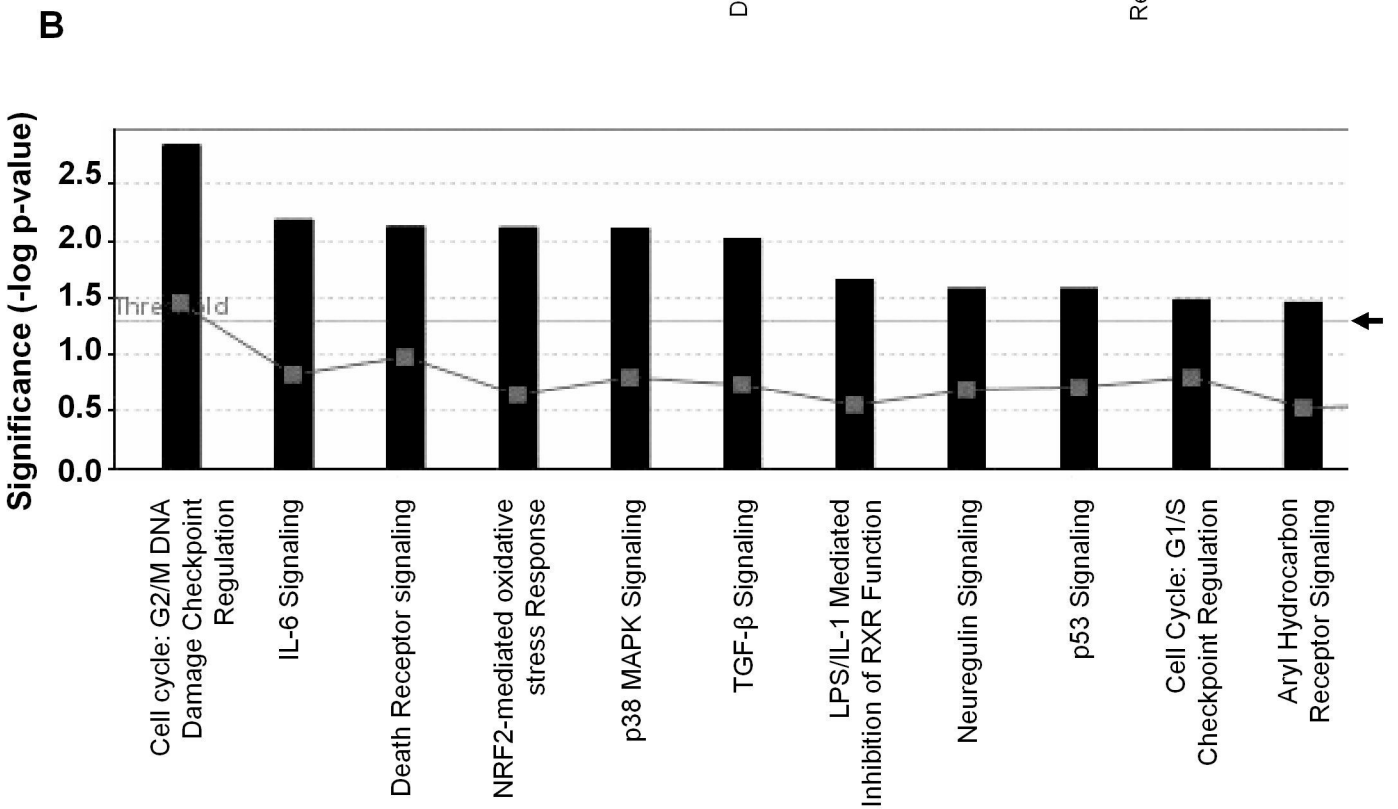
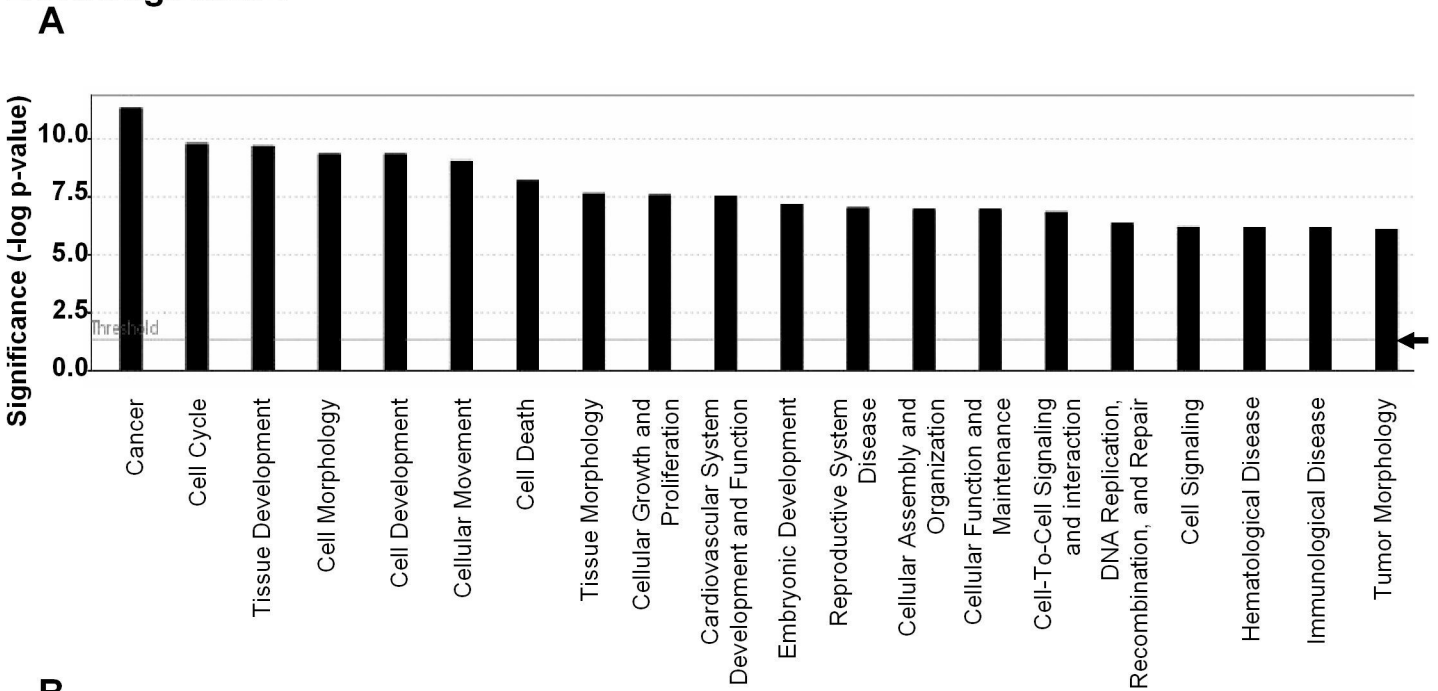


Type of file: figure

Label: Figures

Filename: sfig\_1.pdf

# Supplementary Figure 1. Diverse Transcriptional Effects of SMAD6 Downregulation



(A) The 20 most significant functional categories from Ingenuity Pathway Analysis (IPA). The significance threshold shown in arrow represents  $P = 0.05$ . The set of functions shown below represent  $P < 0.01$ . (B) Significant canonical pathways from IPA. The significance threshold shown in arrow represents  $P = 0.05$ . Closed markers show the ratio between all samples in each pathway.

Type of file: table

Label: Table

Filename: stab\_1-4.pdf

Supplementary Table 1. shRNA Sequence for *Smad6*

shRNA #1	5'-CCGGCGGCGACTTTGGCGAAGTCGTCTCGAGACGACTTCG CCAAAGTCGCCGTTTTT -3' (RHS3979-9586746)
shRNA #2	5'-CCGGCTTACACTGAAACGGAGGCTACTCGAGTAGCCTCCG TTTCAGTGTAAGTTTTT-3' (RHS3979-9586743)
shRNA #3	5'- CCGGGGATTCCCAGCAGCTCTTTGGCTCGAGCCAAGAGCT GCTGGGAATCCTTTTTG-3'

Supplementary Table 2. Expression of SAMD6 and clinical characteristics in non-small cell lung cancer.

<b>Staining Status</b>	<b>No. of Cases</b>	<b>SMAD6</b>	
		<b>+</b>	<b>-</b>
<b>Tumor Scored</b>	<b>242</b>	<b>122</b>	<b>120</b>
<b>Gender</b>	<b>214</b>		
<b>Male</b>		<b>73</b>	<b>79</b>
<b>Female</b>		<b>26</b>	<b>36</b>
<b>Tumor Type</b>	<b>240</b>		
<b>Adanocarcinoma</b>		<b>60</b>	<b>68</b>
<b>Squamous Cell Carcinima</b>		<b>62</b>	<b>52</b>
<b>Stage</b>	<b>178</b>		
<b>I</b>		<b>59</b>	<b>52</b>
<b>II</b>		<b>17</b>	<b>14</b>
<b>III</b>		<b>13</b>	<b>14</b>
<b>IV</b>		<b>4</b>	<b>5</b>

Supplementary Table 3. Upregulated genes by SMAD6 knockdown

Gene ID		Log <sub>2</sub> Ratio shRNA#1/M*	Log <sub>2</sub> Ratio shRNA#3/M*
Extracellular matrix			
NM_000138.1	Fibrillin 1 (Marfan syndrome) (FBN1)	2.86(±0.88)	2.10(±0.67)
NM_002423.2	Matrix metalloproteinase 7 (MMP-7)	1.09(±0.26)	5.15(±0.71)
NM_003255.2	Tissue inhibitor of metalloproteinase 2	1.08(±0.19)	2.36(±0.36)
NM_004353.1	Clade H, member 1 (SERPINH1)	1.95(±0.38)	1.85(±0.26)
Cytokine			
NM_000584.1	Interleukin 8 (IL8)	4.04(±1.47)	2.88(±1.50)
M19154.1	Transforming growth factor-beta-2	2.76(±0.64)	3.14(±0.65)
M37435.1	Macrophage colony-stimulating factor	2.78(±0.54)	1.87(±0.65)
NM_013957.1	Neuregulin 1 (NRG1)	1.76(±0.48)	3.15(±0.44)
Signal transduction			
NM_006398.1	Diubiquitin (UBD)	6.33(±0.31)	4.64(±1.06)
NM_000602.1	Plasminogen activator inhibitor type 1	5.95(±0.35)	3.88(±0.25)
NM_003246.1	Thrombospondin 1	3.77(±0.76)	1.53(±0.37)
NM_005562.1	Laminin, gamma 2	3.64(±1.35)	3.73(±0.53)
NM_002260.2	Killer cell lectin-like receptor subfamily C	3.58(±1.93)	3.95(±1.03)
AF091395.1	Trio isoform mRNA	2.23(±0.25)	1.91(±0.49)
NM_002228.2	v-jun avian sarcoma virus 17 oncogene (JUN)	2.17(±1.65)	2.60(±1.35)
NM_025195.1	G-protein-coupled receptor induced protein	1.85(±0.44)	2.15(±0.61)
X83493.1	Fas/Apo-1	1.82(±0.63)	2.08(±0.74)
NM_013253.1	Dickkopf gene 3 (DKK3)	1.51(±0.39)	2.70(±0.77)
NM_002826.2	Quiescin Q6 (QSCN6)	1.39(±0.42)	2.14(±0.59)
Others			
U17497.1	Proteasome subunit LMP7	2.48(±0.98)	2.55(±0.93)
NM_002852.1	Pentaxin-related gene (PTX3)	2.44(±1.09)	2.05(±0.78)
D42043.1	KIAA0084 protein	2.34(±0.40)	2.40(±0.95)
NM_014890.1	Downregulated in ovarian cancer 1 (DOC1)	2.22(±0.51)	2.87(±0.52)
AI700633	cDNA: FLJ22642 fis, clone HSI06970	1.63(±0.35)	2.18(±0.25)

\* This ratio represent to average and standard deviation.

Supplementary Table 4. Downregulated genes by SMAD6 knockdown

Gene ID		Log <sub>2</sub> Ratio shRNA#1/M*	Log <sub>2</sub> Ratio shRNA#3/M*
<b>Chromatin remodeling</b>			
NM_001067.1	Topoisomerase (DNA) II alpha	-2.74(±0.97)	-3.74(±1.93)
NM_004523.2	Kinesin-like 1 (KNSL1)	-2.42(±1.44)	-2.80(±1.80)
NM_004856.3	Kinesin-like 5 (KNSL5)	-2.06(±0.83)	-1.88(±1.26)
NM_005804.1	Nuclear RNA helicase, (DDXL)	-1.55(±0.32)	-1.05(±0.03)
NM_001809.2	Centromere protein A (17kD) (CENPA)	-1.49(±0.39)	-2.20(±0.69)
<b>Differentiation</b>			
NM_000790.1	Dopa decarboxylase (DDC)	-2.32(±0.27)	-1.43(±0.31)
NM_000435.1	Notch homolog 3 (NOTCH3)	-1.67(±0.28)	-1.23(±0.13)
<b>Transcription/Translation</b>			
NM_004701.2	Cyclin B2 (CCNB2)	-2.10(±0.63)	-2.26(±0.75)
NM_000791.2	Dihydrofolate reductase (DHFR)	-1.63(±0.51)	-2.00(±0.92)
<b>Signal transduction</b>			
NM_001982.1	ERBB3	-2.01(±0.92)	-1.47(±0.86)
NM_004360.1	E-cadherin	-2.26(±0.98)	-3.41(±0.92)
NM_014501.1	Ubiquitin carrier protein (E2-EPF)	-1.37(±0.16)	-1.45(±0.12)
AW157070	Epidermal growth factor receptor	-1.66(±0.27)	-2.62(±0.70)
<b>Others</b>			
NM_000728.1	Calcitonin-related polypeptide	-4.12(±2.59)	-3.31(±1.73)
NM_000709.1	Branched chain keto acid dehydrogenase E1	-1.86(±0.69)	-1.59(±1.10)
AB006955.1	mRNA for AIE-75	-1.81(±0.88)	-2.40(±0.45)
NM_001902	Cystathionase (CTH)	-1.60(±0.36)	-2.18(±0.16)
NM_001360.1	7-dehydrocholesterol reductase (DHCR7)	-1.38(±0.24)	-1.64(±0.24)
NM_003749.1	Insulin receptor substrate-2 (IRS2)	-1.21(±0.22)	-1.02(±0.23)

\* This ratio represent to average and standard deviation.