

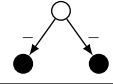
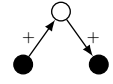
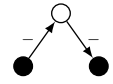
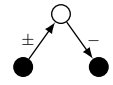
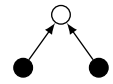
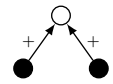
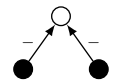
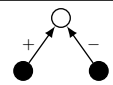
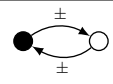
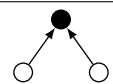
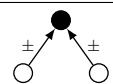
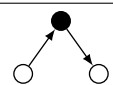
ID	motif	$N_{real}$	$N_{rand} \pm SD$	$P_{value}$	$Z_{score}$
1		1	$0.01 \pm 0.1$	0	9.9
2		15	$7 \pm 4$	0.0134	2.21
3		8	$3 \pm 2$	0.0183	2.09
4		2	$0.3 \pm 0.8$	0.0167	2.13
5		577	$425 \pm 20$	$3.1 \cdot 10^{-14}$	7.50
6		200	$163 \pm 13$	$2.5 \cdot 10^{-3}$	2.80
7		115	$51 \pm 10$	$1.6 \cdot 10^{-10}$	6.29
8		336	$278 \pm 25$	$9.4 \cdot 10^{-3}$	2.35
9		4	$0.7 \pm 0.8$	$1.7 \cdot 10^{-5}$	4.14
10		2341	$1569 \pm 156$	$3.9 \cdot 10^{-7}$	4.94
11		2155	$1246 \pm 128$	$6.2 \cdot 10^{-13}$	7.10
12		24466	$21914 \pm 927$	$2.9 \cdot 10^{-3}$	2.8

Table 1: Significantly over-represented network motifs in HIV-host regulatory network. Black nodes are HIV proteins and white nodes are human proteins. Interactions can either be activations/up-regulations (+), inhibitions/down-regulations (-), signaling/regulation ( $\pm$ ), or both (arrow without sign).  $N_{real}$  is the number of specific motifs found.  $N_{rand} \pm SD$  is the average number and standard deviation of the motif found in one thousand randomized networks.  $P_{value}$  is the probability that  $N_{real}$  or more motifs are found in the randomized networks.  $Z_{score}$  is the number of standard deviations  $N_{rand}$  differs from  $N_{real}$ . Network motifs were classified as significant when  $P_{value} < 0.02$  and  $Z_{score} > 2$ .

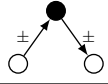
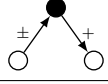
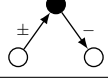
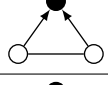
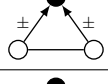
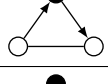
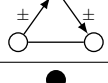
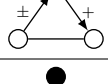
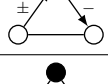
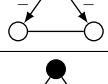
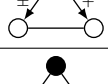
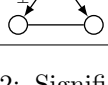
ID	motif	$N_{real}$	$N_{rand} \pm SD$	$P_{value}$	$Z_{score}$
13		482	$374 \pm 48$	0.0123	2.25
14		14718	$12457 \pm 572$	$3.9 \cdot 10^{-5}$	3.95
15		8348	$6709 \pm 377$	$6.8 \cdot 10^{-6}$	4.35
16		74	$16 \pm 6$	0	9.97
17		71	$12 \pm 5$	0	11.0
18		322	$218 \pm 35$	$1.6 \cdot 10^{-3}$	2.94
19		22	$4 \pm 2$	$1.11 \cdot 10^{-16}$	8.28
20		181	$124 \pm 23$	$7.7 \cdot 10^{-3}$	2.43
21		107	$67 \pm 15$	$2.8 \cdot 10^{-3}$	2.77
22		130	$90 \pm 19$	0.0175	2.11
23		30	$16 \pm 6$	0.0135	2.21
24		20	$10 \pm 5$	0.0147	2.18

Table 2: Significantly over-represented network motifs in HIV-host regulatory network. Black nodes are HIV proteins and white nodes are human proteins. Interactions can either be activations/up-regulations (+), inhibitions/down-regulations (-), signaling/regulation ( $\pm$ ), or both (arrow without sign).  $N_{real}$  is the number of specific motifs found.  $N_{rand} \pm SD$  is the average number and standard deviation of the motif found in one thousand randomized networks.  $P_{value}$  is the probability that  $N_{real}$  or more motifs are found in the randomized networks.  $Z_{score}$  is the number of standard deviations  $N_{rand}$  differs from  $N_{real}$ . Network motifs were classified as significant when  $P_{value} < 0.02$  and  $Z_{score} > 2$ .

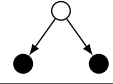
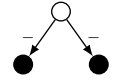
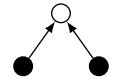
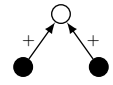
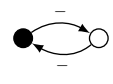
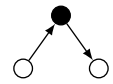
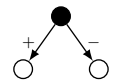
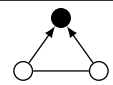
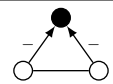
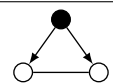
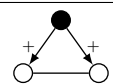
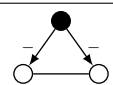
ID	motif	$N_{real}$	$N_{rand} \pm SD$	$P_{value}$	$Z_{score}$
25		35	$23 \pm 5$	0.0114	2.28
26		34	$21 \pm 6$	0.0153	2.16
27		304	$240 \pm 15$	$6.9 \cdot 10^{-6}$	4.35
28		167	$78 \pm 11$	$1.1 \cdot 10^{-16}$	8.19
29		22	$15 \pm 3$	0.0140	2.20
30		42912	$40680 \pm 1031$	0.0151	2.17
31		20912	$19820 \pm 511$	0.0166	2.13
32		77	$39 \pm 11$	$1.9 \cdot 10^{-4}$	3.56
33		72	$36 \pm 10$	$1.7 \cdot 10^{-4}$	3.59
34		659	$402 \pm 44$	$2.7 \cdot 10^{-9}$	5.84
35		324	$131 \pm 27$	$4.5 \cdot 10^{-13}$	7.14
36		175	$74 \pm 17$	$1.4 \cdot 10^{-9}$	5.95

Table 3: Significantly over-represented network motifs in HIV-host signaling network. Black nodes are HIV proteins and white nodes are human proteins. Interactions can either be activations/up-regulations (+), inhibitions/down-regulations (-), signaling/regulation ( $\pm$ ), or both (arrow without sign).  $N_{real}$  is the number of specific motifs found.  $N_{rand} \pm SD$  is the average number and standard deviation of the motif found in one thousand randomized networks.  $P_{value}$  is the probability that  $N_{real}$  or more motifs are found in the randomized networks.  $Z_{score}$  is the number of standard deviations  $N_{rand}$  differs from  $N_{real}$ . Network motifs were classified as significant when  $P_{value} < 0.02$  and  $Z_{score} > 2$ .



ID	motif	HIV protein	human protein	HIV protein
9				
10				
11				
12				
13				
14				
15				
16				

Table 5: Involvement of HIV and human proteins in network motifs of HIV-host regulatory network. HIV nodes in symmetric motifs share the same distribution. Of the human proteins at most only the 10 most frequent ones are shown. Human proteins are identified with a RefSeq protein accession number.

ID	motif	HIV protein	human protein	HIV protein
17				
18				
19				
20				
21				
22				
23				
24				

Table 6: Involvement of HIV and human proteins in network motifs of HIV-host regulatory network. HIV nodes in symmetric motifs share the same distribution. Of the human proteins at most only the 10 most frequent ones are shown. Human proteins are identified with a RefSeq protein accession number.





ID	motif	Biological Process	Cellular Component	Molecular Function
1				
2				
3				
4				
5				
6				
7				
8				
9				

Table 9: Gene Ontology annotation of human proteins involved in network motifs of HIV-human regulatory network.

ID	motif	Biological Process	Cellular Component	Molecular Function
10				
11				
12				
13				

Table 10: Gene Ontology annotation of human proteins involved in network motifs of HIV-human regulatory network.







ID	motif	Biological Process	Cellular Component	Molecular Function
25		<ul style="list-style-type: none"> <li>anti-apoptosis</li> <li>cell proliferation</li> <li>cell differentiation</li> <li>DNA hypermethylation during repressis</li> <li>DNA methylation</li> <li>DNA replication</li> <li>RNA polymerase II transcription</li> <li>cell differentiation</li> <li>cell growth</li> <li>transcription, not immune response</li> <li>transcription of riboflavin</li> </ul>	<ul style="list-style-type: none"> <li>cytoplasm</li> <li>cytosol</li> <li>cell receptor complex</li> <li>cell surface</li> <li>cell adhesion</li> <li>cell junction</li> <li>cytoplasmic vesicle</li> <li>cytoskeleton</li> <li>plasma membrane</li> <li>extracellular matrix</li> <li>extracellular matrix invagination</li> </ul>	<ul style="list-style-type: none"> <li>enzyme activity</li> <li>NF-kappaB binding</li> <li>chemotactic activity</li> <li>conceptor activity</li> <li>ATP binding</li> <li>MHC class II protein binding</li> <li>transcription</li> <li>RNA polymerase activity</li> <li>transcription factor activity</li> <li>transcription factor binding</li> <li>transcription</li> </ul>
26		<ul style="list-style-type: none"> <li>energy processing and production</li> <li>cell proliferation</li> <li>anti-apoptosis</li> <li>cell differentiation</li> <li>DNA hypermethylation during repressis</li> <li>DNA methylation</li> <li>DNA replication</li> <li>RNA polymerase II transcription</li> <li>cell differentiation</li> <li>cell growth</li> <li>transcription, not immune response</li> <li>transcription of riboflavin</li> </ul>	<ul style="list-style-type: none"> <li>cytoplasm</li> <li>cytosol</li> <li>cell receptor complex</li> <li>cell surface</li> <li>cell adhesion</li> <li>cell junction</li> <li>cytoplasmic vesicle</li> <li>cytoskeleton</li> <li>plasma membrane</li> <li>extracellular matrix</li> <li>extracellular matrix invagination</li> </ul>	<ul style="list-style-type: none"> <li>enzyme activity</li> <li>NF-kappaB binding</li> <li>chemotactic activity</li> <li>conceptor activity</li> <li>ATP binding</li> <li>MHC class II protein binding</li> <li>transcription</li> <li>RNA polymerase activity</li> <li>transcription factor activity</li> <li>transcription factor binding</li> <li>transcription</li> </ul>
27		<ul style="list-style-type: none"> <li>G-protein coupled receptor protein signaling</li> <li>DNA methylation</li> <li>cell differentiation</li> <li>cell proliferation</li> <li>DNA hypermethylation during repressis</li> <li>DNA methylation</li> <li>DNA replication</li> <li>RNA polymerase II transcription</li> <li>cell differentiation</li> <li>cell growth</li> <li>transcription, not immune response</li> <li>transcription of riboflavin</li> <li>transcription of riboflavin</li> <li>transcription of riboflavin</li> <li>transcription of riboflavin</li> </ul>	<ul style="list-style-type: none"> <li>cell receptor complex</li> <li>cellular component</li> <li>cytoplasm</li> <li>cytosol</li> <li>cell surface</li> <li>cell adhesion</li> <li>cell junction</li> <li>cytoplasmic vesicle</li> <li>cytoskeleton</li> <li>plasma membrane</li> <li>extracellular matrix</li> <li>extracellular matrix invagination</li> </ul>	<ul style="list-style-type: none"> <li>ATP binding</li> <li>transcription factor activity</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> </ul>
28		<ul style="list-style-type: none"> <li>DNA methylation</li> <li>MARCKS cascade</li> <li>G-protein coupled receptor protein signaling</li> <li>cell differentiation</li> <li>cell proliferation</li> <li>DNA hypermethylation during repressis</li> <li>DNA methylation</li> <li>DNA replication</li> <li>RNA polymerase II transcription</li> <li>cell differentiation</li> <li>cell growth</li> <li>transcription, not immune response</li> <li>transcription of riboflavin</li> <li>transcription of riboflavin</li> <li>transcription of riboflavin</li> <li>transcription of riboflavin</li> </ul>	<ul style="list-style-type: none"> <li>cell junction</li> <li>cellular component</li> <li>cytoplasm</li> <li>cytosol</li> <li>cell surface</li> <li>cell adhesion</li> <li>cell junction</li> <li>cytoplasmic vesicle</li> <li>cytoskeleton</li> <li>plasma membrane</li> <li>extracellular matrix</li> <li>extracellular matrix invagination</li> </ul>	<ul style="list-style-type: none"> <li>ATP binding</li> <li>transcription factor activity</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> <li>ATP binding</li> </ul>
29		<ul style="list-style-type: none"> <li>G-protein coupled receptor signaling</li> <li>cell proliferation</li> <li>cell differentiation</li> <li>DNA hypermethylation during repressis</li> <li>DNA methylation</li> <li>DNA replication</li> <li>RNA polymerase II transcription</li> <li>cell differentiation</li> <li>cell growth</li> <li>transcription, not immune response</li> <li>transcription of riboflavin</li> <li>transcription of riboflavin</li> <li>transcription of riboflavin</li> <li>transcription of riboflavin</li> </ul>	<ul style="list-style-type: none"> <li>cytoplasm</li> <li>cytosol</li> <li>cell receptor complex</li> <li>cell surface</li> <li>cell adhesion</li> <li>cell junction</li> <li>cytoplasmic vesicle</li> <li>cytoskeleton</li> <li>plasma membrane</li> <li>extracellular matrix</li> <li>extracellular matrix invagination</li> </ul>	<ul style="list-style-type: none"> <li>ATP binding</li> <li>G-protein receptor activity</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> <li>DNA binding</li> </ul>

Table 14: Gene Ontology annotation of human proteins involved in network motifs of HIV-human signaling network.



