), the UniProt sequence contains additional N- and C-terminal residues not present in the 1L5G extracellular domain, but is otherwise identical in the aligned region. For $\beta 3$ (right), the UniProt sequence also has extra N- and C-terminal residues compared to 1L5G, with one notable internal difference of four residues at positions 649-653 (UniProt: GALHD; PDB: EPYMT). Conserved residues are highlighted in red, with the alignment visualized in ESPript.

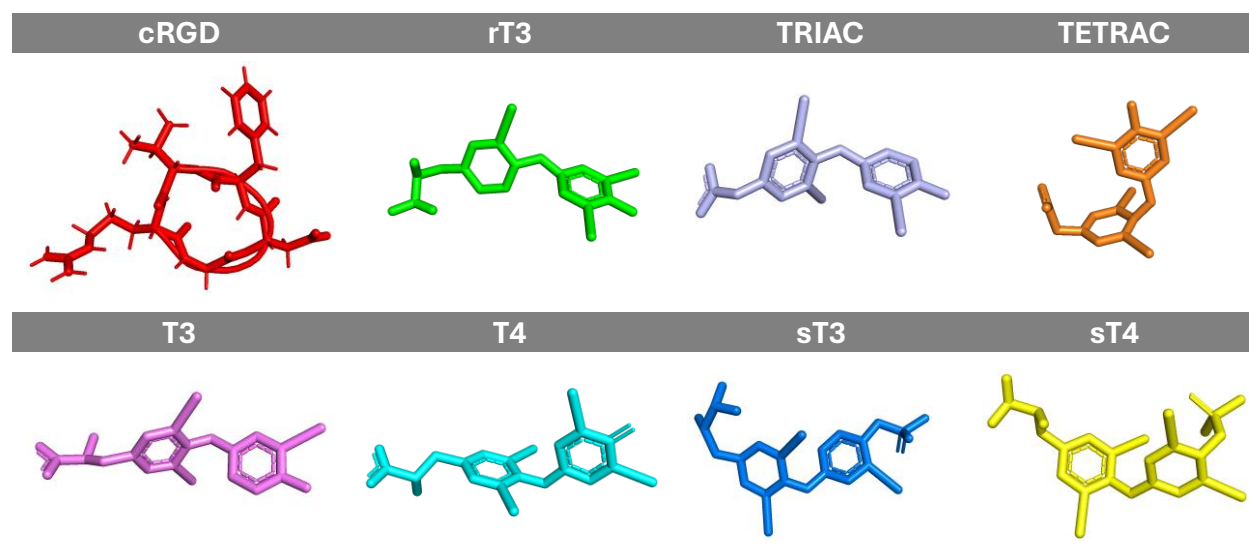
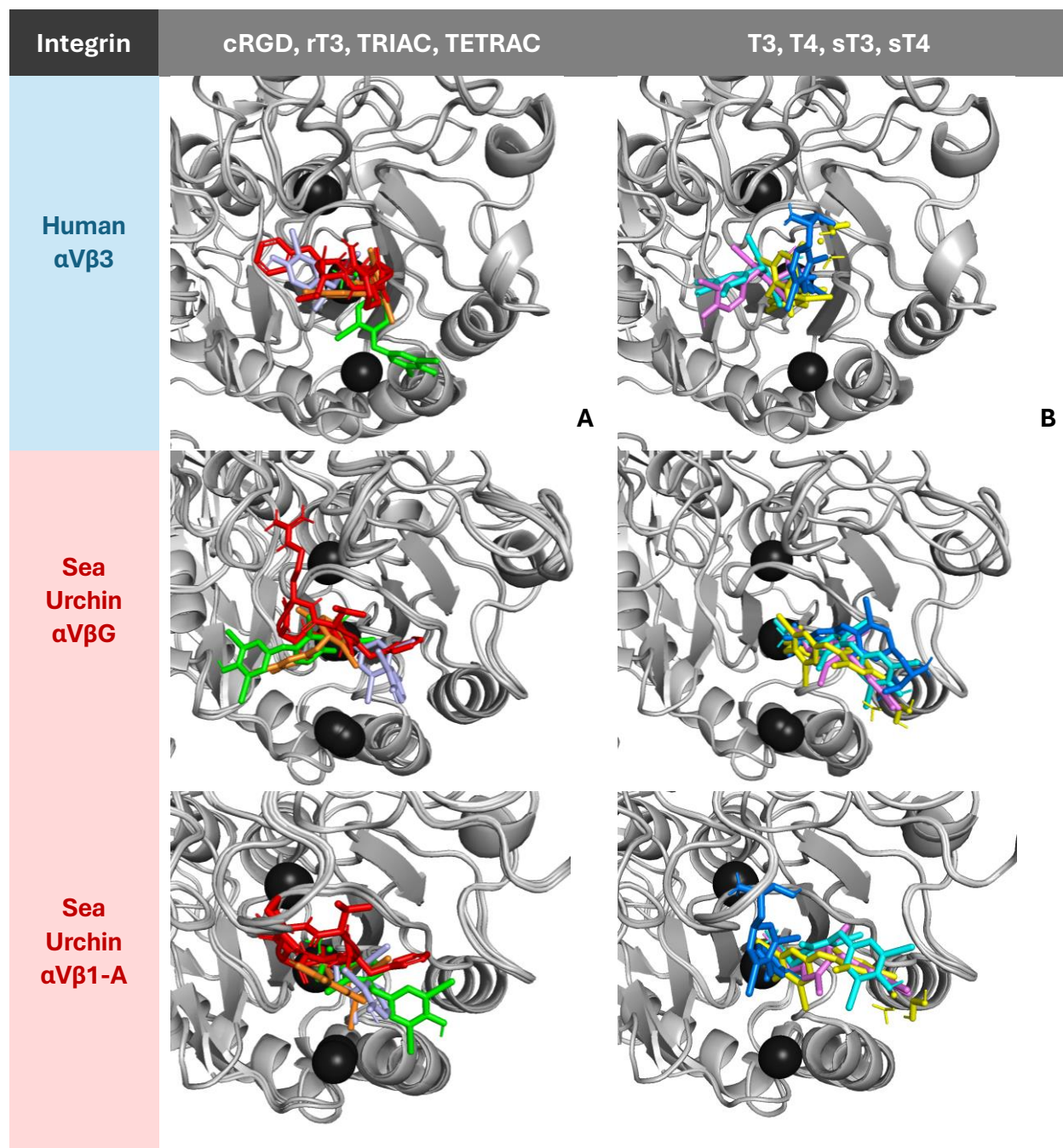


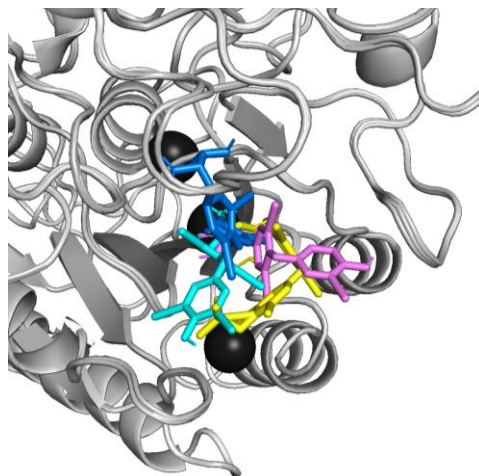
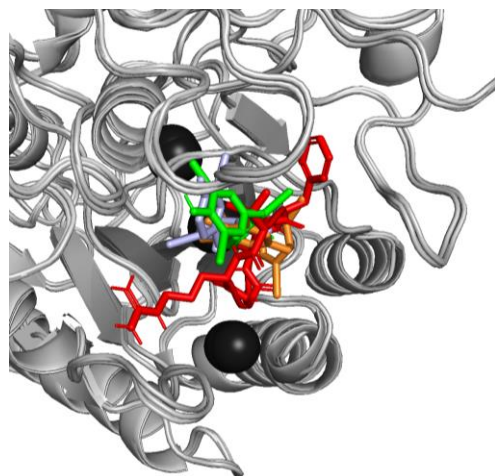
Figure 4. Chemical structures of the ligands used in the HADDOCK docking simulations. Ligands include the reference cyclic RGD peptide (cRGD), known for its high-affinity binding to $\alpha V \beta 3$ integrin, and seven thyroid hormone metabolites: reverse triiodothyronine (rT3), triiodothyroacetic acid (TRIAC), tetraiodothyroacetic acid (TETRAC), triiodothyronine (T3), thyroxine (T4), sulfated triiodothyronine (sT3), and sulfated thyroxine (sT4).



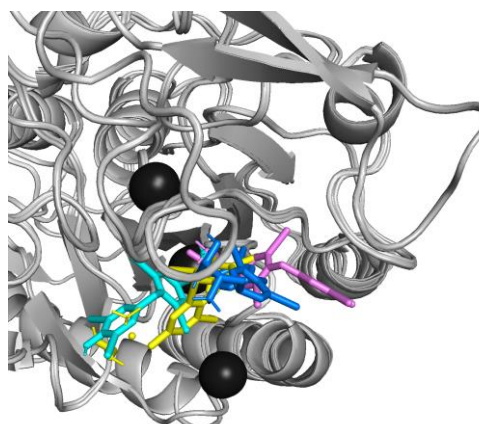
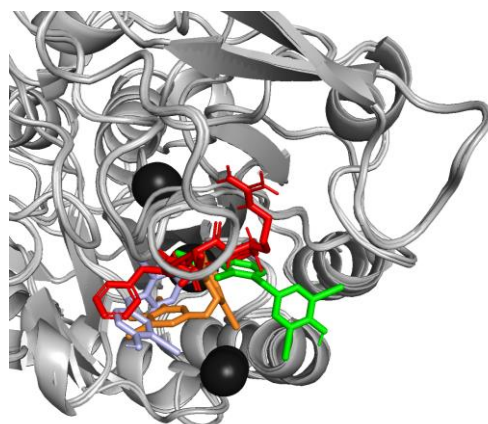
A

B

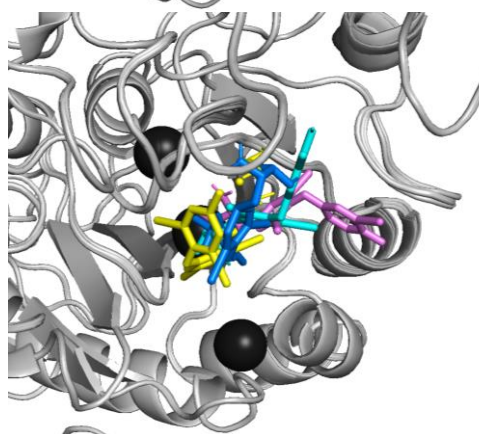
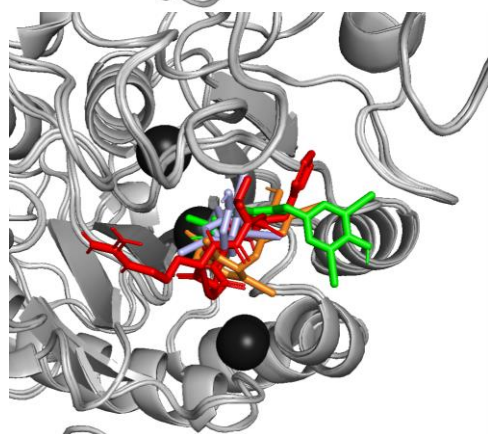
Sea
Urchin
 $\alpha V\beta C$



Sea
Urchin
 $\alpha P\beta G$



Sea
Urchin
 $\alpha P\beta 1-A$



Sea
Urchin
 $\alpha P\beta C$

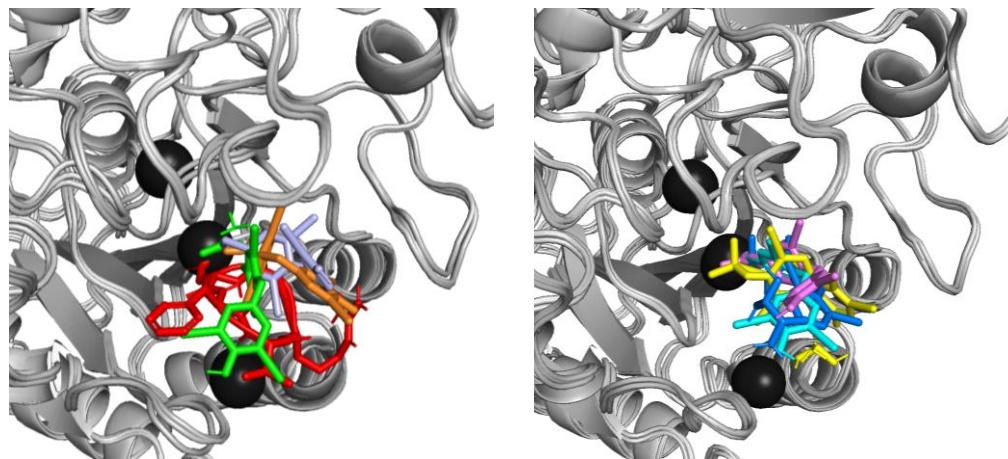


Figure 5. Docking of cRGD, rT3, TRIAC, TETRAC, and thyroid hormones (T3, T4, sT3, sT4) to human $\alpha V\beta 3$ and predicted sea urchin integrin heterodimers. Left panels: cRGD (red), rT3 (green), TRIAC (light purple), and TETRAC (orange) bound at the RGD-binding site. Right panels: T3 (pink), T4 (cyan), sT3 (blue), and sT4 (yellow) bound at the thyroid hormone-binding site. Integrin dimers are shown as grey ribbons, with Mn^{2+} ions as black spheres.

