Automatic Context-Specific Subnetwork Discovery from Large Interaction Networks (Supporting Information) Ashis Saha, Aik Choon Tan, Jaewoo Kang

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S1. Estimated t-score

The Welch's t-test is a widely used metric for measuring the differential expression of a probe or gene (see Eq. S1).

$$t = \frac{\bar{X}_{+} - \bar{X}_{-}}{\sqrt{\frac{\sigma_{+}^{2}}{n_{+}} + \frac{\sigma_{-}^{2}}{n_{-}}}}$$
(S1)

where \bar{X}_+ and \bar{X}_- are the mean expressions, σ_+ and σ_- are the standard deviations, and n_+ and $n_$ are the number of samples of positive and negative classes, respectively. The higher |t| is, the higher the differential power. We use a slightly modified version of the t-test to avoid the noise of the microarray data. We use the median instead of the mean, and we estimate the standard deviation from the interquartile range (IQR) which is defined as the difference between the upper and lower quantiles. The IQR contains 50% of the data within $\frac{1}{2}IQR$ of the median. Our estimation comes from the *empirical rule* - about 68.2% of the values of a normal distribution lie within 1 standard deviation of the mean. The estimated standard deviation ($\hat{\sigma}$) is given by Eq. S2,

$$\hat{\sigma} = \frac{1}{2} \cdot IQR \cdot \frac{68.2}{50} \tag{S2}$$

So, our estimated t-test score (\hat{t}) is given by Eq. S3.

$$\hat{t} = \frac{\tilde{X}_{+} - \tilde{X}_{-}}{\sqrt{\frac{\hat{\sigma}_{+}^{2}}{n_{+}} + \frac{\hat{\sigma}_{-}^{2}}{n_{-}}}}$$
(S3)

where \tilde{X}_+ and \tilde{X}_- are the median expressions, $\hat{\sigma}_+$ and $\hat{\sigma}_-$ are the estimated standard deviations, and n_+ and n_- are the number of samples of positive and negative classes, respectively. The higher $|\hat{t}|$ is, the higher the differential power. We sort the probes of each MIS according to the absolute value of the estimated t-scores $(|\hat{t}|)$ in decreasing order, and select the top five probes as the representative probeset for the corresponding MIS.

S2. Binary Vote

Binary voting is applied when the voting weights for both classes become equal, which would be very infrequent. In the binary voting system, each top MIS casts a vote in favor of either the positive or negative class, i.e., the voting weight for each class will be either 1 or 0. Comparable to weighted voting, which was described in the main paper, binary voting for a new sample is also determined from the closest cluster. The majority class in the closest cluster gets the total vote (weight=1). If $\hat{P}_c > \hat{N}_c$, then $W_i(positive) = 1$ and $W_i(negative) = 0$. Similarly, if $\hat{P}_c < \hat{N}_c$, then $W_i(positive) = 0$ and $W_i(negative) = 1$. If $\hat{P}_c = \hat{N}_c$, the voting weight is determined in the same way, from the normalized number of positive and negative samples in the next closest cluster from x_{new} , and so on. If T, the number of voting MISs, is odd, then $W(positive) = \sum_{i=1}^{T} W_i(positive)$ and $W(negative) = \sum_{i=1}^{T} W_i(negative)$ in binary voting will never be equal. If W(positive) > W(negative), the class, $binary(x_{new})$, predicted from the binary voting is positive; otherwise, it is negative.

$$binary(x_{new}) = \begin{cases} positive & \text{if } W(positive) > W(negative) \\ negative & \text{otherwise} \end{cases}$$
(S4)

S3. Dataset Download Sources

Table S1.	Dataset	Download	Sources
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Dataset Name	Download Source
Leukemia	http://www.broadinstitute.org/cgi-bin/cancer/publications/pub_paper.cgi?
	$mode=view\&paper_id=43$
CNS	http://www.broadinstitute.org/mpr/CNS/
DLBCL	http://www.broadinstitute.org/mpr/lymphoma/
Prostate1	http://www.broadinstitute.org/cgi-bin/cancer/publications/pub_paper.cgi?
	$mode=view\&paper_id=75$
Prostate3	http://www.gnf.org/cancer/prostate (We found the original link broken on 15th
	November 2013. However, an alternative source is available - http://datam.i2r.a-
	star.edu.sg/datasets/krbd/ProstateCancer/ProstateCancer.html.)
Lung	http://datam.i2r.a-star.edu.sg/datasets/krbd/LungCancer/LungCancer-
	Harvard2.html
GCM	http://www.broadinstitute.org/cgi-bin/cancer/publications/pub_paper.cgi?
	mode=view&paper_id=61

S4. An Experiment with the appropriate range

We set the appropriate range, [minRange, maxRange], to generate the molecular interaction subnetworks. We experimented with different ranges and chose the optimal range producing the highest LOOCV accuracy over the datasets. Initially, we set minRange = 3, 5, 7 and maxRange = 15, 20, 25 for KEGG, and minRange = 5, 7, 10 and maxRange = 15, 20, 25 for STRING. Later, we expanded the range list based on the results observed. The results of the MISs with different appropriate ranges using KEGG and STRING are shown in Table S2 and S3, respectively.

Appro. Range	Leu- kemia	CNS	DLBCL	Pros- tate1	Pros- tate3	Lung	GCM	Average
3-15	98.6	82.4	93.5	89.2	100.0	99.5	85.4	92.7
3-20	98.6	73.5	94.8	88.2	100.0	99.5	83.6	91.2
3 - 25	97.2	82.4	94.8	90.2	100.0	99.5	83.9	92.6
5 - 10	97.2	82.4	94.8	91.2	100.0	99.5	84.6	92.8
5 - 15	98.6	85.3	93.5	90.2	100.0	99.5	85.0	93.2
5 - 20	98.6	70.6	94.8	88.2	100.0	99.5	83.6	90.8
5 - 25	97.2	82.4	94.8	90.2	100.0	99.5	83.9	92.6
5 - 30	98.6	82.4	94.8	89.2	100.0	99.5	83.9	92.6
7 - 15	98.6	76.5	96.1	88.2	100.0	99.5	84.6	91.9
7-20	97.2	82.4	94.8	87.3	100.0	99.5	83.6	92.1
7-25	97.2	85.3	94.8	88.2	100.0	99.5	83.6	92.7

Table S2. LOOCV accuracy (%) with different appropriate ranges from KEGG^{*}

'Appro. Range' denotes *appropriate range*. * The optimal appropriate range producing the highest average LOOCV accuracy is shown in **bold** font.

Appro. Range	Leu- kemia	CNS	DLBCL	Pros- tate1	Pros- tate3	Lung	GCM	Average
5-10	97.2	82.4	94.8	91.2	100.0	81.4	98.9	92.3
5 - 15	94.4	85.3	93.5	88.2	100.0	83.6	98.9	92.0
5 - 20	97.2	76.5	89.6	91.2	100.0	82.9	99.5	91.0
5-25	95.8	88.2	94.8	90.2	97.0	84.6	98.3	92.7
5 - 30	97.2	88.2	88.3	91.2	100.0	84.3	98.9	92.6
7 - 15	98.6	76.5	94.8	88.2	97.0	98.3	83.6	91.0
7-20	98.6	76.5	92.2	89.2	100.0	98.9	83.9	91.3
7-25	94.4	82.4	88.3	89.2	97.0	98.3	84.6	90.6
7-30	95.8	82.4	92.2	91.2	100.0	99.5	84.3	92.2
10-20	95.8	79.4	93.5	89.2	100.0	98.9	83.6	91.5
10-25	97.2	79.4	88.3	91.2	100.0	98.3	82.9	91.0
10-30	97.2	79.4	94.8	91.2	100.0	98.9	83.9	92.2

Table S3. LOOCV accuracy (%) with different appropriate ranges from $STRING^*$

'Appro. Range' denotes *appropriate range*. * The optimal appropriate range producing the highest average LOOCV accuracy is shown in **bold** font.

S5. Algorithm Illustration



Figure S1. An illustration of the MIS generation. Let us consider one example of a connected molecular interaction network (MIS) and its community dendrogram as shown in the figure. Let the appropriate range be [5,10]. The size (the total number of leaf nodes) of the dendrogram is 24. As it is greater than the maxRange (10), we divide the dendrogram by removing edge E1 so we are left with two dendrograms (A-Q and R-X). The right dendrogram's (R-X) size is 7 ($5 \le 7 \le 10$), so we take it as an appropriate community (C_3). However, because the left dendrogram's (A-Q) size is above 10, we divide it again by removing edge E_2 . We have to further divide the dendrogram by removing edge E_3 . Thus we get four parts of the original community dendrogram – C_1, C_2, X_1 , and C_3 . Three of their sizes fall within the appropriate range [5,10] ($C_1, C_2, \text{ and } C_3$), so we take them as appropriate communities. However, because X_1 's size is less than 5, we discard it. Now, we shall assign the nodes in X_1 – N, O, P, and Q – individually to their closest communities from the original network. P is 1-hop away from C_1 , so P is merged with C_1 ; N and O are 1-hop away from C_2 , so they are merged with C_2 . In the next iteration, Q is merged with its closest community, C_2 . Thus, we get three MISs – C_1 (A,B,C,D,E,F,P), C_2 (G,H,I,J,K,L,M,N,O,Q), and C_3 (R,S,T,U,V,W,X).

S6. Irregular Network Topology



Figure S2. Topology of two out-of-size MISs generated with an appropriate range of 5-15 from STRING network. A) MIS with 46 nodes has a star topology. B) MIS with 55 nodes is too dense.

S7. Representative probesets of the top MISs

Table S4. Representative probesets of the top MISs from KEGG. MISs generated from KEGG have been ranked by COSSY using all the samples in a dataset, and the representative probesets of the top T MISs have been reported where T is the number of MISs to vote that produced the highest LOOCV accuracy. Each probeset's ID is followed by the corresponding gene symbol in parentheses.

Dataset	T	Rank	Representative probeset of MIS [probeid(gene symb	ol)]
Leukemia	15	1	D87459_at(WASF1), M19283_at(ACTG1),	L33075_at(IQGAP1),
			X74008_at(PPP1CC), X95735_at(ZYX)	
		2	X64072_s_at(ITGB2), M15395_at(ITGB2),	M81695_s_at(ITGAX),
			X80907_at(PIK3R2), X51521_at(EZR)	
		3	D16469_at(ATP6AP1), L09717_at(LAMP2),	M63138_at(CTSD),
			S46622_at(PPP3CC), Z46973_at(PIK3C3)	
		4	M16038_at(LYN), U14588_at(PXN),	X80907_at(PIK3R2),
			X04526_at(GNB1), X77748_at(GRM3)	
		5	U46499_at(MGST1), U77604_at(MGST2),	Y00433_at(GPX1),
			U21689_at(GSTP1), M81118_at(ADH5)	
		6	M22898_at(TP53), U22376_cds2_s_at(MYB),	M65214_s_at(TCF3),
			M38449_s_at(TGFB1), M31523_at(TCF3)	
		7	U14588_at(PXN), M24283_at(ICAM1),	X06318_at(PRKCB),
			S72869_at(CCDC6), X77548_at(NCOA4)	
		8	M16038_at(LYN), M64595_at(RAC2),	M89957_at(CD79B),
			U05259_rna1_at(CD79A), X16316_at(VAV1)	
		9	U29656_at(NME3), U52427_rna1_at(POLR2G),	X15357_at(NPR1),
			X66533_at(GUCY1B3), Y07604_at(NME4)	
		10	M63167_at(AKT1), X80907_at(PIK3R2), M182	55_cds2_s_at(PRKCB),
			M84371_rna1_s_at(CD19), X06318_at(PRKCB)	
		11	$D10495_at(PRKCD),$ $M14676_at(FYN),$	M16038_at(LYN),
			M33195_at(FCER1G), X06318_at(PRKCB)	
		12	$L09708_{at}(C2), M84526_{at}(CFD),$	X05309_at(CR1),
			$M13690_s_at(SERPING1), U28488_s_at(C3AR1)$	
		13	$M27281_at(VEGFA), U09578_at(MAPKAPK3),$	U14588_at(PXN),
			$X80907_at(PIK3R2), Z29090_at(PIK3CA)$	
		14	$L05147_{at}(DUSP3), M22898_{at}(TP53), M2289_{at}(TP53), M228_{at}(TP53), M228_{at}(TP53),$	$X66867_{cds1_{at}}(MAX),$
			$L08895_at(MEF2C), D11327_s_at(PTPN7)$	
		15	$M95678_at(PLCB2), \qquad U03090_at(PLA2G5),$	$X04828_at(GNAI2),$
			$U38545_at(PLD1), X51521_at(EZR)$	
CNS	7	1	$J04177_at(COL11A1), \qquad M55210_at(LAMC1),$	$Z26653_at(LAMA2),$
			$Z74616_s_at(COL1A2), X79683_s_at(LAMB2)$	
		2	$M81933_at(CDC25A), \qquad U31814_at(HDAC2),$	$U18422_at(TFDP2),$
			$L40386_s_at(TFDP2), S49592_s_at(E2F1)$	
		3	$M55210_{at}(LAMC1), X79683_s_at(LAMB2),$	$X07979_at(ITGB1),$
			$U04806_s_at(FLT3LG), L32137_at(COMP)$	
		4	J04111_at(JUN), M92287_at(CCND3),	$L00058_{-}at(MYC),$
			$M25269_at(ELK1), M14745_at(BCL2)$	
		5	L36033_at(CXCL12), U09303_at(EFNB1),	$U27655_at(RGS3),$
			$U81262_at(EFNB2), L06797_s_at(CXCR4)$	

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$\begin{array}{cccccccc} 2 & 34915_at(SLC8A1), & 40435_at(SLC25A6), & 40436_g_at(SLC25A6), \\ & 39123_s_at(TRPC1), & 39124_r_at(TRPC1) \\ 3 & 39775_at(SERPING1), & 40766_at(C4A), & 32249_at(CFHR1), \\ & & 38441_s_at(CD46), & 40282_s_at(CFD) \\ 4 & 41867_at(CREB3L1), & 33134_at(ADCY3), & 1909_at(BCL2), \end{array}$
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4 $41867_{at}(CREB3L1),$ $33134_{at}(ADCY3),$ $1909_{at}(BCL2),$
$41288_at(CALM3), 364_s_at(PLCB3)$
5 $39939_{at}(COL4A6), 32667_{at}(COL4A5), 41755_{at}(COBLL1),$
$37912_{at}(TRAF4), 38042_{at}(PRKCA)$
$6 41867_{at}(CREB3L1), 37733_{at}(MAPK14), 38042_{at}(PRKCA),$
$41288_{at}(CALM3), 1708_{at}(MAPK10)$
$7 = 31824_at(ME1), 35216_at(ME3), 33819_at(LDHB), 41485_at(LDHA),$
837 s.at(ME1)
8 $32(4(_at(ALDH2), 3(707_at(ADH5), 3(708_r_at(ADH5), 2000 + (ALD141)), 3(708_r_at(ADH5), 3(708_r_at($
$30080_at(ALDH1A3), 38/80_at(AKK1A1)$
9 37186 -s_at(ABP1), 41772 _at(MAOA), 32747 _at(ALDH2),
$30132_at(ALDH(AI), 30080_at(ALDHIA3)$ 10 22710 + (LDCAT2) = 28262 + (MDCAT2) = 20206 + (LVDLA1)
$10 33710_{at}(LPOA13), 38202_{at}(MBOA12), 39390_{at}(LYPLA1), \\ 24707_{at}(DDAD2A) 29009_{at}(LDDA12)$
$\frac{34797}{40169} = \frac{34797}{40169} + \frac{30090}{40169} = \frac{30090}{40169} + \frac{30090}{4000} + \frac{3000}{4000} $
$11 40102_S_at(COM1), 40105_L_at(COM1), 105_at(TIID54), \\ 1767 = pt(TCFR2) = 24242 = pt(SDD1)$
$10735_at(10FD5), 54542_5_at(0111)$ $12 \qquad 30054 \text{ at}(CSTM4) = 33306 \text{ at}(CSTP1) = 1120 \text{ at}(CSTM3) = 820 \text{ at}(MCST2)$
556 s.st(CSTM4), 5550 at(CSTM5), 1120 at(CSTM5), 020 at(CSTM5), 1120 at(CSTM5), 020 at(CS
13 33094 g at(MVL6) 32755 at(ACTA2) 41288 at(CALM3)
38298 at(KCNMB1) 33134 at(ADCV3)
14 34138 at(GNAO1) 38042 at(PBKCA) 41288 at(CALM3)
1336 s at(PRKCB) 36918 at(GUCY1A3)
15 34637 f at(ADH1A), 38315 at(ALDH1A2), 40782 at(DHRS3)
37707 i.at(ADH5), 37708 r at(ADH5)
$40682_{at}(GYS2), 37221_{at}(PRKAR2B), 39366 at(PPP1R3C).$
37725_at(PPP1CC), 41288_at(CALM3)

		17	AFFX-HUMGAPDH/M33197_M_at(GAPDH), 33819_at(LDHB),
			40193_at(ENO2), 41485_at(LDHA), 2035_s_at(ENO1)
		18	36917_at(LAMA2), 36929_at(LAMB3), 41755_at(COBLL1),
			33410_at(ITGA6), 37671_at(LAMA4)
		19	34118_at(ATP1B2), 32225_at(ATP1A1), 34377_at(ATP1A2),
			39356_at(NEDD4L), 34915_at(SLC8A1)
		20	1767_s_at(TGFB3), 1735_g_at(TGFB3), 1262_s_at(TGFB2),
		-	41140 at (IFNGR2), 1038 s at (IFNGR1)
		21	1767 s at(TGFB3), $1622 at(MAP2K3), $ $857 at(PPM1A),$
			37408 at(MBC2) 806 at(PLK3)
		22	36686 at(ALDH1A3) $37708 r at(ADH5)$ $1120 at(GSTM3)$
			556 s at(GSTM4) 40071 at(CVP1B1)
		23	41385 at(EPB41L3) $38042 at(PBKCA)$ $1336 s at(PBKCB)$
		20	208 st(CTNNA2) 36174 st(MARCKSL1)
		24	35640 st(CDO1) = 33810 st(LDHR) = 36123 st(TST) = 36124 st(MPST)
		24	$55045_{at}(DD1), 55015_{at}(DD1D), 50125_{at}(151), 50124_{at}(M151), 41485_{at}(DD1A)$
		25	40435 st(SLC25A6) = 40436 st(SLC25A6) = 35818 st(CVCS)
		20	$40450_gat(5L025A0),$ $40450_gat(5L025A0),$ $55010_at(0105),$
		26	$400_at(CASE9), 32000_at(ISEO)$ $41499_at(DDVC)=27102_at(MID2650)=27251_at(IIDD1)=22015_at(IIMDC)$
		20	41422-at(DP15), $3/195$ -at(MIR5056), $5/551$ -at(UPP1), 55015 -at(UMP5), 27202 at(CES1)
		97	37203 = al(OE31) 2414t = t(TIDt) = 26942 = t(TIDt) = 40210 = t(TIDt) = 27720 = t(IICDDt)
		21	$54145_at(1LR0), 50245_at(1LR1), 40510_at(1LR2), 57720_at(RSPD1),$
		00	$\frac{41010 \text{ s}_{\text{a}} (\text{nDFA9})}{27000 \text{ s}_{\text{a}} (\text{ATD})} = \frac{26047 \text{ s}_{\text{a}} (\text{DELA})}{1707 \text{ s}_{\text{a}} (\text{TCED9})} = \frac{1007 \text{ s}_{\text{a}} (\text{DELA})}{1007 \text{ s}_{\text{a}} (\text{DELA})}$
		28	$3/229_at(AIR), 30040_at(RELA), 1/07_S_at(IGFB3), 1290_at(RELA), 1100_4(IDAK1)$
		00	$\frac{1100_{at}(IRAK1)}{1661 + (VLV2)} = \frac{1614}{1614} + \frac{1714}{1614} + \frac{1714}$
		29	$1001_1_at(KLK3), 1013_at(KLK3), 1014_g_at(KLK3), 442_at(MIR3002), 1004_+(ICE0)$
	0	1	$\frac{1004\text{-}at(\text{IGF2})}{20000} + (CTU) = 20010 + (IDUD) = 25242 + (COTT1) = 26124 + (MDCTT)$
Prostate3	3	1	$32902_at(C1H), 33819_at(LDHB), 35343_at(GO11), 30124_at(MPS1),$
		0	$41480_at(LDHA)$
		2	$40372_at(PNLIPRP1),$ $38003_s_at(DGKZ),$ $39044_s_at(DGKD),$
		9	$33802_at(PPAP2B), 38098_at(LPIN1)$ $25110_+(LCATT) = 22710_+(LPCATT2) = 25000_+(CUUZD)$
		3	$35118_at(LCA1), 33710_at(LPCA13), 35228_at(CHKB),$
			$\frac{39396_{at}(LYPLAI), 41176_{at}(LPCATI)}{21000_{at}(LPCATI)} = \frac{39396_{at}(LYPLAI), 41176_{at}(LPCATI)}{21000_{at}(LPCATI)} = \frac{39396_{at}(LPCATI)}{21000_{at}(LPCATI)} = \frac{39396_{at}(LPCATI)}{21000_{at}(LPCATI)} = \frac{39396_{at}(LPCATI)}{21000_{at}(LPCATI)} = \frac{39396_{at}(LPCATI)}{21000_{at}(LPCATI)} = \frac{39396_{at}(LPCATI)}{2100_{at}(LPCATI)} = \frac$
Lung	7	1	$34664_at(FCGR2B), 35822_at(CFB), 39409_at(CIR), 40496_at(CIS),$
		2	$40766_{at}(C4A)$
		2	$33904_{at}(CLDN3), 35276_{at}(CLDN4), 35630_{at}(LLGL2),$
			38482_at(CLDN7), 40973_at(PARD3)
		3	35330_at(FLNC), 36354_at(TNN), 36917_at(LAMA2), 36929_at(LAMB3),
			881_at(ITGB6)
		4	$1810_s_at(PRKCD), \qquad 32046_at(PRKCD), \qquad 33833_at(SPTAN1),$
			767_at(MYH11), 774_g_at(MYH11)
		5	$1810_s_at(PRKCD), \qquad 32046_at(PRKCD), \qquad 41645_at(PLA2G6),$
			33245_at(MAPK13), 33804_at(PTK2B)
		6	1108_s_at(EPHA1), 2039_s_at(FYN), 34329_at(PAK2), 39930_at(EPHB6),
			$40425_at(EFNA1)$
		7	1810_s_at(PRKCD), 32046_at(PRKCD), 33162_at(INSR), 41049_at(IRS1),
			851_s_at(IRS1)
GCM	$2\overline{3}$	1	$X04828_at(GNAI2), X70297_at(CHRNA7), Y10141_s_at(SLC6A3),$
			AA278775_at(APLP2), RC_AA459690_s_at(MPC1)

2	M58603_at(NFKB1), \$75881_c_at(MVB11)_H30	$U33053_at(PKN1),$	U70451_at(MYD88),
3	L76191_at(IRAK1), M1	1717_rna1_at(HSPA1B), $X51757_{-}at(HSPA6)$,
4	L11285_at(MAP2K2), X04828 at(GNAI2) BC A	M21574_at(PDGFRA A147646 s at(METTL)), $X02751_{at}(NRAS)$,
5	D00632_at(GPX3), Y00433 2(CYP2B6), U78310 at(PI	B_at(GPX1), L16991_at ES1)	-2(CYP2C9), M30185_at-
6	D43767_at(CCL17), X55989 rna1 at(ECRP). U	U85767_at(CCL23),	X04828_at(GNAI2),
7	M21056_at(PLA2G1B), U79271 at(AKT3) BC AA	$M34667_{at}(PLCG1),$ A609519 at(MSRA)	U61538_at(CHP1),
8	$L11005_at(AOX1), U89BC AA426643 at(BSL1D1)$	$9606_{at}(PDXK), RC$	C_AA400074_at(DOCK8),
9	$M22995_{at}(RAP1A),$ $M24485_{S} at(CSTP1)_W6$	$M34667_{at}(PLCG1),$ 9543 at(SCML1)	Z15114_at(PRKCG),
10	$M24665_at(05111), woL01087_at(PRKCQ), IM24667_at(PLCC1)_PC_A$	$11285_at(MAP2K2),$	M34353_s_at(ROS1),
11	X55733_at(EIF4B), M BC_AA400766_at(KIAA05	$33666_at(PSG6),$ 56) BC AA416601 s a	M2) M61733_at-2(RPS6KB1), t(ULK3)
12	X81817_at(BCAP31), T69384 at(PER1), RC AA	Z12830_at(SSR1), 443342 s at(TMEM20)	AA093396_at(PHGDH),
13	$M21186_at(CYBA),$ M30448 s at(FBL) U0587	$M55067_at(NCF1B),$ 5 at(IFNGB2)	X77094_at(NCF4),
14	$M16038_{at}(LYN), M$ U78027 ma4 at(BTK) X0	$A34667_{at}(PLCG1),$	U20158_at(LCP2),
15	L76191_at(IRAK1), US	91616_{at} (NFKBIE), CDIR) BC AA261007	X69550_at(ARHGDIA),
16	M11717_rna1_at(HSPA1B)	$, X51757_{at}(HSPA6), $	$AA465601_at(ARFIP1),$
17	A15675_at(A172), AA422. D31766_at(GNPDA1), RC_AA210695_at(PARP14 RC_AA449479 at(BZW2)	RC.), RC	AA035284_at(PDZRN3), C_AA429655_at(TPCN1),
18	$U10473$ _s_at(B4GALT1), U BC AA443841 at(SPRY2)	U28014_at(CASP4), R0 R93273 s at(UXS1)	C_AA429655_at(TPCN1),
19	$X16663_{at}(HCLS1), X$	$01677_{f_at}(GAPDH),$	V00565_s_at-2(ACTB), $MSRA$)
20	U67733_at(PDE2A), Y00 RC_AA609873_at(NECAB	24), RC_AA005515_at(A))486_rna1_at(APRT), 3), M91029_cds2_at(A)	AA318315_at(C6orf106), (PD2 $)$
21	L11285_at(MAP2K2), X02751 at(NBAS) $AA278$	M22995_at(RAP1A),	$M95712_{at}(BRAF),$
22	$M21056_{at}(PLA2G1B),$ $BC \wedge \Lambda 103204 \text{ at}(SOBBS)$	$X04828_{at}(GNAI2),$ $M16038_{at}(IVN)$	$F07806_at(GNAZ),$
23	M95740_at(IDUA), U0373 L33798_at(CACNA1S), RC	$5_{\text{f}} \text{(MAGEA6)}, \text{RC}$ $2_{\text{A}} \text{A459690} \text{(s}_{\text{at}} (\text{MPC})$	_AA193204_at(SORBS2), 1)

Table S5. Representative probesets of the top MISs from STRING. MISs generated from STRING have been ranked by COSSY using all the samples in a dataset, and the representative probesets of the top T MISs have been reported where T is the number of MISs to vote that produced the highest LOOCV accuracy. Each probeset's ID is followed by the corresponding gene symbol in parentheses.

Dataset	Т	Rank	Representative probeset of MIS [probeid(gene symbol)]
Leukemia	5	1	L21954_at(TSPO), M54992_at(CD72), U05259_rna1_at(CD79A),
			X07743_at(PLEK), X97267_rna1_s_at(PTPRCAP)
		2	J03473_at(PARP1), U25435_at(CTCF), X99585_at(SUMO2),
			Z15115_at(TOP2B), M27504_s_at(TOP2B)
		3	X92106_at(BLMH), Z23064_at(SNORD61), Z93784_at(ATXN10),
			M21535_at(ERG), L09209_s_at(APLP2)
		4	L09717_at(LAMP2), M22960_at(CTSA), M74524_at(UBE2A),
			U76992_at(HTATSF1), S79873_s_at(LAMP2)
		5	D87465_at(SPOCK2), D83646_at(MMP16), U14394_at(TIMP3),
			D50477_s_at(MMP16), M32304_s_at(TIMP2)
CNS	5	1	L27560_at(IGFBP5), L42450_at(PDK1), M14745_at(BCL2),
			M65062_at(IGFBP5), M62782_s_at(IGFBP5)
		2	$X04143_at(BGLAP), Z74615_at(COL1A1), D13666_s_at(POSTN),$
			$Z74616_s_at(COL1A2), M55998_s_at(COL1A1)$
		3	$D14838_at(FGF9), L40027_at(GSK3A), M93650_at(PAX6),$
			U07223_at(CHN2), X14474_at(MAPT)
		4	$L06139_at(TEK), M55593_at(MMP2), U89336_cds3_at(AGER),$
			X57766_at(MMP11), U31903_s_at(ATF6B)
		5	M19720_rna2_at(MYCL1), M95929_at(SFXN3), U22377_at(RLF),
			L00058_at(MYC), L07648_at(MXI1)
DLBCL	17	1	$D78134_at(CIRBP), U23803_at(HNRNPA0), M60784_s_at(SNRPA),$
			$X15729_s_at(DDX5), X74874_rna1_s_at(POLR2A)$
		2	J04615_at(SNURF), U08377_at(SFSWAP), U81001_at(SNURF),
			$Z69915_at(RBMXL1), X17567_s_at(SNRPB)$
		3	$D21063_at(MCM2), D80008_at(GINS1), U77949_at(CDC6),$
			$U37426_at(KIF11), X85137_s_at(KIF11)$
		4	$J03909_{at}(IFI30), U15590_{at}(HSPB3), X03934_{at}(CD3D),$
			$X04145_at(CD3G), M23323_s_at(CD3E)$
		5	$D38553_at(NCAPH), D79997_at(MELK), M74558_at(STIL),$
			$X51688_at(CCNA2), X67155_at(KIF23)$
		6	$D87292_at(TST), X02152_at(LDHA), X05409_at(ALDH2),$
			$Z22548_at(PRDX2), M34338_s_at(SRM)$
		7	$J04988_at(HSP90AB1), U12595_at(TRAP1), U24169_at(AIMP2),$
			U41387_at(DDX21), X75861_at(TMBIM6)
		8	$D31890_at(KARS), M63180_at(TARS), U07424_at(FARSA),$
			$U09510_s_at(GARS), U09587_at(GARS)$
		9	$U80040_{at}(ACO2), V00572_{at}(PGK1), X07834_{at}(SOD2),$
			$Z68129_cds1_at(IDH3G), X65965_s_at(SOD2)$
		10	AB003177_at(PSMD9), D26599_at(PSMB2), D38047_at(PSMD8),
			D78151_at(PSMD2), X71874_cds1_at(PSMB10)
		11	$K02268_at(PDYN), L42324_at(GPR18), U94320_at(NPY5R),$
			L07615_at(NPY1R), U28488_s_at(C3AR1)

		12	D64142_at(H1FX), D83243_at(NPAT), L29008_at(SORD),
			M68520_at(CDK2), X03473_at(H1F0)
		13	M33195_at(FCER1G), M37033_at(CD53), M60830_at(EVI2B),
			X62466_at(CD52), U19557_s_at(SERPINB4)
		14	D90084_at(PDHA1), D90086_at(PDHB), U46692_rna1_at(CSTB),
			X56494_at(PKM), L12760_s_at(PCK1)
		15	D21262_at(NOLC1), D25218_at(RRS1), J03798_at(SNRPD1),
			U10323_at(ILF2), X70683_at(SOX4)
		16	D00596_at(TYMS). D25547_at(PCMT1). L16991_at(DTYMK).
		-	X53793_at(PAICS), X59543_at(RRM1)
		17	D14811_at(MAD2L1BP), M86699_at(TTK), U65410_at(MAD2L1),
			U96131_at(TRIP13), L40384_s_at(TRIP13)
Prostate1	17	1	<u>39640_at(GFPT2)</u> , <u>39729_at(PRDX2)</u> , <u>32747_at(ALDH2)</u> ,
			37720_at(HSPD1), 41485_at(LDHA)
		2	34602 at(FCN2), $37085 g at(LYZL6)$, $39590 at(APBA2)$.
		-	40778 at(HSD17B10), 35277 at(SPON1)
		3	41115 s at(BAIAP3) $36943 r at(PLAGL1)$ $38406 f at(PTGDS)$
		0	828 at (PTGER2) 216 at (PTGDS)
		4	39939 at(COL4A6) $32667 at(COL4A5)$ $37890 at(CD47)$
		1	34391 at(IGBP1) 753 $at(NID2)$
		5	35497 at(TSPAN2) $35631 at(POLR2H)$ $33415 at(NME2)$
		0	1980 s at(NME2), 1248 at(POLB2H)
		6	30701 at(PEC3) $30755 at(XBP1)$ $30756 ast(XBP1)$
		0	40856 at(SERPINE1) = 38108 at(FCEI8)
		7	$40000_at(BERTINTT), 50100_at(EGFL0)$ 30252 at(HSDF1) = 22004 at(CIDN2) = 24248 at(SDINT2) = 1512 at(KIK2)
		1	$59555_at(1151_51), 55504_at(OLDIV5), 54546_at(51_1112), 1515_at(KLK5), 575 a at(FDCAM)$
		0	41697 st(CDE9) = 22051 st(ALC9) = 26807 st(MLC1) = 20057 st(DDT)
		0	$41027_{at}(DT2), 52051_{at}(ALG0), 50057_{at}(MLC1), 50057_{at}(DT1), 28050 a st(DTT)$
		0	$30059_{2}at(DTT)$ $30054_{0}at(CSTM4)_{1980_{0}at}(CSTM5)_{1190_{0}at}(CSTM3)_{890_{0}at}(MCST9)$
		9	556 s. st(CSTM4), $1209-at(GSTM5)$, $1120-at(GSTM5)$, $620-at(MGST2)$, $556 s. st(CSTM4)$
		10	$38050 \text{ s}_{2}(\text{MMP23R}) = 35306 \text{ s}_{1}(\text{DHY15}) = 35766 \text{ s}_{1}(\text{KRT18})$
		10	$55950 \pm at(MM25D), 55500 \pm at(DMA15), 55700 \pm at(M116),$
		11	$41200_{at}(\text{AIMI } 2), 1135_{at}(\text{DNORA40})$ 22228 at (HEC1) 25218 at (DDCD10) 25605 at (IVST) 25606 a at (IVST)
		11	$35525_{at}(1151), 55215_{at}(11510), 55555_{at}(1151), 5555_{at}(1151), 5555_{at}($
		19	$\frac{30004_{a0}(\text{KD}11)}{20008_{a0} + (\text{KLPC}3)} = \frac{30007_{a0} + (\text{KLPC}1)}{20007_{a0} + (\text{KLPC}1)} = \frac{40004_{a0} + (\text{STAC})}{40004_{a0} + (\text{STAC})}$
		12	$52200 \pm at(MLRO5), 52297 \pm at(MLRO1), 40024 \pm at(STRO), 40775 \pm t(TTM2A) 41927 \pm t(HLAA)$
		19	$40775_{at}(11M2A), 41257_{at}(11LA-A)$ 26259 $at(CTE1)$ 20215 $at(ANCDT1)$ 22640 $at(ICAM1)$
		15	$50252_at(OIFI), 59515_at(ANGFII), 52040_at(IOAMI),$ 26020 $at(CDM6A)$ 1020 $at(ANCDT1)$
		14	$30939_{\text{al}}(\text{GFMOR}), 1929_{\text{al}}(\text{ANGF11})$ $25071_{\text{al}} * (\text{CMDS}), 25914_{\text{al}} * (\text{UCDH}), 26515_{\text{al}} * (\text{CMF}), 26026_{\text{al}} * (\text{TSTA2})$
		14	50071_{S} at (GND5), $50214_{\text{AU}}(\text{UGDH})$, $50510_{\text{AU}}(\text{GNE})$, $50950_{\text{AU}}(151A5)$,
		15	$41242_{all}(\text{OAF}1)$ $26790_{at}(\text{OAF}1) = 26600_{at}(\text{ND}2\text{O}1) = 27659_{at}(\text{OAF}2) = 1509_{at}(\text{OAF}2)$
		10	$50760_{at}(CLU), 50090_{at}(MASOI), 57056_{at}(GASO), 1596_{g}_{at}(GASO), 1290_{s}_{t}(MME)$
		16	$\frac{1309}{24608} \approx \frac{1}{2} \left(\frac{1}{1000} \frac{1}{1000} \right) = \frac{1}{2} \frac{1}{2} \frac{1}{1000} \frac{1}{1000} \approx \frac{1}{1000} $
		10	$34008_{at}(5NORD95), 34009_{at}(5NORD95), 37345_{at}(117R5), 20192 a at/(TDDC1) 20194 m at/(TDDC1)$
		17	$\frac{99129-5-at}{1 \text{ (I}))))))))))))))))))))))))))))))))))$
		11	$34735_{at}(nUUR1), 37270_{at}(IQGAP2), 38292_{at}(nUMER2),$
Drogtata?	F	1	$\frac{40012_{\text{au}}(\text{UR1}), 1041_{\text{au}}(\text{IQGAF}2)}{41640 \text{ st}(\text{VIDE1}), 24070 \text{ st}(\text{IDD2}), 20409 \text{ st}(\text{EIII.0}), 29726 \text{ st}(\text{WDD1})}$
r rostate3	9	T	$41040_{at}(11FF1)$, $34010_{at}(LDD3)$, $38422_{S}at(FHL2)$, $38130_{at}(WDR1)$, 22549 at (FHI 1)
		0	$\partial 2\partial 4 \Delta_{ab}(\Gamma\Pi LI)$ 27829 st(MMACHC) 41101 st(DALLD) 41105 st(LDD) 1829 st(MCC)
		2	31032 au(MINIAOHO), 41191_au(FALLD), 41192_at(LPP), 1832_at(MOC),
			$(94_at(P1PNb))$

		3	$41626_{at}(TIMELESS), \qquad 37646_{at}(POLD3), \qquad 35326_{at}(YIF1A),$
			$1470_{\text{at}}(\text{POLD2}), 860_{\text{at}}(\text{MSH2})$
		4	37809_at(HOXA9), 41388_at(MEIS2), 32063_at(PBX1), 40763_at(MEIS1),
			$33355_at(PBX1)$
		5	$40118_{at}(ZNF3),$ $33454_{at}(AGRN),$ $34377_{at}(ATP1A2),$
			$37669_s_at(ATP1B1), 39526_at(PAIP2B)$
Lung	5	1	1500_at(WT1), 34218_at(SPEG), 376_at(SEMA3C), 377_g_at(SEMA3C),
-			977_s_at(CDH1)
		2	1661_i_at(KLK3), 1662_r_at(KLK3), 33904_at(CLDN3), 38482_at(CLDN7),
			575_s_at(EPCAM)
		3	2056_at(FGFR1), 2057_g_at(FGFR1), 36522_at(CRTC1),
			39750_at(PARVA), 39930_at(EPHB6)
		4	1237_at(IER3), 33243_at(TNFAIP8), 33900_at(FSTL3),
			35694_at(MAP4K4), 37716_at(CD200)
		5	1564_at(AKT1), 1616_at(FGF9), 32260_at(PEA15), 36095_at(CLIP3),
			36418_at(PRICKLE3)
GCM	11	1	D84110_at(RBPMS), L40393_at(NUMB), R78309_at(ATXN1L),
			RC_AA280004_at(QKI), RC_AA291162_at(SPEN)
		2	X14850_at(H2AFX), Y10262_s_at(EYA3), AA252929_at(H2AFX),
			AA418662_at(RINT1), RC_AA599683_at(EYA3)
		3	X67337_at(CPSF6), X76770_at(PAPOLA), AA259021_s_at(MLLT6),
			RC_AA179826_at(TSEN15), RC_AA463934_at(SF3B4)
		4	L17131_rna1_at(HMGA1), U47054_at(ART3), AA044715_at(ZFR),
			RC_AA256263_at(HNRNPH3), RC_AA449974_at(SEPT4)
		5	AB000816_s_at(ARNTL), T69384_at(PER1), W69582_at(FBXW11),
			RC_AA481037_at(PER3), RC_AA488844_f_at(FBXL3)
		6	L34219_at(RLBP1), M35128_at(CHRM1), M21142_cds2_s_at(GNAS),
			AF007216_at(SLC4A4), RC_AA452263_at(GNA11)
		7	U33053_at(PKN1), Z80787_at(HIST4H4), AA018847_at(NLK),
			AA287291_at(IWS1), RC_AA194257_f_at(BRD1)
		8	Z97054_xpt2_at(HUWE1), AA278775_at(APLP2), AA477046_at(UBA6),
			RC_AA069456_at(PJA2), RC_AA402613_at(PELI3)
		9	U22055_at(SND1), AA028976_at(DLC1), RC_AA233257_at(TGFB1I1),
			RC_AA487576_at(SDPR), RC_AA496366_at(TNS1)
		10	D78134_at(CIRBP), L38696_at(RALY), U03891_at(APOBEC3B),
			X92715_at(ZNF74), M60784_s_at(SNRPA)
		11	U08815_at(SF3A3), U15782_at(CSTF3), X13482_at(SNRPA1),
			X16135_at(HNRNPL), H58970_at(CPSF2)