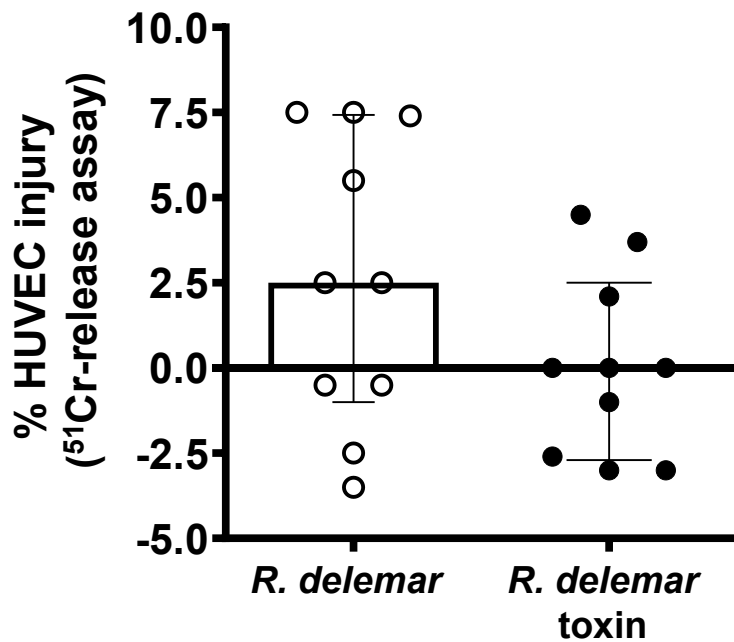# Supplementary Fig. 1

Supplementary Fig. 1. Incubation of lower inoculum of *R. delemar* or its toxin with HUVECs induces minimal to no host cell injury. Data are presented as % ^{51}Cr-released from HUVECs challenged with 1 x 10^5 spores of *R. delemar* or 50 μg/ml of *R. delemar* toxin for 5 hours. Data (n=10/group) are as median $\pm$ interquartile range from three experiments.

Supplementary Fig. 2

```
saporin    VTSITLDLVNPTAGQYSSFVDKIRNNVKDPNLKYGGTDIAVIGPPSKEKFLRINFQSSRG
Mucoricin  ----------------MYFEE---------------------GRLFFIKSQFNGRVL
                            :.::                        ..   *:. :*:.

saporin    TVSLGLKRDNLYVVAYLAMDNTNVNRAYYFRSEITSAESTALFPEATTANQKALEYTEDY
Mucoricin  DVEDGSTEDDANIIVYTQKYEDCLNQLW----------------------RYENGY
           *. * . *: ::.*      :  :*. :                         * :.*

saporin    QSIEKNAQITQGDQSRKELGLGIDLLSTSMEAVNKKARVVKDEARFLLIAIQMTAEAARF
Mucoricin  FINAKSAKV--------------------LDIRGGEMQPESQIIQYAQKMVEEAANQ
             *.*::                        :: ..  :: *:.:: * :*. ***.

saporin    RYIQNLVIKNFPNKFNSENKVIQFEVNWKKISTAIYGDAKNGVFNKDYDFGFGKVRQVKD
Mucoricin  RWAID-----------EDGYIFCEARPDLVLDIQGAEDEDCVPVILYERREGEVSA--N
           *: :           *: *  *.. . :     .: :: *    *:   *:*    :

saporin    LQMGLLMYLGKPK
Mucoricin  QRWELVPFEG---
```

Supplementary Fig. 2. CLUSTAL multiple sequence alignment by MUSCLE (3.8) between mucoricin and saporin from *Saponaria officinalis.* The predicted Type 1 RIP domain in saporin (shown in yellow) aligned with sequence from mucoricin with 10 out of 17 amino acid residues conserved.

Supplementary Table 2. Ten proteins that are structurally similar to mucoricin. The 3-D model of mucoricin was used to identify structurally similar proteins in the protein data bank (PDB) by Tm align.

Rank	PDB Hit	Tm score	RMSD	Identity	Coverage	Protein Description	Classification	Link
1	3ef2D	0.947	1.05	0.166	0.986	*Marasmius oreades* mushroom lectin (MOA) in complex with Gal-alpha(1,3)[Fuc-alpha(1,2)]Gal and Calcium	Sugar binding protein	https://www.rcsb.org/structure/3ef2
2	3vsfA	0.871	1.28	0.248	0.912	1,3 Gal 43A, an exo-beta-1,3-Galactanase from *Clostridium thermocellum*	Sugar binding protein	https://www.rcsb.org/structure/3vsf
3	3pg0A	0.862	1.13	0.295	0.898	3-fold symmetric protein, Three Foil	De novo protein	https://www.rcsb.org/structure/3pg0
4	2x2tA	0.838	1.55	0.157	0.912	*Sclerotinia sclerotiorum* Agglutinin (SSA) in complex with Gal-beta1,3-Galnac	Cell adhesion	https://www.rcsb.org/structure/2x2t
5	3nbeA	0.835	1.6	0.164	0.912	*Clitocybe nebularis* ricin B-like lectin (CNL) in complex with N,N'-diacetyllactosediamine	Sugar binding protein	https://www.rcsb.org/structure/3nbe
6	4g9mA	0.831	1.35	0.223	0.884	Crystal structure of the *Rhizoctonia solani* agglutinin	Sugar binding protein	https://www.rcsb.org/structure/4g9m
7	3phzA	0.827	2.03	0.179	0.912	*Polyporus squamosus* lectin bound to human-type influenza-binding epitope Neu5Aca2-6Galb1-4GlcNAc	Sugar binding protein	https://www.rcsb.org/structure/3phz
8	5xg5A	0.825	1.43	0.099	0.891	Crystal structure of Mitsuba-1 with bound NAcGal	De novo protein	https://www.rcsb.org/structure/5xg5
9	2vseA3	0.825	1.95	0.187	0.905	Structure and mode of action of a mosquitocidal holotoxin (*Lysinibacillus sphaericus*)	Toxin	https://www.rcsb.org/structure/2vse
10	3a23B	0.822	1.54	0.188	0.878	Crystal Structure of beta-L-Arabinopyranosidase complexed with D-galactose	Hydrolase (glycosidase)	https://www.rcsb.org/structure/3a23

Supplementary Table 3: Ricin orthologs in different Mucorales and the presence of vascular leak and RIP motifs

Column headers for the Percent Identity Matrix (1–20):

#	Organism	Accession ID
1	Ricinus communis	NP_001310630.1
2	Choanephora cucurbitarum	OBZ89643.1
3	Rhizopus delemar RA 99-880	EIE81863.1
4	Mucor circinelloides f. circinelloides 1006PhL	EPB83885.1
5	Mucor circinelloides f. lusitanicus	KAF1807713.1
6	Mucor circinelloides f. lusitanicus CBS 277.49	OAD01005.1
7	Rhizopus azygosporus	RCH82711.1
8	Rhizopus microsporus	ORE22231.1
9	Rhizopus stolonifer	RCH89556.1
10	Mucor ambiguus	GAN06585.1
11	Rhizopus microsporus ATCC 52813	XP_023462404.1
12	Rhizopus microsporus var. microsporus	ORE05386.1
13	Phycomyces blakesleeanus NRRL 1555(-)	XP_018295414.1
14	Absidia glauca	SAL96273.1
15	Absidia repens	ORZ12009.1
16	Syncephalastrum racemosum	ORY99019.1
17	Hesseltinella vesiculosa	ORX62783.1
18	Lichtheimia corymbifera JMRC:FSU:9682	CDH57241.1
19	Lichtheimia ramosa	CDS03748.1
20	Parasitella parasitica	CEP13132.1

MUSCLE Sequence Alignment (Percent Identity Matrix):

S.No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1	100	30	30	29	27	27	27	27	27	27	26	26	26	24	23	21	21	20	17	16
2	30	100	81	78	76	76	85	75	75	75	74	74	80	45	45	46	45	47	43	73
3	30	81	100	78	72	72	87	77	77	72	77	77	77	45	48	44	44	48	44	71
4	29	78	78	100	90	90	78	69	69	90	69	69	73	43	45	44	41	45	42	82
5	27	76	72	90	100	100	73	66	66	97	68	68	73	40	43	40	40	42	40	78
6	27	76	72	90	100	100	73	66	66	97	68	68	73	40	43	40	40	42	40	78
7	27	85	87	78	73	73	100	77	77	73	77	77	76	45	46	41	43	48	45	68
8	27	75	77	69	66	66	77	100	100	66	99	99	69	46	45	46	42	45	42	66
9	27	75	77	69	66	66	77	100	100	66	99	99	69	46	45	46	42	45	42	66
10	27	75	72	90	97	97	73	66	66	100	67	67	71	40	43	40	40	42	39	77
11	26	74	77	69	68	68	77	99	99	67	100	100	69	44	45	45	41	44	42	67
12	26	74	77	69	68	68	77	99	99	67	100	100	69	44	45	45	41	44	42	67
13	26	80	77	73	73	73	76	69	69	71	69	69	100	38	41	42	39	42	36	68
14	24	45	45	43	40	40	45	46	46	40	44	44	38	100	69	47	41	42	44	40
15	23	45	48	45	43	43	46	45	45	43	45	45	41	69	100	43	38	39	44	41
16	21	46	44	44	40	40	41	46	46	40	45	45	42	47	43	100	44	46	44	41
17	21	45	44	41	40	40	43	42	42	40	41	41	39	41	38	44	100	56	51	36
18	20	47	48	45	42	42	48	45	45	42	44	44	42	42	39	46	56	100	47	42
19	17	43	44	42	40	40	45	42	42	39	42	42	36	44	44	44	51	47	100	41
20	16	73	71	82	78	78	68	66	66	77	67	67	68	40	41	41	36	42	41	100

Vascular Leak Motifs [(x)D(y)-Motif, x= L, I, G or V; y= V, L or S] and Ribosome Inactivation Motifs (Reported in Ricin):

S.No.	Organisms' Name	Accession ID	LDV	IDV	IDS	GDL	VDV	EAARF Score	EAARF p-value	EAARF Q-value	EAARF Motif in Target Protein	WGRLS Score	WGRLS p-value	WGRLS Q-value	WGRLS Motif in Target Protein
1	Ricinus communis	NP_001310630.1	Yes				Yes	19.81	<0.00001	0.003	EAARF	20.92 / 4.28	<0.00001 / 0.0009	0.001 / 1	WGRLS / RGRLT
2	Choanephora cucurbitarum	OBZ89643.1	Yes					4.25	0.0019	0.59	EAANQ				
3	Rhizopus delemar RA 99-880	EIE81863.1	Yes					4.25	0.0019	0.59	EAANQ	4.28	0.0009	1	EGRLF
4	Mucor circinelloides f. circinelloides 1006PhL	EPB83885.1	Yes					4.25	0.0019	0.59	EAANQ				
5	Mucor circinelloides f. lusitanicus	KAF1807713.1	Yes					4.25	0.0019	0.59	EAANQ				
6	Mucor circinelloides f. lusitanicus CBS 277.49	OAD01005.1	Yes					4.25	0.0019	0.59	EAANQ				
7	Rhizopus azygosporus	RCH82711.1	Yes					4.25	0.0019	0.59	EAANQ				
8	Rhizopus microsporus	ORE22231.1	Yes					4.25	0.0019	0.59	EAANQ				
9	Rhizopus stolonifer	RCH89556.1	Yes					4.25	0.0019	0.59	EAANQ				
10	Mucor ambiguus	GAN06585.1	Yes					4.25	0.0019	0.59	EAANQ				
11	Rhizopus microsporus ATCC 52813	XP_023462404.1	Yes												
12	Rhizopus microsporus var. microsporus	ORE05386.1	Yes												
13	Phycomyces blakesleeanus NRRL 1555(-)	XP_018295414.1		Yes				4.25	0.0019	0.59	EAANQ				
14	Absidia glauca	SAL96273.1	Yes												
15	Absidia repens	ORZ12009.1	Yes				Yes								
16	Syncephalastrum racemosum	ORY99019.1		Yes											
17	Hesseltinella vesiculosa	ORX62783.1				Yes									
18	Lichtheimia corymbifera JMRC:FSU:9682	CDH57241.1		Yes				4.88 / 4.74	0.0009 / 0.0014	0.59 / 0.59	GAAAF / EATRQ				
19	Lichtheimia ramosa	CDS03748.1			Yes			4.88 / 4.74							
20	Parasitella parasitica	CEP13132.1	Yes					4.25	0.0019	0.59	EAANQ				

Note:

1. Protein sequences were aligned using MUSCLE in CLUSTAL format and % sequence identify matrix was generated.

2. Protein sequences were scanned for individual motifs using FIMO (Find Individual Motif Occurrences): Version 5.1.1 tool (http://meme-suite.org).

3. The p-value (threshold p=0.001) of a motif occurrence is defined as the probability of a random sequence of the same length as the motif matching that position of the sequence with as good or better a score.

4. The score (Threshold +0.001) for the match of a position in a sequence to a motif is computed by summing the appropriate entries from each column of the position-dependent scoring matrix that represents the motif.

5. The q-value of a motif occurrence is defined as the false discovery rate if the occurrence is accepted as significant.