Researchers discover potential treatments for common complication following bone marrow transplant

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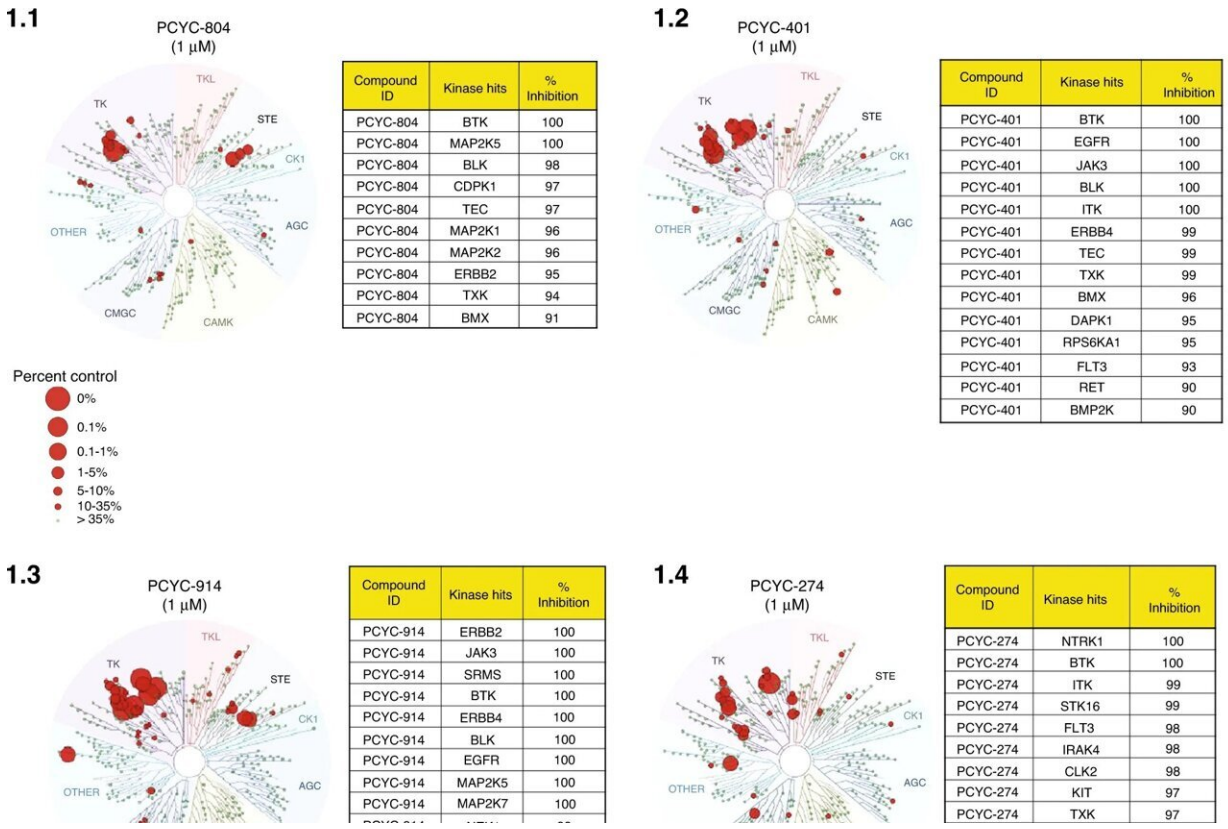

Compound ID	Kinase hits	% Inhibition
PCYC-804	BTK	100
PCYC-804	MAP2K5	100
PCYC-804	BLK	98
PCYC-804	CDPK1	97
PCYC-804	TEC	97
PCYC-804	MAP2K1	96
PCYC-804	MAP2K2	96
PCYC-804	ERBB2	95
PCYC-804	TXK	94
PCYC-804	BMX	91

Compound ID	Kinase hits	% Inhibition
PCYC-401	BTK	100
PCYC-401	EGFR	100
PCYC-401	JAK3	100
PCYC-401	BLK	100
PCYC-401	ITK	100
PCYC-401	ERBB4	99
PCYC-401	TEC	99
PCYC-401	TXK	99
PCYC-401	BMX	96
PCYC-401	DAPK1	95
PCYC-401	RPS6KA1	95
PCYC-401	FLT3	93
PCYC-401	RET	90
PCYC-401	BMP2K	90

Compound ID	Kinase hits	% Inhibition
PCYC-914	ERBB2	100
PCYC-914	JAK3	100
PCYC-914	SRMS	100
PCYC-914	BTK	100
PCYC-914	ERBB4	100
PCYC-914	BLK	100
PCYC-914	EGFR	100
PCYC-914	MAP2K5	100
PCYC-914	MAP2K7	100

Compound ID	Kinase hits	% Inhibition
PCYC-274	NTRK1	100
PCYC-274	BTK	100
PCYC-274	ITK	99
PCYC-274	STK16	99
PCYC-274	FLT3	98
PCYC-274	IRAK4	98
PCYC-274	CLK2	98
PCYC-274	KIT	97
PCYC-274	TXK	97

Kinase binding activity analysis using DiscoverX Kinomescan profiling. 1.1-1.4: Off-target kinase activities were assessed using the commercially available screen from Eurofins. All four test compounds were tested at a high concentration (1 uM) to maximize the sensitivity of the screen. The DiscoverX Kinomescan utilizes an active site-directed competition assay to measure the binding activity of test compounds to 450 human kinases. The assay does not

utilize ATP and is thus not a functional kinase activity screen. 1.5-1.6: After animals in allogeneic groups were dosed with various test compounds at their indicated dose regimens, spleen, and thymus tissue samples were harvested 4 h after the final dose to determine BTK and ITK occupancy levels due to drug-target engagement. Occupancy was determined in the spleen for BTK and thymus for ITK using selective irreversible probes for each target using an ELISA format with MSD detection (see Methods for details). Error bars are shown as SEM. *P* value 0.01 to 0.05 = *, *P* value 0.001 to 0.01 = **, *P* value 0.0001 to 0.001 = ***, *P* value