

**Table S1.** TC values for AKT1 mutational fork in lung adenocarcinoma

Transition	Description	TC
BLOCK 1		
AKT1- GSK3B	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0116
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0116
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0116
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0117
AKT1- RAF1	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0819
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0819
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0822
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0823
AKT1- MAP2K4	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.9034
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.9022
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.9052
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	<b>0.9058</b>
BLOCK 2		
AKT1- GSK3B	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0115
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0116
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0116
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0116
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0117
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0116
AKT1- RAF1	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0815
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0818
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0822
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0819
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0825
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0818
AKT1- MAP2K4	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.8977
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.9004
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	<b>0.9049</b>
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.9022
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.8975
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.9013
BLOCK 3		
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0114

AKT1- GSK3B	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0115
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0115
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0114
AKT1- RAF1	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0806
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0813
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0815
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0808
AKT1- MAP2K4	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.8876
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.8954
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	<b>0.8971</b>
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.8902
BLOCK 3 (special case)		
AKT1- GSK3B	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0076
AKT1- RAF1	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0539
AKT1- MAP2K4	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.5932

**Table S2.** TC values for MAP2K4 mutational fork in lung adenocarcinoma

Transition	Description	TC
BLOCK 1		
MAP2K4- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0779
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0774
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0775
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0778
MAP2K4- MAPK8	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	<b>0.4675</b>
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.465
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4656
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4671
MAP2K4- CRL	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.4545
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.4521
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4527
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4541
BLOCK 2		
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0772



**Table S3.** TC values for MAPK8IP1 mutational fork in lung adenocarcinoma

Transition	Description	TC
BLOCK 1		
MAPK8IP1- MAP3K11	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	<b>0.4056</b>
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.4053
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4053
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4029
MAPK8IP1- MAP2K7	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.2027
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.2026
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.2046
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.2014
MAPK8IP1- MAP4K1	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.3887
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.3884
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.3885
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3862
BLOCK 2		
MAPK8IP1- MAP3K11	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	<b>0.4030</b>
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4026
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3992
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3996
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	<b>0.4030</b>
$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3991	
MAPK8IP1- MAP2K7	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.2014
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.2012
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.1995
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.1997
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.2014
$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.1995	
MAPK8IP1- MAP4K1	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.3862
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.3859
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3826
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3830
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.3863
$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3826	
BLOCK 3		
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	<b>0.3956</b>

MAPK8IP1- MAP3K11	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3889
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3895
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3893
MAPK8IP1- MAP2K7	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.1977
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.1944
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.1947
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.1946
MAPK8IP1- MAP4K1	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.3791
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3727
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3733
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3731
BLOCK 3 (special case)		
MAPK8IP1- MAP3K11	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.1694
MAPK8IP1- MAP2K7	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0846
MAPK8IP1- MAP4K1	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.1623

**Table S4.** TC values for MAP3K11 mutational fork in lung adenocarcinoma

Transition	Description	TC
BLOCK 1		
MAP3K11- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0)$	0.5080
	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.5065
	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	<b>0.5080</b>
MAP3K11- MAP2K7	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0)$	0.4868
	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.4854
	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	0.4868
BLOCK 2		
MAP3K11- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.4978
	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	<b>0.5006</b>
	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.4979
MAP3K11- MAP2K7	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.4770
	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	0.4797
	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.4771
BLOCK 3		

MAP3K11- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.1932
MAP3K11- MAP2K7	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.1852

**Table S5.** TC values for MAPK8 mutational fork in lung adenocarcinoma

Transition	Description	TC
BLOCK 1		
MAPK8- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0)$	0.1679
	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.1676
	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	0.1683
MAPK8- MAPK8IP1	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0)$	<b>0.8259</b>
	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.8243
	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	0.8275
BLOCK 2		
MAPK8- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.1644
	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	0.1658
	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.1649
MAPK8- MAPK8IP1	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.8086
	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	<b>0.8153</b>
	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.8111
BLOCK 3		
MAPK8- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.1932
MAPK8- MAPK8IP1	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.1852

**Table S6.** TC values for KRAS mutational fork in skin cutaneous melanoma

Transition	Description	TC
Block 1		
KRAS-BRAF	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0)$	0.0446
	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.0396
	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	0.0439
KRAS-PIK3CA	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0)$	<b>0.9501</b>
	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.8443

	$TC(T_{\mathbf{JB}}(\mathbf{J}_{\mathbf{AB}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	0.9347
Block 2		
KRAS-BRAF	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{AB}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.0364
	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{AB}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	0.0412
	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{AB}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.0361
KRAS-PIK3CA	$TC(T_{\mathbf{JB}}(\mathbf{J}_{\mathbf{AB}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0)$	0.775
	$TC(T_{\mathbf{JB}}(\mathbf{J}_{\mathbf{AB}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	<b>0.8766</b>
	$TC(T_{\mathbf{JB}}(\mathbf{J}_{\mathbf{AB}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.7679
Block 3		
KRAS-BRAF	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{AB}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.0239
KRAS-PIK3CA	$TC(T_{\mathbf{JB}}(\mathbf{J}_{\mathbf{AB}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.5092

**Table S7.** TC values for AKT1 mutational fork in skin cutaneous melanoma

Transition	Description	TC
BLOCK 1		
AKT1-GSK3B	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0116
	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0116
	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0116
	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0121
AKT1-RAF1	$TC(T_{\mathbf{JB}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0819
	$TC(T_{\mathbf{JB}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0821
	$TC(T_{\mathbf{JB}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0816
	$TC(T_{\mathbf{JB}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0857
AKT1-MAP2K4	$TC(T_{\mathbf{JC}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.9015
	$TC(T_{\mathbf{JC}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.9036
	$TC(T_{\mathbf{JC}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.8989
	$TC(T_{\mathbf{JC}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	<b>0.9436</b>
BLOCK 2		
AKT1-GSK3B	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0115
	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0115
	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0114
	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0115
	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0114
	$TC(T_{\mathbf{JA}}(\mathbf{J}_{\mathbf{ABC}}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0115

AKT1- RAF1	$TC(T_{JB}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 0, M(C) = 0)$	0.0814
	$TC(T_{JB}(J_{ABC})   M(J) = 0, M(A) = 1, M(B) = 1, M(C) = 0)$	0.0810
	$TC(T_{JB}(J_{ABC})   M(J) = 0, M(A) = 0, M(B) = 1, M(C) = 1)$	0.0807
	$TC(T_{JB}(J_{ABC})   M(J) = 1, M(A) = 0, M(B) = 0, M(C) = 1)$	0.081
	$TC(T_{JB}(J_{ABC})   M(J) = 1, M(A) = 0, M(B) = 1, M(C) = 0)$	0.0808
	$TC(T_{JB}(J_{ABC})   M(J) = 0, M(A) = 1, M(B) = 0, M(C) = 1)$	0.0835
AKT1- MAP2K4	$TC(T_{JC}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 0, M(C) = 0)$	0.8963
	$TC(T_{JC}(J_{ABC})   M(J) = 0, M(A) = 1, M(B) = 1, M(C) = 0)$	0.8925
	$TC(T_{JC}(J_{ABC})   M(J) = 0, M(A) = 0, M(B) = 1, M(C) = 1)$	0.8887
	$TC(T_{JC}(J_{ABC})   M(J) = 1, M(A) = 0, M(B) = 0, M(C) = 1)$	0.8923
	$TC(T_{JC}(J_{ABC})   M(J) = 1, M(A) = 0, M(B) = 1, M(C) = 0)$	0.8897
	$TC(T_{JC}(J_{ABC})   M(J) = 0, M(A) = 1, M(B) = 0, M(C) = 1)$	<b>0.8953</b>
BLOCK 3		
AKT1- GSK3B	$TC(T_{JA}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 1, M(C) = 0)$	0.0112
	$TC(T_{JA}(J_{ABC})   M(J) = 0, M(A) = 1, M(B) = 1, M(C) = 1)$	0.0112
	$TC(T_{JA}(J_{ABC})   M(J) = 1, M(A) = 0, M(B) = 1, M(C) = 1)$	0.0111
	$TC(T_{JA}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 0, M(C) = 1)$	0.0112
AKT1- RAF1	$TC(T_{JB}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 1, M(C) = 0)$	0.0789
	$TC(T_{JB}(J_{ABC})   M(J) = 0, M(A) = 1, M(B) = 1, M(C) = 1)$	0.0788
	$TC(T_{JB}(J_{ABC})   M(J) = 1, M(A) = 0, M(B) = 1, M(C) = 1)$	0.0783
	$TC(T_{JB}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 0, M(C) = 1)$	0.0793
AKT1- MAP2K4	$TC(T_{JC}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 1, M(C) = 0)$	0.8694
	$TC(T_{JC}(J_{ABC})   M(J) = 0, M(A) = 1, M(B) = 1, M(C) = 1)$	0.8677
	$TC(T_{JC}(J_{ABC})   M(J) = 1, M(A) = 0, M(B) = 1, M(C) = 1)$	0.8628
	$TC(T_{JC}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 0, M(C) = 1)$	<b>0.8735</b>
BLOCK 3 (special case)		
AKT1- GSK3B	$TC(T_{JA}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 1, M(C) = 1)$	0.0636
AKT1- RAF1	$TC(T_{JB}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 1, M(C) = 1)$	0.1015
AKT1- MAP2K4	$TC(T_{JC}(J_{ABC})   M(J) = 1, M(A) = 1, M(B) = 1, M(C) = 1)$	0.4926

**Table S8.** TC values for MAP2K4 mutational fork in skin cutaneous melanoma

Transition	Description	TC
BLOCK 1		
MAP2K4- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0776
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0770
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0774
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0775
MAP2K4- MAPK8	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	<b>0.4658</b>
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.4621
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4649
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4653
MAP2K4- CRL	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.4529
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.4493
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4520
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4523
BLOCK 2		
MAP2K4- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.0760
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0760
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0767
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0767
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0766
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0760
MAP2K4- MAPK8	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.4561
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4561
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	<b>0.4604</b>
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	<b>0.4604</b>
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4599
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4565
MAP2K4- CRL	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.4434
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4434
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.4476
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4476
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4571
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4538
BLOCK 3		
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.0732

MAP2K4- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0733
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0744
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.0733
MAP2K4- MAPK8	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4396
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.4401
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	<b>0.4465</b>
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4404
MAP2K4- CRL	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.4273
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.4279
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.4340
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4281
BLOCK 3 (special case)		
MAP2K4- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0346
MAP2K4- MAPK8	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.2076
MAP2K4- CRL	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.2018

**Table S9.** TC values for MAPK8IP1 mutational fork in skin cutaneous melanoma

Transition	Description	TC
BLOCK 1		
MAPK8IP1- MAP3K11	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.4028
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.3985
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	<b>0.4050</b>
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.4010
MAPK8IP1- MAP2K7	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.2014
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.1992
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.2024
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.2004
MAPK8IP1- MAP4K1	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.3861
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.3820
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.3882
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3843
BLOCK 2		
MAPK8IP1- MAP3K11	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.3895
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.3922

	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3959
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3930
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	<b>0.3972</b>
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3861
MAPK8IP1- MAP2K7	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.1947
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.1960
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.1979
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.1964
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.1985
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.1930
MAPK8IP1- MAP4K1	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 0)$	0.3733
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.3759
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3794
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3767
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.3807
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3701
BLOCK 3		
MAPK8IP1- MAP3K11	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.3698
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3656
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	<b>0.3761</b>
	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3620
MAPK8IP1- MAP2K7	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.1848
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.1827
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.1880
	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.1809
MAPK8IP1- MAP4K1	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 0)$	0.3544
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3504
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.3605
	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 0, M(\mathbf{C}) = 1)$	0.3469
BLOCK 3 (special case)		
MAPK8IP1- MAP3K11	$TC(T_{JA}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.1113
MAPK8IP1- MAP2K7	$TC(T_{JB}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.0556
MAPK8IP1- MAP4K1	$TC(T_{JC}(\mathbf{J}_{ABC}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1, M(\mathbf{C}) = 1)$	0.1066

**Table S10.** TC values for MAP3K11 mutational fork in skin cutaneous melanoma

Transition	Description	TC
BLOCK 1		
MAP3K11- MAPK8IP3	$TC(T_{JA}(J_{AB}) \mid M(J) = 1, M(A) = 0, M(B) = 0)$	0.4294
	$TC(T_{JA}(J_{AB}) \mid M(J) = 0, M(A) = 1, M(B) = 0)$	0.4350
	$TC(T_{JA}(J_{AB}) \mid M(J) = 0, M(A) = 0, M(B) = 1)$	0.4399
MAP3K11- MAP2K7	$TC(T_{JB}(J_{AB}) \mid M(J) = 1, M(A) = 0, M(B) = 0)$	0.4747
	$TC(T_{JB}(J_{AB}) \mid M(J) = 0, M(A) = 1, M(B) = 0)$	0.4809
	$TC(T_{JB}(J_{AB}) \mid M(J) = 0, M(A) = 0, M(B) = 1)$	<b>0.4863</b>
BLOCK 2		
MAP3K11- MAPK8IP3	$TC(T_{JA}(J_{AB}) \mid M(J) = 1, M(A) = 1, M(B) = 0)$	0.4556
	$TC(T_{JA}(J_{AB}) \mid M(J) = 1, M(A) = 0, M(B) = 1)$	0.4121
	$TC(T_{JA}(J_{AB}) \mid M(J) = 0, M(A) = 1, M(B) = 1)$	0.4229
MAP3K11- MAP2K7	$TC(T_{JB}(J_{AB}) \mid M(J) = 1, M(A) = 1, M(B) = 0)$	<b>0.5037</b>
	$TC(T_{JB}(J_{AB}) \mid M(J) = 1, M(A) = 0, M(B) = 1)$	0.4556
	$TC(T_{JB}(J_{AB}) \mid M(J) = 0, M(A) = 1, M(B) = 1)$	0.4675
BLOCK 3		
MAP3K11- MAPK8IP3	$TC(T_{JA}(J_{AB}) \mid M(J) = 1, M(A) = 1, M(B) = 1)$	0.1430
MAP3K11- MAP2K7	$TC(T_{JB}(J_{AB}) \mid M(J) = 1, M(A) = 1, M(B) = 1)$	0.1581

**Table S11.** TC values for MAPK8 mutational fork in skin cutaneous melanoma

Transition	Description	TC
BLOCK 1		
MAPK8- MAPK8IP3	$TC(T_{JA}(J_{AB}) \mid M(J) = 1, M(A) = 0, M(B) = 0)$	0.1676
	$TC(T_{JA}(J_{AB}) \mid M(J) = 0, M(A) = 1, M(B) = 0)$	0.1661
	$TC(T_{JA}(J_{AB}) \mid M(J) = 0, M(A) = 0, M(B) = 1)$	0.1666
MAPK8- MAPK8IP1	$TC(T_{JB}(J_{AB}) \mid M(J) = 1, M(A) = 0, M(B) = 0)$	<b>0.8240</b>
	$TC(T_{JB}(J_{AB}) \mid M(J) = 0, M(A) = 1, M(B) = 0)$	0.8168
	$TC(T_{JB}(J_{AB}) \mid M(J) = 0, M(A) = 0, M(B) = 1)$	0.8193
BLOCK 2		
MAPK8- MAPK8IP3	$TC(T_{JA}(J_{AB}) \mid M(J) = 1, M(A) = 1, M(B) = 0)$	0.1609
	$TC(T_{JA}(J_{AB}) \mid M(J) = 1, M(A) = 0, M(B) = 1)$	0.1617
	$TC(T_{JA}(J_{AB}) \mid M(J) = 0, M(A) = 1, M(B) = 1)$	0.1595
	$TC(T_{JB}(J_{AB}) \mid M(J) = 1, M(A) = 1, M(B) = 0)$	0.7913

MAPK8- MAPK8IP1	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 0, M(\mathbf{B}) = 1)$	<b>0.7952</b>
	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 0, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.7842
BLOCK 3		
MAPK8- MAPK8IP3	$TC(T_{JA}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.0747
MAPK8- MAPK8IP1	$TC(T_{JB}(\mathbf{J}_{AB}) \mid M(\mathbf{J}) = 1, M(\mathbf{A}) = 1, M(\mathbf{B}) = 1)$	0.3672