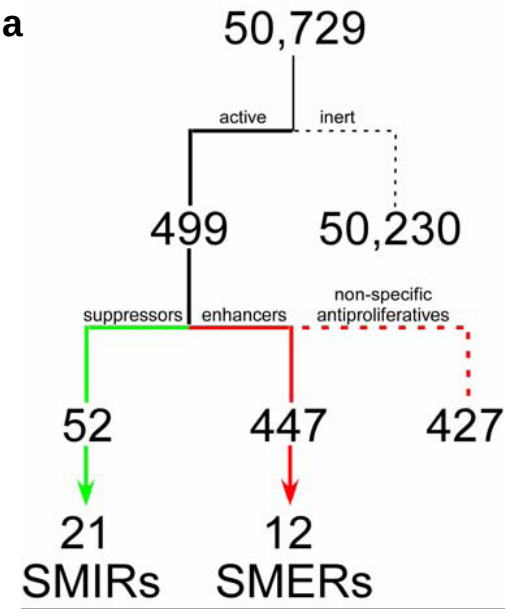
Supplementary Figure 1

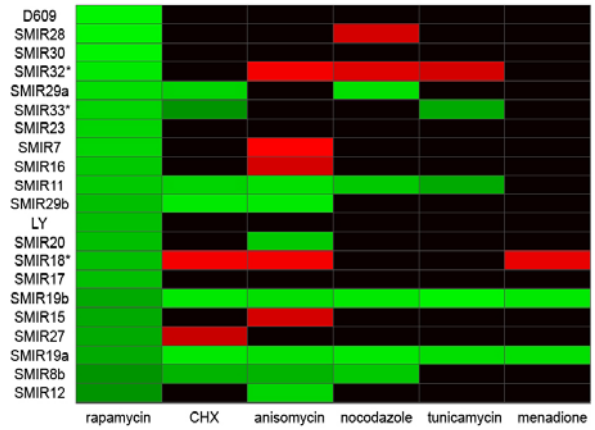
a



b

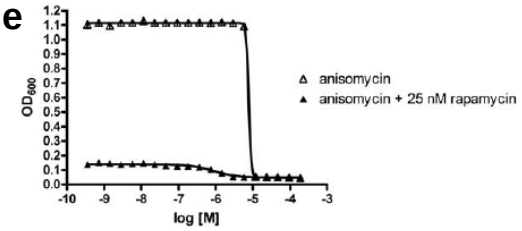
Compound name	EC_{50}	Compound name	EC_{50}
D609	0.412	SMER17	1.3
SMIR28	0.495	SMER20	1.9
SMIR30	0.662	SMER6	3.7
SMIR32*	0.998	SMER26	4.1
SMIR29a	2.0	SMER10	4.9
SMIR33*	3.0	SMER18	17.4
SMIR23	3.3	SMER14	18
SMIR7	4.4	SMER3	24.1
SMIR16	4.8	SMER24	26.6
SMIR11	7.2	SMER22	>50
SMIR29b	9.5	SMER23	>50
LY-83583	10.4	SMER28	>50
SMIR20	11.7		
SMIR18*	12.2		
SMIR19b	14.3		
SMIR15	31.2		
SMIR27	34.1		
SMIR19a	50.4		
SMIR8b	>50		
SMIR12	>50		

c

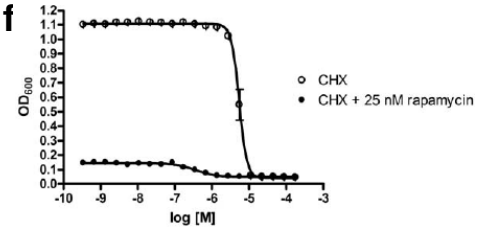


d

e



f



Supplementary Figure 1. Results of a small-molecule screen for suppressors (SMIRs) and enhancers (SMERs) of the cytostatic effects of rapamycin in yeast, and characterisation, potency and selectivity of the identified SMIRs and SMERs.

(**a**) Of 50,729 compounds screened in duplicate in yeast BY4742 strain, 52 (0.001 %) suppressors and 20 (0.0004 %) enhancers were initially identified, of which 21 suppressors and 12 enhancers retested positively. (In cases where multiple structural analogs scored as primary assay positives, a single representative was chosen; exceptions are compounds with a lower-case letter in their name, e.g., SMIR19a). 427 candidate enhancers were subsequently found to be growth-inhibitory as single agents, and were eliminated from further consideration. Library compounds were assessed at approximately 75 μM. The exact concentration varies depending on the molecular weight of each compound.

(**b**) Table summarizing EC_{50} values (listed in descending order of potency) of 21 suppressors of rapamycin (SMIRs) (shown in green) and 12 enhancers of rapamycin (SMERs) (shown in red). Concentrations are listed in micromolar (μM). The EC_{50} of suppression was determined in 50 nM rapamycin; the EC_{50} of enhancement was determined in 20 nM rapamycin. EC_{50} values of asterisked compounds were determined in synthetic media; all other EC_{50} values were determined in rich media.

(**c,d**) Potency and selectivity of 33 small-molecule modifiers of the cytostatic effects of rapamycin (rows) against a panel of 6 assay compounds (columns). Two-dimensional (2D-) heatmaps display negative log-transformed (green) and positive log-transformed (red) EC_{50} values derived from averaged duplicate OD_{600} absorbance measurements of a 2-fold dilution series of SMIRs (**c**) and of SMERs (**d**) treated with either 50 nM (used in **c**) and 20 nM (used in **d**) rapamycin or 555 nM cycloheximide (CHX) or 18.9 μM anisomycin or 16.6 μM nocodazole or 595 nM tunicamycin or 29 μM (used in **c**) and 14.5 μM (used in **d**) menadione. Black indicates no interaction between small-molecule modifiers and assay compounds; intense green corresponds to low half-maximal suppression; intense red corresponds to low half-maximal enhancement.

(**e,f**) Dose-response curves correspond to 2-fold dilutions of either anisomycin (data shown in **e**) or CHX (data shown in **f**) in the presence of 25 nM rapamycin (filled shapes) or vehicle (unfilled shapes).