Diversity at the nuclear envelope: transcription, laminas NPCs and trypanosomes











Oops!!!

Overthinking/attempts to define may be counterproductive

# The average expert is 'roughly as accurate as a dart-throwing chimpanzee.'

Peter Tetlock

# Evolutionary asymmetry



# Evolutionary asymmetry













Sali, Rout and Field 2011















Animal and fungal nuclear pore complexes have species specific structures, but similar protein compositions











# Trypanosomes are highly divergent

African

American

Leishmania



# Trypanosomes are highly divergent





### The nuclear pore complex and the nuclear envelope







#### Comparative Genomic Evidence for a Complete Nuclear Pore Complex in the Last Eukaryotic Common Ancestor

Nadja Neumann<sup>1</sup>, Daniel Lundin<sup>1</sup>, Anthony M. Poole<sup>1,2</sup>

Table 1. Comparison of performance of HMMer-based Nup screen on *Trypanosoma brucei* by reference to published experimental data [32].

Nucleoporins identified					
experimentally by DeGrasse et al. 2009	Nups also identified using HMMer (this study)	Annotation	Returned by HMMer but excluded*	E-value <sup>b</sup>	Notes
Tb10.61.2630	+	Sec13		4.4e-89	
-	Tb11.01.5410	Seh1		9.1e-07	
Tb11.02.2120	+	Aladin		1.1e-12	
Tb09.160.2360	+	Rae1		9.4e-32	
Tb10.6k15.2350	+	Nup155		5.4e-24	
Tb11.02.0460	+	Nup107		0.02	
Tb10.6k15.3670	+	Nup93		0.0012	
Tb1927.4.2880	+	Nup205		0.96	
Tb11.03.0140	+	Nup96/98		0.0012	
Tb11.01.7200	+	Nup62		8.2e-05	
Tb927.4.5200	+	Nup54		1.2e-08	
Tb927.3.3180	-	-	+	0.016	FG repeats
Tb927.3.3540	-	-	+	2.1	FG repeats
Tb11.02.0270	-	-	+	0.16	FG repeats
Tb11.01.2880	-	-	+	1.1	FG repeats
Tb927.4.4310	-	-	+	3.4	FG repeats
Tb927.8.8050	-	-	+	4	FG repeats
Tb11.01.2885	-	-	+	0.0009	FG repeats
Tb11.03.0810	-	-	+	5.8	
Tb10.6k15.1530	-	-	-	ND	
Tb09.211.4780	-	-	-	ND	
Tb09.160.0340	-	-	-	ND	
Tb11.01.7630	-	-	-	ND	
Tb927.7.2300	-	-	-	ND	

<sup>a</sup>Sequence present in HMMer hit list but excluded due to weak similarities (e.g. restricted FG repeats) to known Nups. <sup>b</sup>ND: Sequence not detected in HMMer-based screen.

dok10.1371/journal.pone.0013241.t001

		Opisthokonts	_	_	_	Excavates				
		Dipterans			Vertebrates	Diplomonads	Heterolobosea	Parabasalids	Kinetoplastids	
		Ag	Å.	Ъ	Hs	ซ	Ŋ	≧	ß	5
LOCALIZATION	NUP			-						
Localization	Gle1	~	~							
	Aladin	~	^	~	~		2		×	×
Outoplarmic	Nue	*		*	*		~		*	*
fibrils	Nupee	*	*	*	×					
	Nup214	x	x	x	x		×			x
	Nup358	x	x	×	x					
Scaffold	Nup160	x	x	×	x		×			
	Nup133	x	x	×	x		×			
	Nup107	x	x	×	x	x	×	x	x	x
	Nup75	×	×	×	×	~	×			
	Nup43	x	x	×	x		~			
	Nup37	~	~	- -	^ ¥					
	Seh1	-	Ŷ	Ĵ	Ŷ		~		v	v
	Sec13	^ 	^ 	<u> </u>	^ 		0		<u>`</u>	<u>`</u>
	Nue205	~	~	Ĵ	~	î	~	~	~	~
	Nup205	*	*	*	*		*	*	*	*
	Nupiss	x	×	×	×					
	Nup155	×	×	×	×	×	×	×	×	×
	Nup93	x	×	×	x		×	x	x	×
-	Nup35	×	x	×	×	×		x		
brane	N dc1	x		×	x			x		
	Pom121				x					
	Gp210 Pom152	x	×	×	×		×	x		
	Pom34									
Nuclear ring	Nup96-98	x		×	x	x	x	x	x	×
	Rae1	x	х	х	ж	x	x		x	x
Central	Nup62	x	x	×	x		x	x	x	x
channel	Nup58	x	x	×	x		x			x
	Nup54	x	x	×	x	x	x	x	x	x
Nuclear	Nup50	x	x	×	x		x			
basket	Nup153		×	×	×		x			
	TPR	x	x	×	x		x			
Nups in supergrou	p	31				23				

#### **Comparative Genomic Evidence for a Complete Nuclear** Pore Complex in the Last Eukaryotic Common Ancestor

Nadja Neumann<sup>1</sup>, Daniel Lundin<sup>1</sup>, Anthony M. Poole<sup>1,2</sup>\*

Table 1. Comparison of performance of HMMer-based Nup screen on Trypanosoma brucei by reference to published experimental data [32].

Nucleoporins identified experimentally by	Nups also identified using		Returned by HMMer		
DeGrasse et al. 2009	HMMer (this study)	Annotation	but excluded	E-value"	Notes
Tb10.61.2630	+	Sec13		4.4e-89	
-	Tb11.01.5410	Seh1		9.1e-07	
Tb11.02.2120	+	Aladin		1.1e-12	
Tb09.160.2360	+	Rae1		9.4e-32	
Tb10.6k15.2350	+	Nup155		5.4e-24	
Tb11.02.0460	+	Nup107		0.02	
Tb10.6k15.3670	+	Nup93		0.0012	
Tb1927.4.2880	+	Nup205		0.96	
Tb11.03.0140	+	Nup96/98		0.0012	
Tb11.01.7200	+	Nup62		8.2e-05	
Tb927.4.5200	+	Nup54		1.2e-08	
Tb927.3.3180	-	-	+	0.016	FG repeats
Tb927.3.3540	-	-	+	2.1	FG repeats
Tb11.02.0270	-	-	+	0.16	FG repeats
Tb11.01.2880	_	-	+	1.1	FG repeats
Tb927.4.4310	-	-	+	3.4	FG repeats
Tb927.8.8050	-	-	+	4	FG repeats
Tb11.01.2885	-	-	+	0.0009	FG repeats
Tb11.03.0810	_	-	+	5.8	
Tb10.6k15.1530	-	-	-	ND	
Tb09.211.4780	-	-	-	ND	
Tb09.160.0340	-	-	-	ND	
Tb11.01.7630	-	-	-	ND	
Tb927.7.2300	-	-	-	ND	

<sup>a</sup>Sequence present in HMMer hit list but excluded due to weak similarities (e.g. restricted FG repeats) to known Nups. <sup>b</sup>ND: Sequence not detected in HMMer-based screen.

doi:10.1371/journal.pone.0013241.t001

		Opisthokonts				Excavates				
		Dipterans			Vertebrates	Diplomonads	Heterolobosea	Parabasalids	Kinetoplastids	
		Ag	Am	Dm	Hs	ซ	βN	≧	ß	5
LOCALIZATION	NUP									
	Gle1	x	×	×	x		×			
	Aladin	x		×	x		х		х	x
Cytoplasmic fibrils	Nup88	x	×	×	x					
	Nup214	x	х	х	х		х			x
	Nup358	x	х	×	x					
Scaffold	Nup160	х	х	×	х		×			
	Nup133	х	х	×	х		х			
	Nup107	х	х	х	х	×	х	х	х	x
	Nup75	х	х	×	x		×			
	Nup43	х	х	×	x					
	Nup37	x	x	×	x					
	Seh1	х	х	х	х		×		х	x
	Sec13	x	х	х	х	×	×	х	х	x
	Nup205	х	х	х	х		x	х	х	x
	Nup188	x	x	×	x					
	Nup155	×	x	×	x	×	×	×	x	×
	Nup93	x	x	×	x		×	x	x	x
Transmem-	Nup35 Ndc1	x	×	×	x	×		x		
brane	Pom121				×					
	Gp210	×	x	×	×		×	×		
	Pom152									
	Pom34									
Nuclear ring	Nup96-98	x		×	x	x	x	x	x	x
	Rae1	х	х	х	х	х	х		x	x
Central	Nup62	x	x	×	х		x	x	x	x
channel	Nup58	x	х	х	х		x			x
	Nup54	x	x	×	x	x	x	x	x	×
Nuclear	Nup50	x	x	×	х		x			
basket	Nup153		×	×	×		x			
	TPR	х	х	х	х		х			
Nups in supergro	pup	31	1			23				

#### **Comparative Genomic Evidence for a Complete Nuclear** Pore Complex in the Last Eukaryotic Common Ancestor

Nadja Neumann<sup>1</sup>, Daniel Lundin<sup>1</sup>, Anthony M. Poole<sup>1,2</sup>\*

Table 1. Comparison of performance of HMMer-based Nup screen on Trypanosoma brucei by reference to published experimental data [32].

Nucleoporins identified					
experimentally by DeGrasse et al. 2009	Nups also identified using HMMer (this study)	Annotation	Returned by HMMer but excluded <sup>®</sup>	E-value <sup>b</sup>	Notes
Tb10.61.2630	+	Sec13		4.4e-89	
-	Tb11.01.5410	Seh1		9.1e-07	
Tb11.02.2120	+	Aladin		1.1e-12	
Tb09.160.2360	+	Rae1		9.4e-32	
Tb10.6k15.2350	+	Nup155		5.4e-24	
Tb11.02.0460	+	Nup107		0.02	
Tb10.6k15.3670	+	Nup93		0.0012	
Tb1927.4.2880	+	Nup205		0.96	
Tb11.03.0140	+	Nup96/98		0.0012	
Tb11.01.7200	+	Nup62		8.2e-05	
Tb927.4.5200	+	Nup54		1.2e-08	
Tb927.3.3180	-	-	+	0.016	FG repeats
Tb927.3.3540	-	-	+	2.1	FG repeats
Tb11.02.0270	-	-	+	0.16	FG repeats
Tb11.01.2880	-	-	+	1.1	FG repeats
Tb927.4.4310	-	-	+	3.4	FG repeats
Tb927.8.8050	-	-	+	4	FG repeats
Tb11.01.2885	-	-	+	0.0009	FG repeats
Tb11.03.0810	-	-	+	5.8	
Tb10.6k15.1530	-	-	-	ND	
Tb09.211.4780	-	-	-	ND	
Tb09.160.0340	-	-	-	ND	
Tb11.01.7630	-	-	-	ND	
Tb927.7.2300	-	-	-	ND	

<sup>a</sup>Sequence present in HMMer hit list but excluded due to weak similarities (e.g. restricted FG repeats) to known Nups. <sup>b</sup>ND: Sequence not detected in HMMer-based screen.

doi:10.1371/journal.pone.0013241.t001

		Opisthokonts				Excavates				
		Dipterans			Vertebrates	Diplomonads	Heterolobosea	Parabasalids	Kinetoplastids	
		Ag	4m	Dm	Hs	ซ	Ŋ	≧	12	5
IOCALIZATION	NUD		-	-						
LOCALIZATION	Chal									
	Aladin	×	×	×	×		~		v	×
Cytoplasmic fibrils	Nup88	×	×	×	×		^		^	^
	Nup214	x	x	×	x		×			x
	Nup358	x	x	×	x					
Scaffold	Nup160	x	х	×	x		×			
	Nup133	x	x	×	x		×			
	Nup107	х	х	х	х	×	×	х	х	x
	Nup75	x	x	×	x		×			
	Nup43	x	x	×	x					
	Nup37	x	х	×	х					
	Seh1	х	x	×	x		×		x	×
	Sec13	х	х	×	х	×	×	х	х	x
	Nup205	х	х	х	х		×	х	х	х
	Nup188	x	x	×	x					_
	Nup155	×	х	×	х	×	×	x	х	×
	Nup93	x	x	×	x		×	х	х	×
	Nup35	х	х	х	х	×		х		
Transmem- brane	Ndc1	x		×	×			x		
	Pom121				х					
	Gp210 Pom152	×	×	×	×		×	×		
	Pom34									
Nuclear ring	Nup96-98	x		×	×	x	x	x	x	×
	Rae1	х	х	х	х	х	х		x	x
Central	Nup62	x	x	×	x		x	x	x	×
channel	Nup58	x	x	×	х		х			×
	Nup54	x	х	×	x	x	х	x	x	×
Nuclear	Nup50	x	x	×	×		x			
basket	Nup153		×	×	×		x			
	TPR	x	x	×	х		x			
Nups in supergro	up	31				23				



β-propeller								0	
15 million	Tb10.61.2630	TbSec13	41.6		Sec13	Sec13		85	outer
	Tb11.02.2120	TbNup48	48.4			ALADIN		9	ings.
	Tb11.01.7630	TbNup109	108.7	TA HEMANE A THE REPORT OF A CONTRACT OF A	Nup120/133	Nup160/133			
	Тъ927.7.2300	TbNup132	132.3	an de la balancia de la baladad da la desta de la desta de la constante de balancia.	Nup120/133	Nup160/133		85	inner & outer rings
a-solenoid	Tb10.6k15.2350	TbNup144	144.3	1. Markada, M. J. (1998). An Additional Control (1998). An Addition of the Action o	Nup157/170	Nup155	~	7	
as the second	Tb09.211.4780	TbNup82	82.4		Nup84/85	Nup107/75			
Stor 6 Sea	Tb11.02.0460	TbNup89	89.1	n a mar air ann an cuireann ann ann ann ann ann ann ann ann ann	Nup84/85	Nup107/75		L	
	Tb10.6k15.3670	TbNup96	96.5	a a fuir a share a shar	NIC96	Nup93		E	inner & outer rings
	Tb10.6k15.1530	TbNup181	181.5	is. Sidde bu callain a thumbhachtadh a bha th an Annachtadh anna a' cuide	Nup188/192	Nup188/205	~	7	
β-sandwich	Tb927.4.2880	TbNup225	225.5	te dan menangkanak antar akan dana baharan berakan kemanak melanakan sebuah dan kemanakan dan kemanak	Nup188/192	Nup188/205	Ű.	, I	
200 · · · · · · · · · · · · · · · · · ·	Tb11.03.0140	TbNup158	158.3		Nup145	Nup98/96		8E	outer rings/ FG nups
SONGE /	Tb927.4.4310	TbNup64	64.2	na ta da		١	T	7	
× /	Tb927.8.8050	TbNup75	74.8	u					
	Tb927.3.3180	TbNup98	98.1	L/A. 1. 1			E.	RE	FG nups
FG-repeat	Tb11.01.2885	TbNup140	140.3	Let 1			× 1	7	
~ ~ ~ ~	Tb11.01.2880	TbNup149	149.2	الله المراجع ا		)			
Surang /	ТЬ11.01.7200	TbNup53a	52.7		Nsp1/Nup116	Nup62	0	0	
	Tb927.3.3540	TbNup53b	52.8	and the life second				8-	FC
/	Tb11.02.0270	TbNup59	58.8	All dramme to Million				S-	PG nups
colled-coil	Tb927.4.5200	TbNup62	62.4		Nup57	Nup58	U	U	
Commercia	( Tb09.160.0340	TbNup92	92.3	A AND VIEW DIS A CAMPAGE AND A CAMPACITY OF A CAMPACITY	Mip	Tpr )		de_	nuclear
Manufacture	Tb11.03.0810	TbNup110	109.7		Mip	Tpr		E -	basket
								1	

Classes of nucleoporins Scaffold FG repeat

Only 3 major fold types β-propellers a-solenoid Disordered FG-repeat



Obado et al in prep

## NUP84 complex



## NUP84 complex pullout



Nups41 and 152 appear to be trypanosome specific

### NUP84 complex pullout



Nups41 and 152 appear to be trypanosome specific



-Sec13 Nup41 -Sec13



⊣Sec13 Nup41

-Sec13 Nup41



51kD

39kD

Sec13

Sec13 Nup41



⊣Sec13 Nup41 -Sec13



Nup	R ave	R Err	N (R)	Z ave	Z Err	N (Z)
Nup62	37.5	5.0	26	±12.5	2.5	52
Nup64	26.3	3.8	21	±6.2	6.3	58
Nup98	27.5	5.0	41	±10.0	5.0	94
Nup76	42.5	2.5	30	±10.0	5.0	60
Nup89	40.0	5.0	43	±16.2	6.3	120
Nup119	31.2	3.8	37	±11.3	3.8	65
Nup110	25.0	5.0	23	-36.2	18.8	73



#### Affinity Captured Nucleoporins

TbNup	Gene ID	S. cerevisiae Homolog	H. sapiens Homolog	Homo- dimer	TbNup132	TbNup109	TbNup89	TbNup158	TbNup152	TbSec13	TbNup41	TbNup119	TbNup144	TbNup225	TbNup181	TbNup65	TbNup96	TbNup53a	ucequvia I ThNin62	TbNup76	TbNup140	TbNup149	TbNup64	TbNup75	ThM: ThM: ThM: ThM: ThM: ThM: ThM: ThM:	ThMin110	Tbnup92
TbNup132	Tb927.7.2300	Nup120/Nup133	Nup160/Nup133																								
TbNup109	Tb927.11.15990	Nup120/Nup133	Nup160/Nup133										<u></u>	tor I	ina												
TbNup89	Tb927.11.2950	Nup84/Nup85	Nup107/Nup75										Oui	err	ing												
TbNup89	Tb927.11.2950	Nup84/Nup85	Nup107/Nup75																	S	caff	old	Con	nec	tion		
TbNup82	Tb927.9.14240	Nup84/Nup85	Nup107/Nup75																			to B	ack	ot			
TbNup158	Tb927.11.980	Nup145	Nup98/96													Inn	Di Di	ina				100	USA	Cl			
TbNup152	Tb927.10.9650	Nup120/Nup133	Nup160/Nup133													////		ng									
TbSec13	Tb927.10.14180	Sec13	Sec13																								
TbNup41	Tb927.10.2320	-	Nup37/Nup43																								
TbNup119	Tb927.11.9780	Nup157/170	Nup155	Y																							
TbNup144	Tb927.10.8170	Nup170/Nup157	Nup155																								
TbNup225	Tb927.4.2880	Nup188/Nup192	Nup188/Nup205				Oute	or / Ir	ner	Rin	n																
TbNup181	Tb927.10.8910	Nup188/Nup192	Nup188/Nup205				ould	onn	octio	0n	9																
TbNup65	Tb927.10.3810	Nup53	Nup35				C	.01110	cin	UII																	
TbNup96	Tb927.10.7060	Nic96	Nup93	Y																							
TbNup53a	Tb927.11.15560	Nsp1/Nup57/Nup49	Nup62/Nup58/Nup54	ļ	0	itor	Dine	- / NJ	m 74	6 ( 0	mn	Joy															
TbNup53b	Tb927.3.3540	Nsp1/Nup57/Nup49	Nup62/Nup58/Nup54	ļ	0	lei	ппу				μηρ	лех	·								Ν.,	n76	Con	nnl	av		
TbNup62	Tb927.4.5200	Nsp1/Nup57/Nup49	Nup62/Nup58/Nup54	ŀ				onne		m											NU	070	COII	iipi	28		
TbNup76	Tb927.8.6250	Nup82	Nup88	Y							Sc	off	Jd	Cor	noc	tion											
TbNup140	Tb927.11.11090	Nup159	Nup214								50																
TbNup149	Tb927.11.11080	Nup159	Nup214								to	Ba.	ѕке	τάI	GA	ups											
TbNup64	Tb927.4.4310																										
TbNup75	Tb927.8.8050																										
TbNup98	Tb927.3.3180																										
TbNup110	Tb927.11.330	Mlp1	Tpr	Y																							
TbNup92	TB927.9.1340	Mlp2	Tpr	Y																							

### Many subcomplexes have conserved and divergent units












Animal and fungal nuclear pore complexes have species specific structures, but similar protein compositions



















#### How did the nuclear envelope arise?





#### pre-FECA/FECA

Membrane capper

Fenestrations

Subunit duplication

More gating

FG Gate

### LECA/post-LECA



More asymm More elaboration

Additional fxn

Asymmetry

#### The nuclear pore complex and the nuclear envelope



Fold Type		Accession N	ucleoporin	Mass (kDa)		Homologs S. cerevisiae H. sapiens		Homolog Positions		
β-propeller										
69-22	{	Tb10.61.2630	TbSec13	41.6		Sec13	Sec13			
	$\leq 1$	Tb11.02.2120	TbNup48	48.4			ALADIN	-	de-	outer
		Tb11.01.7630	TbNup109	108.7	, I A TA MANA AT THE IS AN A REPORT OF	Nup120/133	Nup160/133		9	rings
	23	Tb927.7.2300	TbNup132	132.3	a shi a kulo da kalada da shekara kulo kala kulo kulo kulo kulo kala kulo kala kulo kulo k	Nup120/133	Nup160/133 )	-la		
$\alpha$ -solenoid		Tb10.6k15.2350	TbNup144	144.3	n i han aladh, an an an ann an ann an ann an ann an an	Nup157/170	Nup155	3	E	inner rings
. Steller		Tb09.211.4780	TbNup82	82.4	Land Karana menerika sa Angkarana Jawa Karan	Nup84/85	Nup107/75		de_	outer
and the set		Tb11.02.0460	TbNup89	89.1		Nup84/85	Nup107/75	-20	÷	rings
		Tb10.6k15.3670	TbNup96	96.5	a da la companya da la companya da comp	Nic96	Nup93		1	
		Tb10.6k15.1530	TbNup181	181.5	in. A the first of bits we dealed the first of	Nup188/192	Nup188/205	3	12	inner rings
β-sandwich		Tb927.4.2880	TbNup225	225.5	le i de la de la constante da la constante de la constante de la constante e constante da las de la del second	Nup188/192	Nup188/205	7	7	
<b>E</b> NDA		Tb11.03.0140	TbNup158	158.3		Nup145	Nup98/96	3	(t	outer rings/ FG nups
and the	/ /	Tb927.3.3180	TbNup98	98.1		FG Re	peat	0	1	
		Tb11.01.2880	TbNup149	149.2	All and a second s	Grou	рВ			
		Tb927.4.4310	TbNup64	64.2		Í				
FG-repeat		Tb927.8.8050	TbNup75	74.8						
- mail		Tb11.01.2885	TbNup140	140.3			)	j.	Ē	FG nups
-		Tb11.01.7200	TbNup53a	52.7		FG Repeat Group A		77	7	
		Tb927.3.3540	TbNup53b	52.8	يجيد الله الشيب					
	1	Tb11.02.0270	TbNup59	58.8						
coiled-coil		Tb927.4.5200	TbNup62	62.4		)				
Company	/ (	Tb09.160.0340	TbNup92	92.3	. The first states for the second states of the second states of the second states of the second states of the	Mlp	Tpr )	-	de_	nuclear
Contraction of the second	{	Tb11.03.0810	TbNup110	109.7	ATTING TO THE MATCHING WATER AND A TO	Mlp	Tpr )	-30	-	basket

Fold Type		Accession Nucleoporin Mass (kDa)		Mass (kDa)		Homologs S. cerevisiae H. sapiens		Homolog Positions		
β-propeller										
692	5	Tb10.61.2630	TbSec13	41.6		Sec13	Sec13			
	_ (	Tb11.02.2120	TbNup48	48.4			ALADIN	-	de-	outer
	(	Tb11.01.7630	TbNup109	108.7	, I A TA MARA II. JA, IA JAAN TANI MARANA MARANA II ALA ATA	Nup120/133	Nup160/133	~	-	rings
	23	Tb927.7.2300	TbNup132	132.3	a chu a bhainn air bhliadh aine chu abh a mhainn a bhainn a bhainn bh	Nup120/133	Nup160/133 )	-la	-l-	
$\alpha$ -solenoid	/ (	Tb10.6k15.2350	) TbNup144	144.3	n i de della di ne ne cellenti i di devide e della d	Nup157/170	Nup155	· _3	Ę۲.	inner rings
	(	Tb09.211.4780	TbNup82	82.4	ter a de la verte de la constante de la constan	Nup84/85	Nup107/75			outer
Aller See .		Tb11.02.0460	TbNup89	89.1		Nup84/85	Nup107/75		\$ <del>-</del>	rings
	-{	Tb10.6k15.3670	) TbNup96	96.5	, but name a state a st	Nic96	Nup93			
$\langle \rangle$		Tb10.6k15.1530	TbNup181	181.5	in - A hide die verheite is stelle bekeinde die der Kallen von die	Nup188/192	Nup188/205		ÊΞ	inner
β-sandwich	$\langle  $	Tb927.4.2880	TbNup225	225.5	te o de la filia de nare de las las de la filia de la deficie de la deficie de la filia de la filia de la fili	Nup188/192	Nup188/205	9	7	
in the second		Tb11.03.0140	TbNup158	158.3		Nup145	Nup98/96	- 3	()=	outer rings FG nups
and the	1	Tb927.3.3180	TbNup98	98.1		FGR	epeat	0	1	
/		Tb11.01.2880	TbNup149	149.2		Grou	ир В			
/	1	Tb927.4.4310	TbNup64	64.2		Í				
FG-repeat		Tb927.8.8050	TbNup75	74.8	a dala a construction de la construcción de la construcción de la construcción de la construcción de la constru					
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	(	Tb11.01.2885	TbNup140	140.3				3	(E	FG nups
	(	Tb11.01.7200	TbNup53a	52.7		FG R Gro	epeat up A	7	7	
	$\langle  $	Tb927.3.3540	TbNup53b	52.8	يريد الله الشريب					
	1	Tb11.02.0270	TbNup59	58.8						
coiled-coil		Tb927.4.5200	TbNup62	62.4		)				
Commercia	(	Tb09.160.0340	TbNup92	92.3		Mlp	Tpr )	-	de-	nuclear
HORAL DEVICE	- {	Tb11.03.0810	TbNup110	109.7	ATT I WALLAND AND A MARKED AND A	Mlp	Tpr	-93	-	basket

### TbNup110 interacts with TbNup92, NUP-2 and NAP-1







Spectrin  $\beta$ 



# TbNup92 is a cell cycle-regulated protein and associates with the spindle















#### TbNup92 modulates mRNA levels, but not promoter activity



#### Evolution of TbNup92



#### Evolution of TbNup92



#### Evolution of TbNup92



#### The nuclear pore complex and the nuclear envelope



NUP-1





Rout and Field JBC 2001

#### NUP-1 forms a cage



duBois, Horden, Field, Rout

#### NUP-1 forms a cage



duBois, Horden, Field, Rout

#### Nuclear pore positioning and VSG repression requires NUP-1





duBois et al., PLoS Biology 2011

Hours post-induction

24

48

0

-0.5

6

#### Nuclear pore positioning and VSG repression requires NUP-1





duBois et al., PLoS Biology 2011

Hours post-induction

24

48

0

-0.5

6

#### NUP-1 interacts with the NPC and additional IF proteins



#### Maishman et al., in preparation

# NUP-1 NUP-2



# NUP-1 NUP-2



# Relative dimensions of human and trypanosome nuclei and lamina proteins



# NPC NUP-1 DNA



NPC: Nup98 C-terminus NUP-1: C-terminus

# NPC NUP-1 DNA



NPC: Nup98 C-terminus NUP-1: C-terminus

# NPC NUP-1 DNA



NPC: Nup98 C-terminus NUP-1: C-terminus



#### NMCPs (nuclear matrix constituent proteins)



Koreny and Field (submitted)
# NUP-1





Koreny and Field





Dinoflagellate Symbiodinium goreaui Oomycete Phytophthora infestans

## Evolution of the nuclear envelope



## Evolution of the nuclear envelope



## Evolution of the nuclear envelope





## How did the nuclear envelope arise?



## Conclusions

Trypanosome NPC is symmetrical, lacking the cytoplasmic mRNA export machinery.

Alternative mechanisms for membrane attachment.

Subunit flexibility within NPC substructures.

Alternate lamina systems in trypanosomes and plants.

Original lamina most likely lamin system.

### Acknowledgments

Cordula Boehm ThankGod Ebenezer Ludek Koreny Samson Obado Divya Venkatesh Ning Zhang Martin Zoltner

#### Alumni

Vincent Adung'a Moazzam Ali Harriet Allison Clare Allen Wei-Lian Chung Jeff deGrasse Kelly duBois Joel Dacks Helen I. Field Carme Gabernet-Castello Catarina Gadhela Belinda Hall Jennifer Holden Lila Koumandou Ka-Fai Leung Jennifer Lumb Luke Maishman Paul Manna Gareth Morgan Senthil Natesan Darren Nesbeth Amanda O'Reilly Arun Pal Tatiana Seergenko Francois Valentin Ya-Nan Wang

### Collaborators

Vincent Adung'a (Nairobi) John Aitchison (Seattle) Mark Carrington (Cambridge) Brian T. Chait (New York) Joel B. Dacks (Edmonton) Catarina Gadelha (Nottingham) David Horn (Dundee) Steve Kelly (Oxford) Miguel Navarro (Granada) Michael P. Rout (New York)

### Support

The Wellcome Trust Marie Curie Fellowships The Cambridge Commonwealth Fund Bill and Melinda Gates Foundation National Institutes of Health (USA) The Medical Research Council (UK) The Leverhulme Trust



Coulson plot generator http://sourceforge.net/projects/coulson/



Euglena genome project http://euglenadb.org



RNAit http://trypanofan.bioc.cam.ac.uk/ trypanofan/main/

### Euglena gracilis



### Trypanosoma brucei



http://goo.gl/E7Em6

Dundee

