Electronic supplementary material for "Beyond cancer genes: colorectal cancer as robust intrinsic states formed by molecular interactions"

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CONTENTS

I. NETWORK CONSTRUCTION

A. Molecular pathways underlying genetic risks

Up to one third of CRC are likely related to inheritance. First degree relatives of patients with CRC have a 2- to 4-fold risk of developing neoplasm compared with the general population [1–6]. One example clearly showing the extensiveness of heredity in CRC is the research conducted in Utah [4]. Utah has the lowest incidence of CRC in the United States for both men and women [7]. Since the Church of Jesus Christ of Latter-day Saints, which the majority of its residents belong to, has a health code against the use of coffee, tea, alcohol, and tobacco, presumable risk factors due to diet are excluded to some degree.

Between 2% to 5% of CRC arise with lynch syndrome, adenomatous and hamartomatous polyposis syndromes which demonstrate Mendelian inheritance pattern [6]. The genes responsible for these disorders have been identified and carriers of the pathogenic mutations have a high lifetime risk of cancers. Among the overlapped genes with the ones identified in somatic mutations [8] is adenomatous polyposis coli (APC), which encodes a protein repressing canonical Wnt signaling pathway at several levels. Another ones are involved in TGF-β signaling, such as Smad4 and BMPR1A [6, 8]. Except for APC, KRAS, p53, most of somatic mutations in oncogene and tumor suppressors happen at low frequencies. Possibly, canonical Wnt signaling and TGF-β signaling pathways are the critical ones for CRC development while others work as additional contributors.

The predisposed genetic condition in these studies has implications. The vast majority of the gene variants for CRC, mostly not yet identified, carry out normal physiological functions which are not grossly affected, therefore not critical by themselves. The combined effect of the gene variants can be additive, possibly through interactions. Therefore, it is necessary for us to extend the search for molecules for CRC development beyond current genetic studies. Also, a method to account for the cooperation may be helpful.

B. Identify molecules and pathways from gastrointestinal track development

Canonical Wnt signaling pathway, which is implicated in genetic study of CRC has an important role in controlling patterning and proliferation of gastrointestinal track (GI) at embryonic stage. In the study of familial and sporadic colon cancers, association between the GI tract and the canonical Wnt pathway was first established [9, 10]. Mutations in the components of this pathway that result in tumor formation are those that leading to stabilization of beta-catenin and hence constitutive activation of the pathway. Mouse models with interruption in various components elucidated role of Wnt pathway in development [10]. For example, disruption of Tcf4 resulted in depletion of the epithelial stem cell compartment in the crypts of the small intestine [11].

We searched for molecules interacting with Wnt pathways in order to include feedbacks into the network. Wnt signaling is active in posterior endoderm in early mouse development and induces Cdx2 [12], a cell fate switch of intestinal specification in the endoderm [13]. Wnt is a transient process and appears to be repressed by Cdx2 after differentiation [13] while activation of Wnt signaling is sufficient enough to induce intestinal differentiation of embryonic stem cell-derived endoderm, specifically inducing posterior small intestine and large intestine fate [11]. The interaction of Cdx2 and Wnt pathway is complex that only 18% of the genes induced by Wnt activation were induced by Cdx2 while larger degree of overlap was observed between genes down-regulated by them, suggesting additional pathways may also play a role.

Endoderm-mesoderm interaction exists throughout GI developmental process [14]. Gut endoderm was able to induce smooth muscle differentiation in non-gut mesoderm, possibly through secreted molecule Sonic Hedgehog (SHH) [15]. SHH signaling has a dual role in proliferation and differentiation, as over-expression of SHH transgenic mice lead to increased cell proliferation of gut mesoderm as well as smooth muscle specification [16]. The endodermal signal, such as SHH, BMP4 allows the epithelial lumen to be surrounded by mesoderm specified to form visceral mesoderm [14]. Similar to Wnt pathway, hedgehog pathway was also found in cancer progress by induction of epithelial-mesenchymal transition. Through the expression of the transcription factor Gli1, hedgehog ultimately activates Snail and drives cancer invasion [17]. Another important signaling pathway in GI development is Notch. Notch regulates adult intestinal development by controlling the balance between secretory and absorptive cell types [18]. Notch activation in the embryonic foregut results in reversible defects in villus morphogenesis and loss of the proliferative progenitor compartment [18]. SNotch signaling pathway is also proposed to play an important role in cancer invasion [19]. These important pathways for developmental process and cancer also interact. For example, Notch may directly suppress Hedgehog via Hes1 mediated inhibition of Gli1 transcription [20]. In addition to Wnt, SHH, Notch, which are important for developmental process, we include other molecules for GI development, such as those of GATA, Hox family.

C. Immune response and its possible active role in CRC

CRC is a type of cancer which demonstrates apparent association with inflammation [21, 22]. Both ulcerative colitis and Crohns colitis are at increased risk of developing CRC [22]. Colitis-associated colorectal cancer affects individuals at a younger age than the general population and the risk for developing CRC increases with longer duration of colitis. Inflammation is known to induce cellular stress as well as to modify microenvironment. In the context of network, we found indications that in the case of CRC, inflammation might not entirely be a passive response to stress and irritation, but possibly form an aberrant intracellular feedback. In adult human, Cdx2 is only detected in intestinal epithelial cells [23]. It is aberrantly expressed in most cases of acute myeloid leukemia and promotes leukemogenesis [24], and associated with Hox dysregulation expressions [24]. Another possible feedback link to inflammation in CRC is frequently observed Runx1 expression [25, 26]. Runx1 is a gastric [27] gene which also indispensable in hematopoiesis and associates with the myeloid leukemia [28]. In fact, aberrant developmental process is shown to be involved in carcinogenesis through epithelial-mesenchymal transition [17, 19]. We found no fundamental reason that aberrant developmental process in cancer is limited to epithelial-mesenchymal transition not that of leukemogenesis. The activation of pathways in leukemogenesis might lead to additional contribution to inflammation through receptors and cytokines usually observed in leukocytes. We included molecules and pathways known to interact with molecules such as Cdx2 and Hox family in acute myeloid leukemia in the network for necessary feedbacks to molecules of interest.

D. Key nuclear receptors in GI development and inflammation

Normal intestinal function also requires a number of nuclear receptors. Their expression and activities may also be altered by inflammation [22, 29]. PPARγ ligands have been shown to inhibit intestinal inflammation [30, 31]. Glucocorticoids affect development of the gastrointestinal mucosa in addition to their anti-inflammation function [32]. Given the importance of glucocorticoids in GI track, the repressors of glucocorticoid pathway are also of interests. The NR4A subgroup of nuclear receptors might be considered early response genes which are induced by a large set of stimuli, such as growth factors, fatty acids, cytokines [33]. NR4As have anti-inflammation role through induction of iκB [34]. In addition, NR4As are also antagonists of glucocorticoids pathway [35], which is also anti-inflammatory. Thus inflammation stimuli NR4As and glucocorticoids form a complex relationship. There are at least two possible relations of NR4As to CRC. First, activation of NR4As favors angiogenesis [36]. Second, NR4As might interfere with nuclear signaling through competing with binding partners, such as VDR and RXR [33, 37]. Unlike the extensive research on signaling pathways in developmental processes such as Wnt, SHH and Notch, research on nuclear receptor signaling pathways in CRC is less mature. In the network model, we included only the ones which seem to be most important.

Table S1. Molecular interactions in the CRC endogenous network. Molecules and pathways are grouped according to their roles in cell cycle, apoptosis, differentiation, nuclear receptor signaling, immune response, growth factors, stress response, and interaction with extracellular matrix. NR: nuclear receptor signaling. ECM: molecules and pathways interact with extracellular matrix. Detailed description and references are shown in Table S2.

	Nodes	Activator	Inhibitor
Cell Cycle	Cyclin D/Cdk4,6	E2F; EGFR; Pu.1; Myc	p21; p53
	Cyclin E/Cdk2	E2F; Myc	p21; p27; PTEN
	E2F	E2F; Myc	p21
	Myc	E2F; MAPK; Notch; pRb; SHH; Wnt	AP2; p53; TGF-β
	p21	AP2; Gata1/2; HNF4α; p53; Runx1; TGF-β; TNF-α; GR	Akt; Hes1; Myc
	p27	E-Cadherin; Gata1/2; PTEN; TGF-β; NR4A	Akt; Hes1; Myc
	pRb	Cyclin D/Cdk4,6; Cyclin E/Cdk2	
	Ras	EGFR; FGFR2; IL-6; VEGF; IR; HGF	p53; GR
Apoptosis	Bad	p53; TNF-α	Akt; MAPK; NF-κB; p21
	Bax	Bim; p53	Akt; Bcl-2; Sox4
	Bcl-2	Integrin; NF-κB; VEGF	Caspase 3; p53; TGF-β
	Bcl-xL	EGFR; NF-κB; Stat5	Caspase 3
	Bim		Akt; MAPK
	Caspase 3	Bad; Cytochrome C; Fas; TNF-α	NF-κB; XIAP
	Cytochrome C	Bad; Bax; Caspase 3	Bcl-2; Bcl-xL; p21
	Fas	TNF-α	Ras
	XIAP	Akt; Integrin; MAPK; NF-κB; RARs	Caspase 3; Cytochrome C
Differentiation	C/EBPα	C/EBPβ; HNF4α; NOG; Runx1	HIF; IL-1; MAPK; Notch; SHH; Stat5; NR2F2
	C/EBPβ	AP2; IL-1; MAPK	Hoxa3; TGF-β
	Cdx2	BMP; c-Jun; Gata1/2; HNF1; HNF4α; MAPK; Sox2; Wnt	C/EBPβ; Sox9; Stat3; TGF-β
	Foxa1	AP2; Foxa2; RARs	Sox4
	Foxa2	C/EBPα; RARs; SHH	Akt; PRDM14
	Gata1/2	Cdx2; Notch; Stat3	c-Jun; Hes1; Hoxa10; VEGF; Pu.1
	Gata4/6	PKA; Sox7; Wnt	c-Jun; Hey2; PRDM14; Sox2
	Hes1	Notch; TGF-β	
	Hey2	Notch	
	HNF1	HNF4α; Notch	C/EBPα
	HNF4α	C/EBPα; Cdx2; E-Cadherin; Gata4/6; HNF1; Stat5; NR2F2	MAPK; NF-κB; p53; PKA; Sox2; Stat3; IR; NR4A
	Hoxa10	BMP; Hoxa9; Stat5	Cdx2; IL-1
	Hoxa3	c-Jun; RARs; Wnt	Stat3
	Hoxa5	Cdx2; Hoxa10; RARs	Runx1
	Hoxa9	C/EBPα; Notch; Stat5	NF-κB; TGF-β
	PGC-1	C/EBPβ	p53; Akt; c-Jun
	PRDM14	Stat3	
	Pu.1	C/EBPα; Runx1	Gata1/2; Sox4
	Runx1	BMP; Cdx2; c-Jun; Gata1/2; Sox2; Notch	Hoxa3; Stat5
	Runx2	BMP; Hoxa10; Runx1	C/EBPβ; FGFR3; Notch; Stat5; NR2F2; TGF-β
	Sox2	AP2; FGFR2; Stat3; Wnt	p21; Cdx2
	Sox4	Sox7; Stat5; TGF-β; Wnt	C/EBPα
	Sox7	BMP; c-Jun; VEGF	PRDM14
	Sox9	AP2; BMP; FGFR3; Notch; PKA; SHH; TGF-β; Wnt	c-Jun; IL-1; NF-κB; RARs
NR	PPARγ	C/EBPα; C/EBPβ	RARs; SHH; Stat5; TGF-β; TNF-α; NR2F2
	GR	HNF1; TGF-β	NR4A; NR2F2
	NR4A	EGFR; VEGF; Runx1	HNF4α; GR
	RARs	AP2; PPARγ	MAPK; NR2F2
	NR2F2	Gata4/6; HNF4α; MAPK; SHH; Wnt; GR	
Immune Response	G-CSFR	C/EBPα; NF-κB; Pu.1	GR
	IL-1	C/EBPβ; NF-κB; OPN	Akt; C/EBPα
	IL-10	Fas; TNF-α	IL-10
	IL-3	C/EBPα; Gata1/2; Runx1	
	IL-6	C/EBPβ; Hoxa3; NF-κB; NGAL	HNF4α; RARs; Sox2
	iκB	NF-κB; TGF-β; NR4A; GR	Akt; EGFR; Fas; TNF-α
	NF-κB	C/EBPβ; CCK; IL-1; TNF-α	Cdx2; Foxa1; IL-10; iκB; PPARγ; Sox2; IR
	Stat3	CCK; FGFR2; FGFR3; G-CSFR; FGFR4; Gast; IL-6; OPN; VEGF; HGF	Gata1/2; PPARγ; PTEN; RARs
	Stat5	FGFR2; IL-3; VEGF; IR; G-CSFR	HNF4α; Runx1; Runx2; TGF-β
	TGF-β	Hoxa10; Hoxa3; Hoxa9; NOG; OPN; p53; Sox7; Stat3; TNF-α	Gata4/6; NF-κB; RARs; Sox2; Stat5; NR2F2
	TNF-α	IL-1; NF-κB	IL-10
Growth Factors	BMP	EGFR; FGFR2; Gata4/6; Runx1	HNF4α; NOG; TGF-β; NR2F2
	CCK	C/EBPβ; Cdx2; Gast; Gata4/6; IL-1; IR	
	EGFR	Myc; Runx1; Sox4; HIF	PTEN
	FGF2	Hoxa10; HSPG2	
	FGF4/8	SHH	Notch
	FGF7	HSPG2; IL-1	
	FGF9	Sox9	
	FGFR2	FGF2; FGF7; Hoxa10; Runx2	PRDM14
	FGFR3	FGF9	
	FGFR4	FGF4/8; FGF9	
	Gast	Sox2; TGF-β; Wnt	
	HGF	c-Jun; NF-κB; HIF	GR; TGF-β
	IR	C/EBPα; PPARγ; SHH; Wnt	Notch; TNF-α
	VEGF	Gata4/6; HIF; PGC-1; Stat3; TGF-β; NR2F2; NR4A	RARs; Sox9; Notch; Runx1
Stress Response	Akt	CCK; c-Jun; EGFR; FGFR2; Notch; NF-κB; PKA; Ras; RARs; IR; HGF	PTEN
	AP2	C/EBPβ; RARs; NR2F2	
	c-Jun	Akt; CCK; EGFR; FGFR3; Runx1; TNF-α	C/EBPα; Mkp2; GR
	HIF	Akt; Stat3; NR4A	p53
	MAPK	FGFR2; FGFR3; Integrin; NF-κB; PPARγ; Ras; NR2F2	PTEN; TGF-β
	Mkp2	Hoxa10	
	PKA	Akt; EGFR; TGF-β	p53
	PTEN	AP2; p53; PPARγ	NF-κB; Stat3
	p53	AP2; Myc; PPARγ; PTEN; RARs	Akt; Notch; Sox4
ECM	E-Cadherin	AP2; Cdx2; Foxa1; Foxa2; HNF4α	Akt; TGF-β; EGFR; HIF; SHH; Stat3; TNF-α
	HSPG2	Runx2; TGF-β	
	Integrin	EGFR; MAPK; TNF-α; VEGF	Myc; Ras; SHH
	Notch	NF-κB; Cdx2; FGFR2; HNF1; MAPK; Stat3	BMP; C/EBPα; E-Cadherin; Hoxa5; NR2F2
	NGAL	Runx1; TNF-α	
	NOG	SHH; Sox9; Wnt	FGFR2
	OPN	Runx1; Runx2; TGF-β	PGC-1
	SHH	Foxa1; Sox2; TGF-β	BMP; FGFR2; Foxa2; Hes1
	Wnt	EGFR; FGFR2; FGFR3; Gata4/6; PGC-1; Sox4; TGF-β; IR; HGF	Cdx2; HNF4α; Sox7; Sox9

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F. Network definition and reference for molecular interactions

Table S2. Molecular interactions in the CRC network with references.

	Activated By	Inhibited By	Notes
Cell Cycle			
Cyclin D/Cdk4,6	E2F [1], EGFR [2], Myc [1], Pu.1 [3]	p21 [1, 4], p53 [1]	
Cyclin E/Cdk2	E2F [1], Myc [5]	PTEN [1], p21 [1, 4], p27 [1, 4]	
E2F	E2F [1], Myc [1]	p21 [4]	
Myc	E2F [6], MAPK [6, 7], Notch [8], SHH [9], Wnt [10], pRb [6]	AP2 [11], TGF-β [12, 13], p53 [6]	
p21	AP2 [14], GR [15], Gata1/2 [16], HNF4α [17], Runx1 [18], TGF-β [13], TNF-α [19], p53 [6, 19]	Akt [4], Hes1 [20], Myc [19, 21]	
p27	E-Cadherin [22], Gata1/2 [23], NR4A [24], PTEN [25], TGF-β [26]	Akt [25], Hes1 [27], Myc [6]	
pRb	Cyclin D/Cdk4,6 [1, 28], Cyclin E/Cdk2 [1, 28]		Retinoblastoma protein phosphorylation
Ras	EGFR [29], FGFR2 [30], HGF [31], IL-6 [32, 33], IR [34], VEGF [35, 36]	GR [37], p53 [38]	
Apoptosis			
Bad	TNF-α [39], p53 [40]	Akt [41], MAPK [41], NF-κB [42], p21 [43]	
Bax	Bim [44], p53 [45, 46]	Akt [47], Bcl-2 [48], Sox4 [49]	
Bcl-2	Integrin [50], NF-κB [51], VEGF [52]	Caspase 3 [52], TGF-β [53], p53 [54]	
Bcl-xL	EGFR [55], NF-κB [56], Stat5 [57]	Caspase 3 [58]	
Bim		Akt [41], MAPK [41]	
Caspase 3	Bad [59, 60], Cytochrome C [46, 52, 61], Fas [62], TNF-α [63]	NF-κB [64], XIAP [46, 52, 65, 66]	
Cytochrome C	Bad [52], Bax [52], Caspase 3 [46, 52, 65, 67]	Bcl-2 [68, 69], Bcl-xL [68, 70], p21 [71, 72]	Cytochrome C, Apaf-1, and Caspase 9 complex
Fas	TNF-α [73]	Ras [74]	
XIAP	Akt [66], Integrin [75], MAPK [76], NF-κB [67, 77], RARs [78]	Caspase 3 [46, 52, 54, 65–67], Cytochrome C [46, 52, 67]	X-linked inhibitor of apoptosis
Differentiation			
C/EBPα	C/EBPβ [79], HNF4α [80], NOG [81], Runx1 [82]	HIF [83], IL-1 [84], MAPK [85], NR2F2 [86], Notch [87], SHH [88], Stat5 [89]	
C/EBPβ	AP2 [90], IL-1 [84], MAPK [91]	Hoxa3 [92], TGF-β [93]	

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	Activated By	Inhibited By	Notes
Cdx2	BMP [94], Gata1/2 [95, 96], HNF1 [97], HNF4α [98], MAPK [99], Sox2 [100], Wnt [101], c-Jun [102]	*C/EBPβ [102, 103], Sox9 [104], Stat3 [105], TGF-β [106]	*C/EBPβ downregulate Cdx2 by c-Fos upregulation
Foxa1	AP2 [107], Foxa2 [108], RARs [109, 110]	Sox4 [111]	
Foxa2	C/EBPα [112], RARs [109], SHH [113]	Akt [114], PRDM14 [115]	
Gata1/2	Cdx2 [116], Notch [117], Stat3 [118]	Hes1 [119], Hoxa10 [120], Pu.1 [121, 122], VEGF [123], c-Jun [124]	
Gata4/6	PKA [125], Sox7 [126], Wnt [127]	Hey2 [128], PRDM14 [115], Sox2 [100, 126, 129], c-Jun [130]	
Hes1	Notch [119], TGF-β [131]		
Hey2	Notch [132]		
HNF1	HNF4α [133], Notch [134]	C/EBPα [135]	
HNF4α	C/EBPα [85], Cdx2 [98], E-Cadherin [136], Gata4/6 [137], HNF1 [133], NR2F2 [138], Stat5 [139]	IR [140], MAPK [141], NF-κB [142], *NR4A [143, 144], PKA [140], Sox2 [145], Stat3 [146], p53 [147]	*indirect through competing available p300
Hoxa10	BMP [148], Hoxa9 [149], *Stat5 [150, 151]	Cdx2 [152], IL-1 [153]	*indirect
Hoxa3	RARs [154, 155], Wnt [156], c-Jun [157]	Stat3 [158]	
Hoxa5	Cdx2 [159], Hoxa10 [120], RARs [155]	Runx1 [160]	
Hoxa9	C/EBPα [161, 162], Notch [163], Stat5 [161]	NF-κB [164], TGF-β [165]	
PGC-1	C/EBPβ [166]	Akt [167], c-Jun [168], p53 [169]	
PRDM14	Stat3 [170]		
Pu.1	C/EBPα [171], Runx1 [172, 173]	Gata1/2 [121, 122], Sox4 [174]	
Runx1	BMP [175], Cdx2 [116], Gata1/2 [176], Notch [177], Sox2 [178], c-Jun [179]	Hoxa3 [92, 180], Stat5 [181, 182]	
Runx2	BMP [13], Hoxa10 [148], *Runx1 [183]	C/EBPβ [184], FGFR3 [185], NR2F2 [186], Notch [187], Stat5 [182], TGF-β [183]	*indirect
Sox2	AP2 [188], FGFR2 [189], Stat3 [100], Wnt [190]	*Cdx2 [191], p21 [192]	*indirect
Sox4	Sox7 [193], Stat5 [194], TGF-β [195, 196], Wnt [193]	C/EBPα [197]	
Sox7	BMP [198], VEGF [199], c-Jun [200]	PRDM14 [201]	
Sox9	AP2 [202], BMP [203], FGFR3 [204], Notch [134, 205], PKA [206], SHH [207], TGF-β [208], Wnt [104, 209]	IL-1 [210], NF-κB [210, 211], RARs [211, 212], c-Jun [213]	
Nuclear Receptor (NR)			
PPARγ	C/EBPα [214], C/EBPβ [215]	NR2F2 [86], RARs [216], SHH [88], Stat5 [217], TGF-β [216], TNF-α [218]	
GR	HNF1 [219], TGF-β [220]	NR2F2 [221], NR4A [222]	

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	Activated By	Inhibited By	Notes
NR4A	EGFR [24], Runx1 [223], VEGF [224]	GR [225], *HNF4α [143, 144]	*indirect through competing available p300
RARs	AP2 [226], PPARγ [227]	MAPK [228], NR2F2 [229]	Retinoic acid receptor signaling
NR2F2	GR [221], Gata4/6 [230, 231], HNF4α [138], MAPK [232], SHH [233], Wnt [86]		
Immune Response			
G-CSR	C/EBPα [234], NF-κB [235], Pu.1 [236]	GR [237]	
IL-1	C/EBPβ [238], NF-κB [239], OPN [240]	Akt [241], C/EBPα [242]	Interleukin 1
IL-10	Fas [239], TNF-α [239]	IL-10 [239]	Interleukin 10
IL-3	C/EBPα [243], Gata1/2 [244], Runx1 [245–247]		Interleukin 3
IL-6	C/EBPβ [248], Hoxa3 [249], NF-κB [250], NGAL [251]	HNF4α [146], RARs [252], Sox2 [253]	Interleukin 6
iκB	GR [237], NF-κB [77, 254, 255], NR4A [256], TGF-β [257]	Akt [258], EGFR [259], Fas [260], TNF-α [77, 254, 255]	
NF-κB	C/EBPβ [261], CCK [262, 263], IL-1 [77, 254, 255, 264], TNF-α [77, 254, 255]	Cdx2 [265], Foxa1 [107], IL-10 [266], IR [267], PPARγ [268], Sox2 [269], iκB [77, 254, 255]	
Stat3	CCK [270], FGFR2 [271], FGFR3 [272], FGFR4 [273], G-CSR [274], Gast [275], HGF [31], IL-6 [276], OPN [277], VEGF [278]	Gata1/2 [279], PPARγ [280], PTEN [281, 282], RARs [283]	
Stat5	FGFR2 [284], G-CSR [274], IL-3 [57], IR [285], VEGF [286]	HNF4α [139], Runx1 [181], Runx2 [181], TGF-β [287]	
TGF-β	Hoxa10 [288], Hoxa3 [92], Hoxa9 [289], NOG [290], OPN [290], Sox7 [291], Stat3 [292], TNF-α [13, 293], p53 [294, 295]	Gata4/6 [296], NF-κB [13], NR2F2 [297], RARs [298], Sox2 [299], Stat5 [300]	Transforming growth factor beta
TNF-α	IL-1 [77, 254, 255], NF-κB [77, 254, 255]	IL-10 [77, 254, 255]	
Growth Factors			
BMP	EGFR [301], FGFR2 [302], Gata4/6 [303], Runx1 [304]	HNF4α [305], NOG [306], NR2F2 [307], TGF-β [308]	
CCK	C/EBPβ [309], Cdx2 [310], Gast [309, 311], Gata4/6 [312], IL-1 [313–315], IR [316]		
EGFR	HIF [317], Myc [318], Runx1 [319], Sox4 [196]	PTEN [320]	
FGF2	HSPG2 [321], Hoxa10 [288]		Fibroblast growth factor 2

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	Activated By	Inhibited By	Notes
FGF4/8	SHH [322]	Notch [323]	
FGF7	HSPG2 [321], IL-1 [324]		Fibroblast growth factor 7
FGF9	Sox9 [325]		
FGFR2	FGF2 [271], FGF7 [271], Hoxa10 [288], Runx2 [326]	PRDM14 [327]	Fibroblast growth factor receptor 2
FGFR3	FGF9 [328]		
FGFR4	FGF4/8 [329], FGF9 [329]		
Gast	Sox2 [145], TGF-β [330, 331], Wnt [330, 331]		
HGF	HIF [31], NF-κB [332], c-Jun [332]	GR [333], TGF-β [333]	
IR	C/EBPα [214], PPARγ [334], SHH [335], Wnt [336]	Notch [337], TNF-α [338]	
VEGF	Gata4/6 [339], HIF [340], NR2F2 [341], NR4A [342], PGC-1 [343], Stat3 [344–346], TGF-β [347, 348]	Notch [349], RARs [350], Runx1 [351], Sox9 [352]	Vascular endothelial growth factor

Stress Response

Akt	CCK [311, 353], EGFR [354], FGFR2 [271], HGF [31], IR [355], NF-κB [41, 255], Notch [356], PKA [357], RARs [358], Ras [359], c-Jun [360]	PTEN [361]	
AP2	C/EBPβ [362], NR2F2 [363], RARs [364]		Activating Protein 2 (AP-2)
c-Jun	Akt [365], CCK [366], EGFR [367], FGFR3 [185], Runx1 [179], TNF-α [368]	C/EBPα [369], GR [370, 371], Mkp2 [372]	
HIF	Akt [41, 373], NR4A [374], Stat3 [346]	p53 [373]	Hypoxia-inducible factors
MAPK	FGFR2 [375], FGFR3 [376], Integrin [377, 378], NF-κB [7], NR2F2 [232], PPARγ [379], Ras [35]	PTEN [361, 378], TGF-β [380]	Mitogen-activated protein kinase signaling
Mkp2	Hoxa10 [381]		
PKA	Akt [382], EGFR [383], TGF-β [384, 385]	p53 [386]	
PTEN	AP2 [387], PPARγ [388], p53 [389]	NF-κB [390], Stat3 [281]	
p53	AP2 [391], Myc [35], PPARγ [392], PTEN [393], RARs [392, 394]	Akt [35], Notch [395], Sox4 [396]	

ECM (Extracellular Matrix)

E-Cadherin	AP2 [397], Cdx2 [398], Foxa1 [109, 399], Foxa2 [399], HNF4α [400]	Akt [401, 402], EGFR [403], HIF [404, 405], SHH [406], Stat3 [275, 407], TGF-β [408], TNF-α [409]	

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	Activated By	Inhibited By	Notes
HSPG2	Runx2 [410], TGF-β [411]		
Integrin	EGFR [50, 377], MAPK [412], TNF-α [377, 413], VEGF [50, 377]	Myc [414], Ras [415], SHH [416]	
Notch	Cdx2 [417, 418], FGFR2 [419], HNF1 [97], MAPK [420], NF-κB [421], Stat3 [422]	BMP [423], C/EBPα [424], E-Cadherin [425], Hoxa5 [426], NR2F2 [427]	
NGAL	Runx1 [428], TNF-α [429]		
NOG	SHH [430], Sox9 [431], Wnt [430]	FGFR2 [432]	Noggin
OPN	Runx1 [428], Runx2 [428], TGF-β [433]	*PGC-1 [434, 435]	Osteopontin, *indirect
SHH	Foxa1 [108], Sox2 [178], TGF-β [436]	BMP [437, 438], FGFR2 [439], Foxa2 [108], Hes1 [440]	Sonic hedgehog pathway
Wnt	EGFR [441], FGFR2 [441], FGFR3 [441], Gata4/6 [442], HGF [443, 444], IR [445], PGC-1 [446], Sox4 [196], TGF-β [447]	Cdx2 [448, 449], HNF4α [450, 451], Sox7 [452, 453], Sox9 [454]	

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II. NETWORK MODELING

A. Modeling the network dynamics by mathematical equations

We use nonlinear Hill type function to implement coarse-grained activation and inhibition between different agents. The dynamical equation for the concentration/activities of agents $\mathbf{x} = (x_1, x_2, \ldots, x_m)$ under the influence of the other agents takes the following form:

$$\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x}) - \frac{\mathbf{x}}{\tau} \; . \tag{1}$$

This expression is consistent with chemical rate equations. A main simplification is that the natural protein degradation time is set to be unity for all proteins: $\tau = 1$. If the agent x_2 activates agent x_1, function $f_1(x_2)$ is assigned as the form

$$f_1(x_2) = \frac{a \cdot x_2^n}{1 + a \cdot x_2^n} \; , \tag{2}$$

while for the inhibition on x_1 by x_2

$$f_1(x_2) = \frac{1}{1 + a \cdot x_2^n} \; . \tag{3}$$

If there are multiple activations x_2, x_3 and inhibitions x_4, x_5 to x_1, we have

$$f_1(x_2, \ldots, x_5) = \frac{a \cdot (x_2^n + x_3^n)}{1 + a \cdot (x_2^n + x_3^n)} \times \frac{1}{1 + a \cdot (x_4^n + x_5^n)} \; . \tag{4}$$

The values for each agent is normalized from zero to one. One may notice that our equations guarantee that the values of agents will not go beyond the internal from zero to one while evolving with time. The values for the parameters are typically chosen to be $a = 10$ and $n = 3$. We demonstrate in the following that our results are robust under random parameter tests.

1. *A full list of equations for the network dynamics*

We list below all equations for the network dynamics described in Table S2:

$$\frac{dx_{Cyclin\ D/Cdk4,6}}{dt} = \frac{a \cdot (x_{E2F}^n + x_{Myc}^n + x_{Pu.1}^n + x_{EGFR}^n)}{1 + a \cdot (x_{E2F}^n + x_{Myc}^n + x_{Pu.1}^n + x_{EGFR}^n)} \times \frac{1}{1 + a \cdot (x_{p21}^n + x_{p53}^n)} - x_{Cyclin\ D/Cdk4,6}$$

$$
\begin{aligned}
\frac{dx_{Cyclin\ E/Cdk2}}{dt} &= \frac{a \cdot (x^n_{E2F} + x^n_{Myc})}{1 + a \cdot (x^n_{E2F} + x^n_{Myc})} \times \frac{1}{1 + a \cdot (x^n_{p21} + x^n_{p27} + x^n_{PTEN})} - x_{Cyclin\ E/Cdk2} \\
\frac{dx_{E2F}}{dt} &= \frac{a \cdot (x^n_{E2F} + x^n_{Myc})}{1 + a \cdot (x^n_{E2F} + x^n_{Myc})} \times \frac{1}{1 + a \cdot (x^n_{p21})} - x_{E2F} \\
\frac{dx_{Myc}}{dt} &= \frac{a \cdot (x^n_{E2F} + x^n_{pRb} + x^n_{MAPK} + x^n_{Notch} + x^n_{SHH} + x^n_{Wnt})}{1 + a \cdot (x^n_{E2F} + x^n_{pRb} + x^n_{MAPK} + x^n_{Notch} + x^n_{SHH} + x^n_{Wnt})} \times \frac{1}{1 + a \cdot (x^n_{TGF-\beta} + x^n_{AP2} + x^n_{p53})} - x_{Myc} \\
\frac{dx_{p21}}{dt} &= \frac{a \cdot (x^n_{Gata1/2} + x^n_{HNF4\alpha} + x^n_{Runx1} + x^n_{GR} + x^n_{TGF-\beta} + x^n_{TNF-\alpha} + x^n_{AP2} + x^n_{p53})}{1 + a \cdot (x^n_{Gata1/2} + x^n_{HNF4\alpha} + x^n_{Runx1} + x^n_{GR} + x^n_{TGF-\beta} + x^n_{TNF-\alpha} + x^n_{AP2} + x^n_{p53})} \times \frac{1}{1 + a \cdot (x^n_{Myc} + x^n_{Hes1} + x^n_{Akt})} - x_{p21} \\
\frac{dx_{p27}}{dt} &= \frac{a \cdot (x^n_{Gata1/2} + x^n_{NR4A} + x^n_{TGF-\beta} + x^n_{PTEN} + x^n_{E-Cadherin})}{1 + a \cdot (x^n_{Gata1/2} + x^n_{NR4A} + x^n_{TGF-\beta} + x^n_{PTEN} + x^n_{E-Cadherin})} \times \frac{1}{1 + a \cdot (x^n_{Myc} + x^n_{Hes1} + x^n_{Akt})} - x_{p27} \\
\frac{dx_{pRb}}{dt} &= \frac{a \cdot (x^n_{Cyclin\ D/Cdk4,6} + x^n_{Cyclin\ E/Cdk2})}{1 + a \cdot (x^n_{Cyclin\ D/Cdk4,6} + x^n_{Cyclin\ E/Cdk2})} - x_{pRb} \\
\frac{dx_{Ras}}{dt} &= \frac{a \cdot (x^n_{IL-6} + x^n_{EGFR} + x^n_{FGFR2} + x^n_{HGF} + x^n_{IR} + x^n_{VEGF})}{1 + a \cdot (x^n_{IL-6} + x^n_{EGFR} + x^n_{FGFR2} + x^n_{HGF} + x^n_{IR} + x^n_{VEGF})} \times \frac{1}{1 + a \cdot (x^n_{GR} + x^n_{p53})} - x_{Ras} \\
\frac{dx_{Bad}}{dt} &= \frac{a \cdot (x^n_{TNF-\alpha} + x^n_{p53})}{1 + a \cdot (x^n_{TNF-\alpha} + x^n_{p53})} \times \frac{1}{1 + a \cdot (x^n_{p21} + x^n_{NF-\kappa B} + x^n_{Akt} + x^n_{MAPK})} - x_{Bad} \\
\frac{dx_{Bax}}{dt} &= \frac{a \cdot (x^n_{Bim} + x^n_{p53})}{1 + a \cdot (x^n_{Bim} + x^n_{p53})} \times \frac{1}{1 + a \cdot (x^n_{Bcl-2} + x^n_{Sox4} + x^n_{Akt})} - x_{Bax} \\
\frac{dx_{Bcl-2}}{dt} &= \frac{a \cdot (x^n_{NF-\kappa B} + x^n_{VEGF} + x^n_{Integrin})}{1 + a \cdot (x^n_{NF-\kappa B} + x^n_{VEGF} + x^n_{Integrin})} \times \frac{1}{1 + a \cdot (x^n_{Caspase\ 3} + x^n_{TGF-\beta} + x^n_{p53})} - x_{Bcl-2} \\
\frac{dx_{Bcl-xL}}{dt} &= \frac{a \cdot (x^n_{NF-\kappa B} + x^n_{Stat5} + x^n_{EGFR})}{1 + a \cdot (x^n_{NF-\kappa B} + x^n_{Stat5} + x^n_{EGFR})} \times \frac{1}{1 + a \cdot (x^n_{Caspase\ 3})} - x_{Bcl-xL} \\
\frac{dx_{Bim}}{dt} &= \frac{1}{1 + a \times (x^n_{Akt} + x^n_{MAPK})} - x_{Bim} \\
\frac{dx_{Caspase\ 3}}{dt} &= \frac{a \cdot (x^n_{Bad} + x^n_{Cytochrome\ C} + x^n_{Fas} + x^n_{TNF-\alpha})}{1 + a \cdot (x^n_{Bad} + x^n_{Cytochrome\ C} + x^n_{Fas} + x^n_{TNF-\alpha})} \times \frac{1}{1 + a \cdot (x^n_{XIAP} + x^n_{NF-\kappa B})} - x_{Caspase\ 3} \\
\frac{dx_{Cytochrome\ C}}{dt} &= \frac{a \cdot (x^n_{Bad} + x^n_{Bax} + x^n_{Caspase\ 3})}{1 + a \cdot (x^n_{Bad} + x^n_{Bax} + x^n_{Caspase\ 3})} \times \frac{1}{1 + a \cdot (x^n_{p21} + x^n_{Bcl-2} + x^n_{Bcl-xL})} - x_{Cytochrome\ C} \\
\frac{dx_{Fas}}{dt} &= \frac{a \cdot (x^n_{TNF-\alpha})}{1 + a \cdot (x^n_{TNF-\alpha})} \times \frac{1}{1 + a \cdot (x^n_{Ras})} - x_{Fas} \\
\frac{dx_{XIAP}}{dt} &= \frac{a \cdot (x^n_{RARs} + x^n_{NF-\kappa B} + x^n_{Akt} + x^n_{MAPK} + x^n_{Integrin})}{1 + a \cdot (x^n_{RARs} + x^n_{NF-\kappa B} + x^n_{Akt} + x^n_{MAPK} + x^n_{Integrin})} \times \frac{1}{1 + a \cdot (x^n_{Caspase\ 3} + x^n_{Cytochrome\ C})} - x_{XIAP} \\
\frac{dx_{C/EBP\alpha}}{dt} &= \frac{a \cdot (x^n_{C/EBP\beta} + x^n_{HNF4\alpha} + x^n_{Runx1} + x^n_{NOG})}{1 + a \cdot (x^n_{C/EBP\beta} + x^n_{HNF4\alpha} + x^n_{Runx1} + x^n_{NOG})} \times \frac{1}{1 + a \cdot (x^n_{NR2F2} + x^n_{IL-1} + x^n_{Stat5} + x^n_{HIF} + x^n_{MAPK} + x^n_{Notch} + x^n_{SHH})} \\
&\quad - x_{C/EBP\alpha} \\
\frac{dx_{C/EBP\beta}}{dt} &= \frac{a \cdot (x^n_{IL-1} + x^n_{AP2} + x^n_{MAPK})}{1 + a \cdot (x^n_{IL-1} + x^n_{AP2} + x^n_{MAPK})} \times \frac{1}{1 + a \cdot (x^n_{Hoxa3} + x^n_{TGF-\beta})} - x_{C/EBP\beta} \\
\frac{dx_{Cdx2}}{dt} &= \frac{a \cdot (x^n_{Gata1/2} + x^n_{HNF1} + x^n_{HNF4\alpha} + x^n_{Sox2} + x^n_{BMP} + x^n_{c-Jun} + x^n_{MAPK} + x^n_{Wnt})}{1 + a \cdot (x^n_{Gata1/2} + x^n_{HNF1} + x^n_{HNF4\alpha} + x^n_{Sox2} + x^n_{BMP} + x^n_{c-Jun} + x^n_{MAPK} + x^n_{Wnt})} \\
&\quad \times \frac{1}{1 + a \cdot (x^n_{C/EBP\beta} + x^n_{Sox9} + x^n_{Stat3} + x^n_{TGF-\beta})} - x_{Cdx2} \\
\frac{dx_{Foxa1}}{dt} &= \frac{a \cdot (x^n_{Foxa2} + x^n_{RARs} + x^n_{AP2})}{1 + a \cdot (x^n_{Foxa2} + x^n_{RARs} + x^n_{AP2})} \times \frac{1}{1 + a \cdot (x^n_{Sox4})} - x_{Foxa1} \\
\frac{dx_{Foxa2}}{dt} &= \frac{a \cdot (x^n_{C/EBP\alpha} + x^n_{RARs} + x^n_{SHH})}{1 + a \cdot (x^n_{C/EBP\alpha} + x^n_{RARs} + x^n_{SHH})} \times \frac{1}{1 + a \cdot (x^n_{PRDM14} + x^n_{Akt})} - x_{Foxa2} \\
\frac{dx_{Gata1/2}}{dt} &= \frac{a \cdot (x^n_{Cdx2} + x^n_{Stat3} + x^n_{Notch})}{1 + a \cdot (x^n_{Cdx2} + x^n_{Stat3} + x^n_{Notch})} \times \frac{1}{1 + a \cdot (x^n_{Hes1} + x^n_{Hoxa10} + x^n_{Pu.1} + x^n_{VEGF} + x^n_{c-Jun})} - x_{Gata1/2} \\
\frac{dx_{Gata4/6}}{dt} &= \frac{a \cdot (x^n_{Sox7} + x^n_{PKA} + x^n_{Wnt})}{1 + a \cdot (x^n_{Sox7} + x^n_{PKA} + x^n_{Wnt})} \times \frac{1}{1 + a \cdot (x^n_{Hey2} + x^n_{PRDM14} + x^n_{Sox2} + x^n_{c-Jun})} - x_{Gata4/6} \\
\frac{dx_{Hes1}}{dt} &= \frac{a \cdot (x^n_{TGF-\beta} + x^n_{Notch})}{1 + a \cdot (x^n_{TGF-\beta} + x^n_{Notch})} - x_{Hes1} \\
\frac{dx_{Hey2}}{dt} &= \frac{a \cdot (x^n_{Notch})}{1 + a \cdot (x^n_{Notch})} - x_{Hey2} \\
\frac{dx_{HNF1}}{dt} &= \frac{a \cdot (x^n_{HNF4\alpha} + x^n_{Notch})}{1 + a \cdot (x^n_{HNF4\alpha} + x^n_{Notch})} \times \frac{1}{1 + a \cdot (x^n_{C/EBP\alpha})} - x_{HNF1} \\
\frac{dx_{HNF4\alpha}}{dt} &= \frac{a \cdot (x^n_{C/EBP\alpha} + x^n_{Cdx2} + x^n_{Gata4/6} + x^n_{HNF1} + x^n_{NR2F2} + x^n_{Stat5} + x^n_{E-Cadherin})}{1 + a \cdot (x^n_{C/EBP\alpha} + x^n_{Cdx2} + x^n_{Gata4/6} + x^n_{HNF1} + x^n_{NR2F2} + x^n_{Stat5} + x^n_{E-Cadherin})} \\
&\quad \times \frac{1}{1 + a \cdot (x^n_{Sox2} + x^n_{NR4A} + x^n_{NF-\kappa B} + x^n_{Stat3} + x^n_{IR} + x^n_{MAPK} + x^n_{PKA} + x^n_{p53})} - x_{HNF4\alpha}
\end{aligned}
$$

$$\frac{dx_{Hoxa10}}{dt} = \frac{a\cdot(x^n_{Hoxa9}+x^n_{Stat5}+x^n_{BMP})}{1+a\cdot(x^n_{Hoxa9}+x^n_{Stat5}+x^n_{BMP})}\times\frac{1}{1+a\cdot(x^n_{Cdx2}+x^n_{IL-1})}-x_{Hoxa10}$$

$$\frac{dx_{Hoxa3}}{dt} = \frac{a\cdot(x^n_{RARs}+x^n_{c-Jun}+x^n_{Wnt})}{1+a\cdot(x^n_{RARs}+x^n_{c-Jun}+x^n_{Wnt})}\times\frac{1}{1+a\cdot(x^n_{Stat3})}-x_{Hoxa3}$$

$$\frac{dx_{Hoxa5}}{dt} = \frac{a\cdot(x^n_{Cdx2}+x^n_{Hoxa10}+x^n_{RARs})}{1+a\cdot(x^n_{Cdx2}+x^n_{Hoxa10}+x^n_{RARs})}\times\frac{1}{1+a\cdot(x^n_{Runx1})}-x_{Hoxa5}$$

$$\frac{dx_{Hoxa9}}{dt} = \frac{a\cdot(x^n_{C/EBP\alpha}+x^n_{Stat5}+x^n_{Notch})}{1+a\cdot(x^n_{C/EBP\alpha}+x^n_{Stat5}+x^n_{Notch})}\times\frac{1}{1+a\cdot(x^n_{NF-\kappa B}+x^n_{TGF-\beta})}-x_{Hoxa9}$$

$$\frac{dx_{PGC-1}}{dt} = \frac{a\cdot(x^n_{C/EBP\beta})}{1+a\cdot(x^n_{C/EBP\beta})}\times\frac{1}{1+a\cdot(x^n_{Akt}+x^n_{c-Jun}+x^n_{p53})}-x_{PGC-1}$$

$$\frac{dx_{PRDM14}}{dt} = \frac{a\cdot(x^n_{Stat3})}{1+a\cdot(x^n_{Stat3})}-x_{PRDM14}$$

$$\frac{dx_{Pu.1}}{dt} = \frac{a\cdot(x^n_{C/EBP\alpha}+x^n_{Runx1})}{1+a\cdot(x^n_{C/EBP\alpha}+x^n_{Runx1})}\times\frac{1}{1+a\cdot(x^n_{Gata1/2}+x^n_{Sox4})}-x_{Pu.1}$$

$$\frac{dx_{Runx1}}{dt} = \frac{a\cdot(x^n_{Cdx2}+x^n_{Gata1/2}+x^n_{Sox2}+x^n_{BMP}+x^n_{c-Jun}+x^n_{Notch})}{1+a\cdot(x^n_{Cdx2}+x^n_{Gata1/2}+x^n_{Sox2}+x^n_{BMP}+x^n_{c-Jun}+x^n_{Notch})}\times\frac{1}{1+a\cdot(x^n_{Hoxa3}+x^n_{Stat5})}-x_{Runx1}$$

$$\frac{dx_{Runx2}}{dt} = \frac{a\cdot(x^n_{Hoxa10}+x^n_{Runx1}+x^n_{BMP})}{1+a\cdot(x^n_{Hoxa10}+x^n_{Runx1}+x^n_{BMP})}\times\frac{1}{1+a\cdot(x^n_{C/EBP\beta}+x^n_{NR2F2}+x^n_{Stat5}+x^n_{TGF-\beta}+x^n_{FGFR3}+x^n_{Notch})}-x_{Runx2}$$

$$\frac{dx_{Sox2}}{dt} = \frac{a\cdot(x^n_{Stat3}+x^n_{FGFR2}+x^n_{AP2}+x^n_{Wnt})}{1+a\cdot(x^n_{Stat3}+x^n_{FGFR2}+x^n_{AP2}+x^n_{Wnt})}\times\frac{1}{1+a\cdot(x^n_{p21}+x^n_{Cdx2})}-x_{Sox2}$$

$$\frac{dx_{Sox4}}{dt} = \frac{a\cdot(x^n_{Sox7}+x^n_{Stat5}+x^n_{TGF-\beta}+x^n_{Wnt})}{1+a\cdot(x^n_{Sox7}+x^n_{Stat5}+x^n_{TGF-\beta}+x^n_{Wnt})}\times\frac{1}{1+a\cdot(x^n_{C/EBP\alpha})}-x_{Sox4}$$

$$\frac{dx_{Sox7}}{dt} = \frac{a\cdot(x^n_{BMP}+x^n_{VEGF}+x^n_{c-Jun})}{1+a\cdot(x^n_{BMP}+x^n_{VEGF}+x^n_{c-Jun})}\times\frac{1}{1+a\cdot(x^n_{PRDM14})}-x_{Sox7}$$

$$\begin{aligned}\frac{dx_{Sox9}}{dt} &= \frac{a\cdot(x^n_{TGF-\beta}+x^n_{BMP}+x^n_{FGFR3}+x^n_{AP2}+x^n_{PKA}+x^n_{Notch}+x^n_{SHH}+x^n_{Wnt})}{1+a\cdot(x^n_{TGF-\beta}+x^n_{BMP}+x^n_{FGFR3}+x^n_{AP2}+x^n_{PKA}+x^n_{Notch}+x^n_{SHH}+x^n_{Wnt})}\\&\quad\times\frac{1}{1+a\cdot(x^n_{RARs}+x^n_{IL-1}+x^n_{NF-\kappa B}+x^n_{c-Jun})}-x_{Sox9}\end{aligned}$$

$$\frac{dx_{PPAR\gamma}}{dt} = \frac{a\cdot(x^n_{C/EBP\alpha}+x^n_{C/EBP\beta})}{1+a\cdot(x^n_{C/EBP\alpha}+x^n_{C/EBP\beta})}\times\frac{1}{1+a\cdot(x^n_{RARs}+x^n_{NR2F2}+x^n_{Stat5}+x^n_{TGF-\beta}+x^n_{TNF-\alpha}+x^n_{SHH})}-x_{PPAR\gamma}$$

$$\frac{dx_{GR}}{dt} = \frac{a\cdot(x^n_{HNF1}+x^n_{TGF-\beta})}{1+a\cdot(x^n_{HNF1}+x^n_{TGF-\beta})}\times\frac{1}{1+a\cdot(x^n_{NR4A}+x^n_{NR2F2})}-x_{GR}$$

$$\frac{dx_{NR4A}}{dt} = \frac{a\cdot(x^n_{Runx1}+x^n_{EGFR}+x^n_{VEGF})}{1+a\cdot(x^n_{Runx1}+x^n_{EGFR}+x^n_{VEGF})}\times\frac{1}{1+a\cdot(x^n_{HNF4\alpha}+x^n_{GR})}-x_{NR4A}$$

$$\frac{dx_{RARs}}{dt} = \frac{a\cdot(x^n_{PPAR\gamma}+x^n_{AP2})}{1+a\cdot(x^n_{PPAR\gamma}+x^n_{AP2})}\times\frac{1}{1+a\cdot(x^n_{NR2F2}+x^n_{MAPK})}-x_{RARs}$$

$$\frac{dx_{NR2F2}}{dt} = \frac{a\cdot(x^n_{Gata4/6}+x^n_{HNF4\alpha}+x^n_{GR}+x^n_{MAPK}+x^n_{SHH}+x^n_{Wnt})}{1+a\cdot(x^n_{Gata4/6}+x^n_{HNF4\alpha}+x^n_{GR}+x^n_{MAPK}+x^n_{SHH}+x^n_{Wnt})}-x_{NR2F2}$$

$$\frac{dx_{G-CSR}}{dt} = \frac{a\cdot(x^n_{C/EBP\alpha}+x^n_{Pu.1}+x^n_{NF-\kappa B})}{1+a\cdot(x^n_{C/EBP\alpha}+x^n_{Pu.1}+x^n_{NF-\kappa B})}\times\frac{1}{1+a\cdot(x^n_{GR})}-x_{G-CSR}$$

$$\frac{dx_{IL-1}}{dt} = \frac{a\cdot(x^n_{C/EBP\beta}+x^n_{NF-\kappa B}+x^n_{OPN})}{1+a\cdot(x^n_{C/EBP\beta}+x^n_{NF-\kappa B}+x^n_{OPN})}\times\frac{1}{1+a\cdot(x^n_{C/EBP\alpha}+x^n_{Akt})}-x_{IL-1}$$

$$\frac{dx_{IL-10}}{dt} = \frac{a\cdot(x^n_{Fas}+x^n_{TNF-\alpha})}{1+a\cdot(x^n_{Fas}+x^n_{TNF-\alpha})}\times\frac{1}{1+a\cdot(x^n_{IL-10})}-x_{IL-10}$$

$$\frac{dx_{IL-3}}{dt} = \frac{a\cdot(x^n_{C/EBP\alpha}+x^n_{Gata1/2}+x^n_{Runx1})}{1+a\cdot(x^n_{C/EBP\alpha}+x^n_{Gata1/2}+x^n_{Runx1})}-x_{IL-3}$$

$$\frac{dx_{IL-6}}{dt} = \frac{a\cdot(x^n_{C/EBP\beta}+x^n_{Hoxa3}+x^n_{NF-\kappa B}+x^n_{NGAL})}{1+a\cdot(x^n_{C/EBP\beta}+x^n_{Hoxa3}+x^n_{NF-\kappa B}+x^n_{NGAL})}\times\frac{1}{1+a\cdot(x^n_{HNF4\alpha}+x^n_{Sox2}+x^n_{RARs})}-x_{IL-6}$$

$$\frac{dx_{i\kappa B}}{dt} = \frac{a\cdot(x^n_{GR}+x^n_{NR4A}+x^n_{NF-\kappa B}+x^n_{TGF-\beta})}{1+a\cdot(x^n_{GR}+x^n_{NR4A}+x^n_{NF-\kappa B}+x^n_{TGF-\beta})}\times\frac{1}{1+a\cdot(x^n_{Fas}+x^n_{TNF-\alpha}+x^n_{EGFR}+x^n_{Akt})}-x_{i\kappa B}$$

$$\frac{dx_{NF-\kappa B}}{dt} = \frac{a\cdot(x^n_{C/EBP\beta}+x^n_{IL-1}+x^n_{TNF-\alpha}+x^n_{CCK})}{1+a\cdot(x^n_{C/EBP\beta}+x^n_{IL-1}+x^n_{TNF-\alpha}+x^n_{CCK})}\times\frac{1}{1+a\cdot(x^n_{Cdx2}+x^n_{Foxa1}+x^n_{Sox2}+x^n_{PPAR\gamma}+x^n_{IL-10}+x^n_{i\kappa B}+x^n_{IR})}-x_{NF-\kappa B}$$

$$\begin{aligned}\frac{dx_{Stat3}}{dt} &= \frac{a\cdot(x^n_{G-CSR}+x^n_{IL-6}+x^n_{CCK}+x^n_{FGFR2}+x^n_{FGFR3}+x^n_{FGFR4}+x^n_{Gast}+x^n_{HGF}+x^n_{VEGF}+x^n_{OPN})}{1+a\cdot(x^n_{G-CSR}+x^n_{IL-6}+x^n_{CCK}+x^n_{FGFR2}+x^n_{FGFR3}+x^n_{FGFR4}+x^n_{Gast}+x^n_{HGF}+x^n_{VEGF}+x^n_{OPN})}\\&\quad\times\frac{1}{1+a\cdot(x^n_{Gata1/2}+x^n_{PPAR\gamma}+x^n_{RARs}+x^n_{PTEN})}-x_{Stat3}\end{aligned}$$

$$\frac{dx_{Stat5}}{dt} = \frac{a\cdot(x^n_{G-CSR}+x^n_{IL-3}+x^n_{FGFR2}+x^n_{IR}+x^n_{VEGF})}{1+a\cdot(x^n_{G-CSR}+x^n_{IL-3}+x^n_{FGFR2}+x^n_{IR}+x^n_{VEGF})}\times\frac{1}{1+a\cdot(x^n_{HNF4\alpha}+x^n_{Runx1}+x^n_{Runx2}+x^n_{TGF-\beta})}-x_{Stat5}$$

$$\begin{aligned}
\frac{dx_{TGF-\beta}}{dt} &= \frac{a\cdot(x_{Hoxa10}^n + x_{Hoxa3}^n + x_{Hoxa9}^n + x_{Sox7}^n + x_{Stat3}^n + x_{TNF-\alpha}^n + x_{p53}^n + x_{NOG}^n + x_{OPN}^n)}{1 + a\cdot(x_{Hoxa10}^n + x_{Hoxa3}^n + x_{Hoxa9}^n + x_{Sox7}^n + x_{Stat3}^n + x_{TNF-\alpha}^n + x_{p53}^n + x_{NOG}^n + x_{OPN}^n)} \\
&\quad \times \frac{1}{1 + a\cdot(x_{Gata4/6}^n + x_{Sox2}^n + x_{RARs}^n + x_{NR2F2}^n + x_{NF-\kappa B}^n + x_{Stat5}^n)} - x_{TGF-\beta} \\
\frac{dx_{TNF-\alpha}}{dt} &= \frac{a\cdot(x_{IL-1}^n + x_{NF-\kappa B}^n)}{1 + a\cdot(x_{IL-1}^n + x_{NF-\kappa B}^n)} \times \frac{1}{1 + a\cdot(x_{IL-10}^n)} - x_{TNF-\alpha} \\
\frac{dx_{BMP}}{dt} &= \frac{a\cdot(x_{Gata4/6}^n + x_{Runx1}^n + x_{EGFR}^n + x_{FGFR2}^n)}{1 + a\cdot(x_{Gata4/6}^n + x_{Runx1}^n + x_{EGFR}^n + x_{FGFR2}^n)} \times \frac{1}{1 + a\cdot(x_{HNF4\alpha}^n + x_{NR2F2}^n + x_{TGF-\beta}^n + x_{NOG}^n)} - x_{BMP} \\
\frac{dx_{CCK}}{dt} &= \frac{a\cdot(x_{C/EBP\beta}^n + x_{Cdx2}^n + x_{Gata4/6}^n + x_{IL-1}^n + x_{Gast}^n + x_{IR}^n)}{1 + a\cdot(x_{C/EBP\beta}^n + x_{Cdx2}^n + x_{Gata4/6}^n + x_{IL-1}^n + x_{Gast}^n + x_{IR}^n)} - x_{CCK} \\
\frac{dx_{EGFR}}{dt} &= \frac{a\cdot(x_{Myc}^n + x_{Runx1}^n + x_{Sox4}^n + x_{HIF}^n)}{1 + a\cdot(x_{Myc}^n + x_{Runx1}^n + x_{Sox4}^n + x_{HIF}^n)} \times \frac{1}{1 + a\cdot(x_{PTEN}^n)} - x_{EGFR} \\
\frac{dx_{FGF2}}{dt} &= \frac{a\cdot(x_{Hoxa10}^n + x_{HSPG2}^n)}{1 + a\cdot(x_{Hoxa10}^n + x_{HSPG2}^n)} - x_{FGF2} \\
\frac{dx_{FGF4/8}}{dt} &= \frac{a\cdot(x_{SHH}^n)}{1 + a\cdot(x_{SHH}^n)} \times \frac{1}{1 + a\cdot(x_{Notch}^n)} - x_{FGF4/8} \\
\frac{dx_{FGF7}}{dt} &= \frac{a\cdot(x_{IL-1}^n + x_{HSPG2}^n)}{1 + a\cdot(x_{IL-1}^n + x_{HSPG2}^n)} - x_{FGF7} \\
\frac{dx_{FGF9}}{dt} &= \frac{a\cdot(x_{Sox9}^n)}{1 + a\cdot(x_{Sox9}^n)} - x_{FGF9} \\
\frac{dx_{FGFR2}}{dt} &= \frac{a\cdot(x_{Hoxa10}^n + x_{Runx2}^n + x_{FGF2}^n + x_{FGF7}^n)}{1 + a\cdot(x_{Hoxa10}^n + x_{Runx2}^n + x_{FGF2}^n + x_{FGF7}^n)} \times \frac{1}{1 + a\cdot(x_{PRDM14}^n)} - x_{FGFR2} \\
\frac{dx_{FGFR3}}{dt} &= \frac{a\cdot(x_{FGF9}^n)}{1 + a\cdot(x_{FGF9}^n)} - x_{FGFR3} \\
\frac{dx_{FGFR4}}{dt} &= \frac{a\cdot(x_{FGF4/8}^n + x_{FGF9}^n)}{1 + a\cdot(x_{FGF4/8}^n + x_{FGF9}^n)} - x_{FGFR4} \\
\frac{dx_{Gast}}{dt} &= \frac{a\cdot(x_{Sox2}^n + x_{TGF-\beta}^n + x_{Wnt}^n)}{1 + a\cdot(x_{Sox2}^n + x_{TGF-\beta}^n + x_{Wnt}^n)} - x_{Gast} \\
\frac{dx_{HGF}}{dt} &= \frac{a\cdot(x_{NF-\kappa B}^n + x_{c-Jun}^n + x_{HIF}^n)}{1 + a\cdot(x_{NF-\kappa B}^n + x_{c-Jun}^n + x_{HIF}^n)} \times \frac{1}{1 + a\cdot(x_{GR}^n + x_{TGF-\beta}^n)} - x_{HGF} \\
\frac{dx_{IR}}{dt} &= \frac{a\cdot(x_{C/EBP\alpha}^n + x_{PPAR\gamma}^n + x_{SHH}^n + x_{Wnt}^n)}{1 + a\cdot(x_{C/EBP\alpha}^n + x_{PPAR\gamma}^n + x_{SHH}^n + x_{Wnt}^n)} \times \frac{1}{1 + a\cdot(x_{TNF-\alpha}^n + x_{Notch}^n)} - x_{IR} \\
\frac{dx_{VEGF}}{dt} &= \frac{a\cdot(x_{Gata4/6}^n + x_{PGC-1}^n + x_{NR4A}^n + x_{NR2F2}^n + x_{Stat3}^n + x_{TGF-\beta}^n + x_{HIF}^n)}{1 + a\cdot(x_{Gata4/6}^n + x_{PGC-1}^n + x_{NR4A}^n + x_{NR2F2}^n + x_{Stat3}^n + x_{TGF-\beta}^n + x_{HIF}^n)} \\
&\quad \times \frac{1}{1 + a\cdot(x_{Runx1}^n + x_{Sox9}^n + x_{RARs}^n + x_{Notch}^n)} - x_{VEGF} \\
\frac{dx_{Akt}}{dt} &= \frac{a\cdot(x_{Ras}^n + x_{RARs}^n + x_{NF-\kappa B}^n + x_{CCK}^n + x_{EGFR}^n + x_{FGFR2}^n + x_{HGF}^n + x_{IR}^n + x_{c-Jun}^n + x_{PKA}^n + x_{Notch}^n)}{1 + a\cdot(x_{Ras}^n + x_{RARs}^n + x_{NF-\kappa B}^n + x_{CCK}^n + x_{EGFR}^n + x_{FGFR2}^n + x_{HGF}^n + x_{IR}^n + x_{c-Jun}^n + x_{PKA}^n + x_{Notch}^n)} \\
&\quad \times \frac{1}{1 + a\cdot(x_{PTEN}^n)} - x_{Akt} \\
\frac{dx_{AP2}}{dt} &= \frac{a\cdot(x_{C/EBP\beta}^n + x_{RARs}^n + x_{NR2F2}^n)}{1 + a\cdot(x_{C/EBP\beta}^n + x_{RARs}^n + x_{NR2F2}^n)} - x_{AP2} \\
\frac{dx_{c-Jun}}{dt} &= \frac{a\cdot(x_{Runx1}^n + x_{TNF-\alpha}^n + x_{CCK}^n + x_{EGFR}^n + x_{FGFR3}^n + x_{Akt}^n)}{1 + a\cdot(x_{Runx1}^n + x_{TNF-\alpha}^n + x_{CCK}^n + x_{EGFR}^n + x_{FGFR3}^n + x_{Akt}^n)} \times \frac{1}{1 + a\cdot(x_{C/EBP\alpha}^n + x_{GR}^n + x_{Mkp2}^n)} - x_{c-Jun} \\
\frac{dx_{HIF}}{dt} &= \frac{a\cdot(x_{NR4A}^n + x_{Stat3}^n + x_{Akt}^n)}{1 + a\cdot(x_{NR4A}^n + x_{Stat3}^n + x_{Akt}^n)} \times \frac{1}{1 + a\cdot(x_{p53}^n)} - x_{HIF} \\
\frac{dx_{MAPK}}{dt} &= \frac{a\cdot(x_{Ras}^n + x_{PPAR\gamma}^n + x_{NR2F2}^n + x_{NF-\kappa B}^n + x_{FGFR2}^n + x_{FGFR3}^n + x_{Integrin}^n)}{1 + a\cdot(x_{Ras}^n + x_{PPAR\gamma}^n + x_{NR2F2}^n + x_{NF-\kappa B}^n + x_{FGFR2}^n + x_{FGFR3}^n + x_{Integrin}^n)} \times \frac{1}{1 + a\cdot(x_{TGF-\beta}^n + x_{PTEN}^n)} - x_{MAPK} \\
\frac{dx_{Mkp2}}{dt} &= \frac{a\cdot(x_{Hoxa10}^n)}{1 + a\cdot(x_{Hoxa10}^n)} - x_{Mkp2} \\
\frac{dx_{PKA}}{dt} &= \frac{a\cdot(x_{TGF-\beta}^n + x_{EGFR}^n + x_{Akt}^n)}{1 + a\cdot(x_{TGF-\beta}^n + x_{EGFR}^n + x_{Akt}^n)} \times \frac{1}{1 + a\cdot(x_{p53}^n)} - x_{PKA} \\
\frac{dx_{PTEN}}{dt} &= \frac{a\cdot(x_{PPAR\gamma}^n + x_{AP2}^n + x_{p53}^n)}{1 + a\cdot(x_{PPAR\gamma}^n + x_{AP2}^n + x_{p53}^n)} \times \frac{1}{1 + a\cdot(x_{NF-\kappa B}^n + x_{Stat3}^n)} - x_{PTEN} \\
\frac{dx_{p53}}{dt} &= \frac{a\cdot(x_{Myc}^n + x_{PPAR\gamma}^n + x_{RARs}^n + x_{AP2}^n + x_{PTEN}^n)}{1 + a\cdot(x_{Myc}^n + x_{PPAR\gamma}^n + x_{RARs}^n + x_{AP2}^n + x_{PTEN}^n)} \times \frac{1}{1 + a\cdot(x_{Sox4}^n + x_{Akt}^n + x_{Notch}^n)} - x_{p53} \\
\frac{dx_{E-Cadherin}}{dt} &= \frac{a\cdot(x_{Cdx2}^n + x_{Foxa1}^n + x_{Foxa2}^n + x_{HNF4\alpha}^n + x_{AP2}^n)}{1 + a\cdot(x_{Cdx2}^n + x_{Foxa1}^n + x_{Foxa2}^n + x_{HNF4\alpha}^n + x_{AP2}^n)}
\end{aligned}$$

$$\times \frac{1}{1 + a \cdot (x_{Stat3}^n + x_{TGF-\beta}^n + x_{TNF-\alpha}^n + x_{EGFR}^n + x_{Akt}^n + x_{HIF}^n + x_{SHH}^n)} - x_{E-Cadherin}$$

$$\frac{dx_{HSPG2}}{dt} = \frac{a \cdot (x_{Runx2}^n + x_{TGF-\beta}^n)}{1 + a \cdot (x_{Runx2}^n + x_{TGF-\beta}^n)} - x_{HSPG2}$$

$$\frac{dx_{Integrin}}{dt} = \frac{a \cdot (x_{TNF-\alpha}^n + x_{EGFR}^n + x_{VEGF}^n + x_{MAPK}^n)}{1 + a \cdot (x_{TNF-\alpha}^n + x_{EGFR}^n + x_{VEGF}^n + x_{MAPK}^n)} \times \frac{1}{1 + a \cdot (x_{Myc}^n + x_{Ras}^n + x_{SHH}^n)} - x_{Integrin}$$

$$\frac{dx_{Notch}}{dt} = \frac{a \cdot (x_{Cdx2}^n + x_{HNF1}^n + x_{NF-\kappa B}^n + x_{Stat3}^n + x_{FGFR2}^n + x_{MAPK}^n)}{1 + a \cdot (x_{Cdx2}^n + x_{HNF1}^n + x_{NF-\kappa B}^n + x_{Stat3}^n + x_{FGFR2}^n + x_{MAPK}^n)}$$

$$\times \frac{1}{1 + a \cdot (x_{C/EBP\alpha}^n + x_{Hoxa5}^n + x_{NR2F2}^n + x_{BMP}^n + x_{E-Cadherin}^n)} - x_{Notch}$$

$$\frac{dx_{NGAL}}{dt} = \frac{a \cdot (x_{Runx1}^n + x_{TNF-\alpha}^n)}{1 + a \cdot (x_{Runx1}^n + x_{TNF-\alpha}^n)} - x_{NGAL}$$

$$\frac{dx_{NOG}}{dt} = \frac{a \cdot (x_{Sox9}^n + x_{SHH}^n + x_{Wnt}^n)}{1 + a \cdot (x_{Sox9}^n + x_{SHH}^n + x_{Wnt}^n)} \times \frac{1}{1 + a \cdot (x_{FGFR2}^n)} - x_{NOG}$$

$$\frac{dx_{OPN}}{dt} = \frac{a \cdot (x_{Runx1}^n + x_{Runx2}^n + x_{TGF-\beta}^n)}{1 + a \cdot (x_{Runx1}^n + x_{Runx2}^n + x_{TGF-\beta}^n)} \times \frac{1}{1 + a \cdot (x_{PGC-1}^n)} - x_{OPN}$$

$$\frac{dx_{SHH}}{dt} = \frac{a \cdot (x_{Foxa1}^n + x_{Sox2}^n + x_{TGF-\beta}^n)}{1 + a \cdot (x_{Foxa1}^n + x_{Sox2}^n + x_{TGF-\beta}^n)} \times \frac{1}{1 + a \cdot (x_{Foxa2}^n + x_{Hes1}^n + x_{BMP}^n + x_{FGFR2}^n)} - x_{SHH}$$

$$\frac{dx_{Wnt}}{dt} = \frac{a \cdot (x_{Gata4/6}^n + x_{PGC-1}^n + x_{Sox4}^n + x_{TGF-\beta}^n + x_{EGFR}^n + x_{FGFR2}^n + x_{FGFR3}^n + x_{HGF}^n + x_{IR}^n)}{1 + a \cdot (x_{Gata4/6}^n + x_{PGC-1}^n + x_{Sox4}^n + x_{TGF-\beta}^n + x_{EGFR}^n + x_{FGFR2}^n + x_{FGFR3}^n + x_{HGF}^n + x_{IR}^n)}$$

$$\times \frac{1}{1 + a \cdot (x_{Cdx2}^n + x_{HNF4\alpha}^n + x_{Sox7}^n + x_{Sox9}^n)} - x_{Wnt}$$

B. Robustness of the modeling results

1. *Random parameter tests*

The results and details of the random parameter tests are summarized in Fig. S2.

2. *Robustness tests by using alternative forms of equations*

We use two alternative forms of differential equations to verify the robustness [1] of the attractors we obtained.

a. Alternative form (a) The first alternative form can be expressed as, for each x_i:

$$\frac{dx_i}{dt} = -x_i + \frac{1}{|act|} \left(\sum_{u \in act} \frac{a \cdot x_u^n}{1 + a \cdot x_u^n} \right) \cdot \frac{1}{1 + a \cdot (\sum_{v \in inh} x_v^n)} \tag{5}$$

where $i = 1, \ldots, 89$, *act* represents the set of all nodes that activate x_i and *inh* the set of nodes that inhibit x_i, and $|act|$ here means the total number of nodes in *act*. For instance, if x_2, x_3, x_4 activate x_1 and x_5, x_6 inhibit x_1, we have

$$\frac{dx_1}{dt} = -x_1 + \frac{1}{3}\left(\frac{a \cdot x_2^n}{1 + a \cdot x_2^n} + \frac{a \cdot x_3^n}{1 + a \cdot x_3^n} + \frac{a \cdot x_4^n}{1 + a \cdot x_4^n}\right) \cdot \frac{1}{1 + a \cdot (x_5^n + x_6^n)} \tag{6}$$

Using *Euler method*, all 10 attractors are obtained (See Table S4).

b. Alternative form (b) A formal representation for the second form would be, for each x_i:

$$\frac{dx_i}{dt} = -x_i + \frac{a \cdot (\sum_{u \in act} x_u)^n}{1 + a \cdot (\sum_{u \in act} x_u)^n} \cdot \frac{1}{1 + a \cdot (\sum_{v \in inh} x_v)^n} \tag{7}$$

where $i = 1, \ldots, 89$, act represents the set of all nodes that activate x_i and inh the set of nodes that inhibit x_i. For example, if x_2, x_3, x_4 activate x_1 and x_5, x_6 inhibit x_1, we have

$$\frac{dx_1}{dt} = -x_1 + \frac{a \cdot (x_2 + x_3 + x_4)^n}{1 + a \cdot (x_2 + x_3 + x_4)^n} \cdot \frac{1}{1 + a \cdot (x_5 + x_6)^n} \; . \tag{8}$$

By using *Euler method*, 9 attractors are found with values listed in Table S5. Among them, 8 attractors directly correspond to those obtained in in Table S3. Interestingly, we also found a limit cycle attractor. The averaged value along one period of the limit cycle is put in Table S5. It has features of both S5 and S6.

3. Comparison with Boolean dynamics

Boolean network modeling as an effective and simple tool have been used for the modeling of biological networks [2] and endogenous molecular-cellular networks [3–5]. To test the robustness of the attractors obtained from differential equations, we employed Boolean network with threshold functions to model our network as well. Each x_i has two states, ON $x_i = 1$ or OFF $x_i = 0$. The dynamics of the Boolean network is defined as

$$x_i(t+1) = \begin{cases} 0 & \sum_j r_{ij} x_j(t) <= 0 \\ 1 & \sum_j r_{ij} x_j(t) > 0 \end{cases}$$

where the adjacent matrix R for the network has elements r_{ij}. $r_{ij} = 1$ represents that node i is activated by node j, and $r_{ij} = -100$ denotes node i is inhibited by node j. Inhibition is dominant in our model corresponds to a usual biological situation. We show that the attractors obtained from differential equations are consistent Boolean network modeling in Table S6.

C. Transitions between attractors

There are different ways of implementing transitions between attractors. They may be classified as: a) stochastic transition as a result of internal fluctuation. For two attractors connected by a saddle point, the most probable path of the stochastic transition usually go through the saddle point. The landscape (Fig. 3(a)) demonstrates the connections between attractors by saddle and other unstable fixed points as a roadmap of stochastic transitions. b) induced transition by external perturbation. Perturbations may cause by environmental change or drug treatment. These perturbations can be impulsive, continuous, or has a specific pattern. The effects are able to be carried out based on our modeling results. The whole phase space (each point in the space represents a distinct state of the system) is separated by attractive basins of the attractors, which means, for instance, starting inside the basin of S1, the system will go to S1 afterwards. As an illustration, for a given attractor, we enumerate the combinations of 3 nodes with down-regulation to 0 and up-regulation to 1 separately to generate perturbed starting positions that may fall into other attractive basins. Following the trajectories calculated by Euler method, we obtain the attractor the system will finally reach. Systematic investigation on induced switching between all 10 attractors is performed. Part of the results is drawn in Fig. 3(b). It suggests new biomarkers for CRC.

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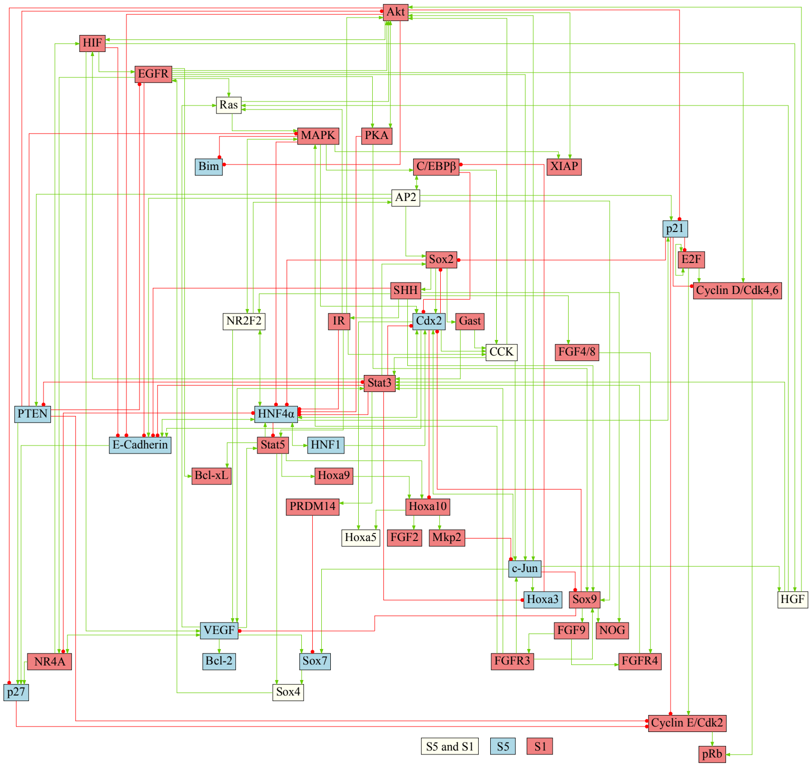
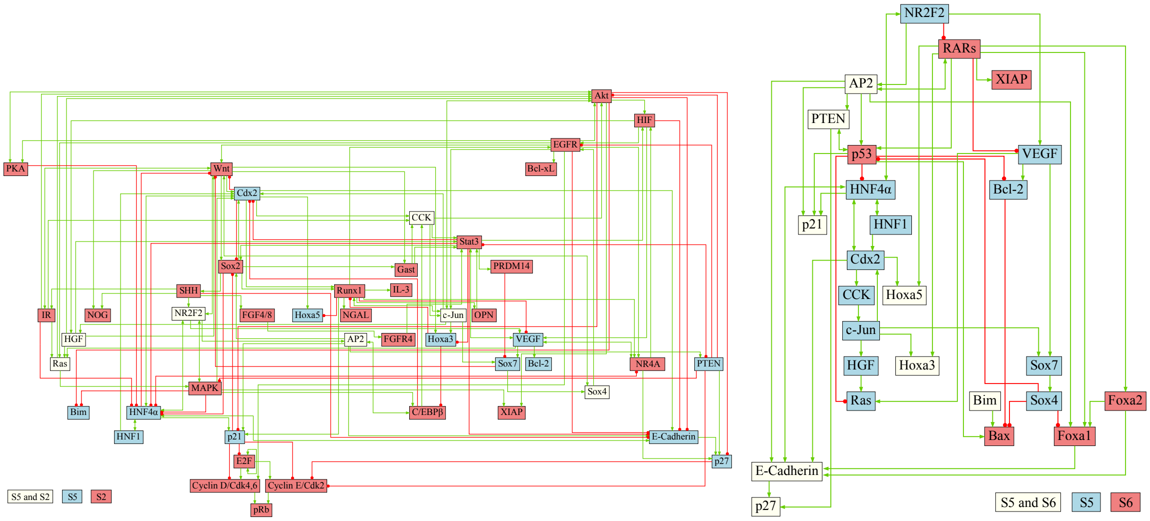
III. MORE SUPPLEMENTARY FIGURES AND TABLES



(a)Active nodes in S5 and S1



(b)Active nodes in S5 and S2

(c)Active nodes in S5 and S6

Fig. S1. Effective sub-networks between attractors. Effective sub-networks by selecting active nodes (> 0.5). Effective network for attractors (S5, S1), (S5, S2) and (S5, S6) (see Fig. 2) are overlaid in (a), (b), and (c). S1 and S2 are possible CRC like attractor. S5 is a normal intestine like attractor. S6 is mis-differentiated like attractor. The first graph shows that attractors S1 and S5 have few nodes in common. These two attractors form a kind of ”switch” since the interactions between their specific active nodes are mostly inhibitory. They are mutually suppressing at network level. The third graph suggests that stress signaling through p53 is a potential source for mis-differentiation.

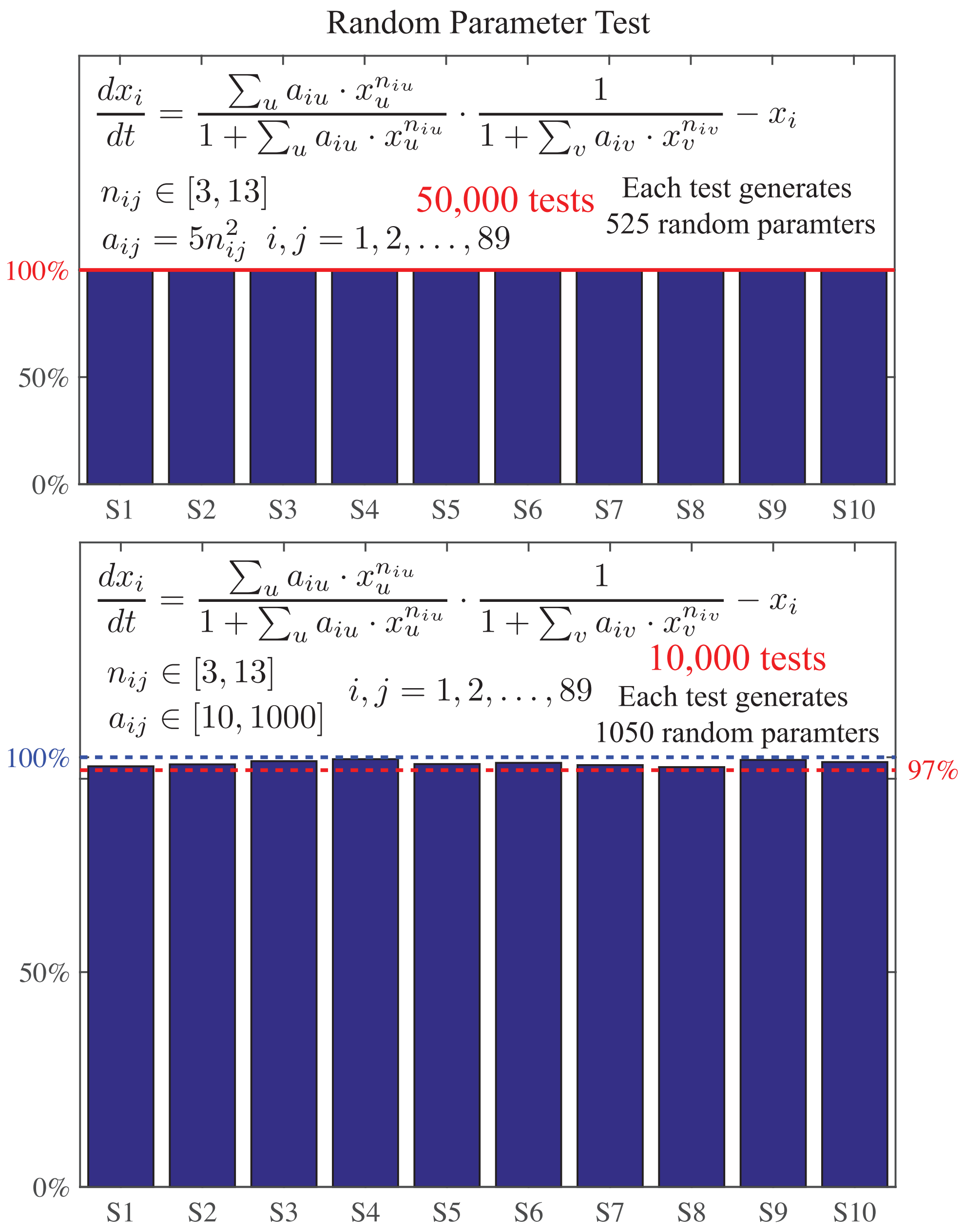


Fig. S2. Recurrence rate of attractors under random parameters. In the first test, we use the equations that enable different n_{ij} for each of the 525 interactions $i, j = 1, \ldots, 89$, where agent j to agent i has an interaction. With uniformly distributed real random numbers $n_{ij} \in [3, 13]$ and $a_{ij} = 5n_{ij}^2$, 50,000 tests show that all 10 attractors have 100% recurrence rate. In the second test, we also allow a_{ij} and n_{ij} are independent. Under the setting, we generate 10,000 sets (each set has $525 \times 2 = 1050$ random numbers) of random parameters with $a_{ij} \in [10, 1000]$, and $n_{ij} \in [3, 13]$, put into the equations, and calculate attractors using Euler method. The recurrence rate of each attractor calculated in Table S3 are shown here: the rates for all attractors are above 97%. Note that the $\sum_u$ means summation over all nodes activating node i and the $\sum_v$ means summation over all nodes inhibiting node i.

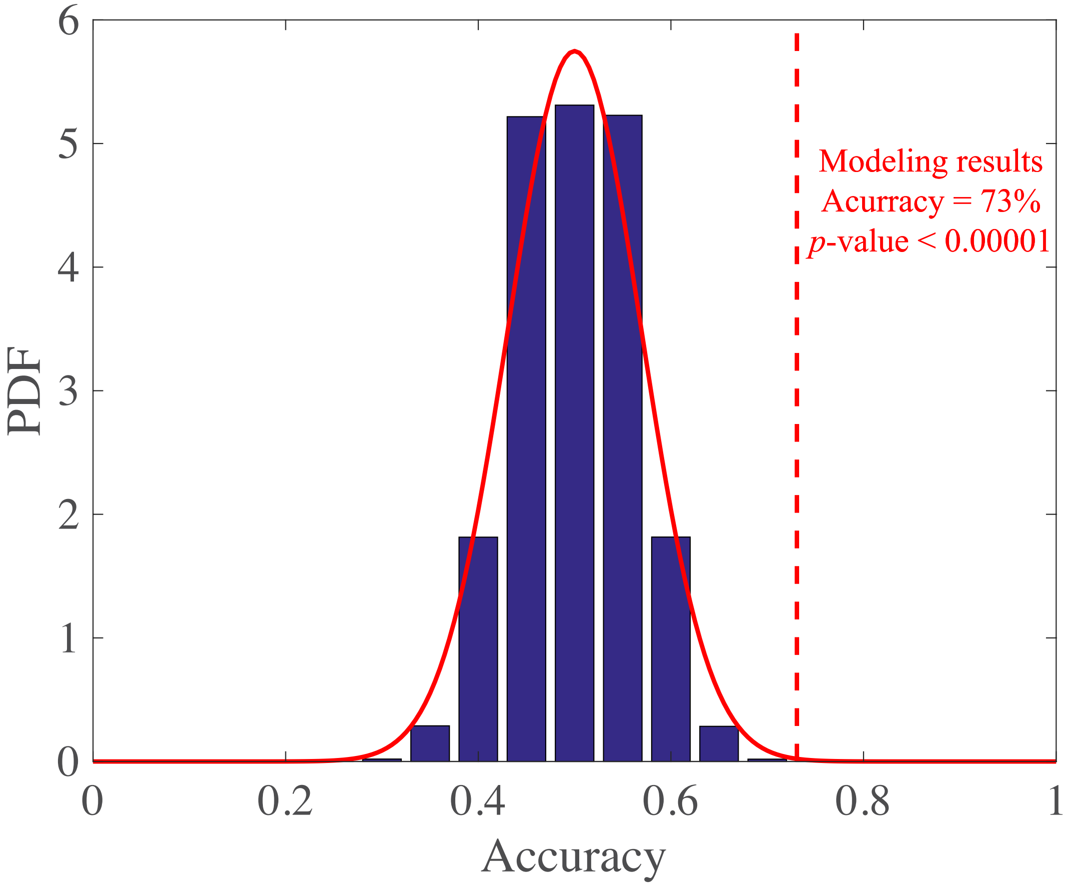


Fig. S3. Hypothesis test of modeling results *vs.* random guess. We generate one million random vectors consisting of 1 and -1. The distribution of the accuracy in comparing with the microarray data is shown here. We use a threshold value 5% for processing data (see Materials and Methods) with 78 genes determined as upregulated or downregulated in cancer. The modeling results have an accuracy rate 73% that corresponds to p-value < 0.00001.

Table S3. Molecular profile of computed attractors

	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10
Cyclin D/Cdk4,6	0.93	0.93	0.88	0.89	0.00	0.00	0.93	0.93	0.89	0.88
Cyclin E/Cdk2	0.85	0.84	0.01	0.01	0.00	0.00	0.84	0.85	0.01	0.01
E2F	0.86	0.86	0.01	0.01	0.00	0.00	0.86	0.86	0.01	0.01
Myc	0.10	0.10	0.10	0.10	0.00	0.00	0.10	0.10	0.10	0.10
p21	0.09	0.09	0.09	0.09	0.90	0.93	0.09	0.09	0.09	0.09
p27	0.09	0.09	0.09	0.09	0.90	0.93	0.09	0.09	0.09	0.09
pRb	0.93	0.93	0.87	0.88	0.00	0.00	0.93	0.93	0.88	0.87
Ras	0.95	0.96	0.95	0.96	0.89	0.00	0.96	0.95	0.96	0.95
Bad	0.00	0.00	0.00	0.00	0.00	0.10	0.00	0.00	0.00	0.00
Bax	0.00	0.00	0.00	0.00	0.07	0.94	0.00	0.00	0.00	0.00
Bcl-2	0.01	0.02	0.01	0.02	0.82	0.00	0.00	0.00	0.00	0.00
Bcl-xL	0.93	0.90	0.93	0.90	0.05	0.00	0.13	0.13	0.13	0.13
Bim	0.05	0.05	0.05	0.05	0.95	0.99	0.05	0.05	0.05	0.05
Caspase 3	0.00	0.00	0.00	0.00	0.00	0.00	0.85	0.85	0.85	0.85
Cytochrome C	0.00	0.00	0.00	0.00	0.00	0.10	0.84	0.83	0.84	0.83
Fas	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
XIAP	0.95	0.95	0.95	0.95	0.09	0.86	0.07	0.07	0.07	0.07
C/EBPα	0.02	0.03	0.02	0.03	0.11	0.02	0.03	0.02	0.03	0.02
C/EBPβ	0.94	0.93	0.94	0.93	0.13	0.12	0.93	0.94	0.93	0.94
Cdx2	0.04	0.05	0.04	0.05	0.88	0.02	0.05	0.04	0.05	0.04
Foxa1	0.12	0.11	0.12	0.11	0.11	0.95	0.11	0.12	0.11	0.12
Foxa2	0.05	0.05	0.05	0.05	0.03	0.86	0.05	0.05	0.05	0.05
Gata1/2	0.10	0.09	0.10	0.09	0.07	0.00	0.09	0.10	0.09	0.10
Gata4/6	0.05	0.04	0.05	0.04	0.13	0.00	0.04	0.05	0.04	0.05
Hes1	0.00	0.01	0.00	0.01	0.02	0.02	0.01	0.00	0.01	0.00
Hey2	0.00	0.01	0.00	0.01	0.00	0.00	0.01	0.00	0.01	0.00
HNF1	0.00	0.01	0.00	0.01	0.86	0.01	0.01	0.00	0.01	0.00
HNF4α	0.02	0.02	0.02	0.02	0.87	0.09	0.02	0.02	0.02	0.02
Hoxa10	0.92	0.01	0.92	0.01	0.00	0.00	0.01	0.92	0.01	0.92
Hoxa3	0.00	0.10	0.00	0.10	0.84	0.87	0.10	0.00	0.10	0.00
Hoxa5	0.87	0.00	0.87	0.00	0.85	0.87	0.00	0.87	0.00	0.87
Hoxa9	0.86	0.02	0.86	0.02	0.03	0.00	0.02	0.86	0.02	0.86
PGC-1	0.09	0.05	0.09	0.05	0.00	0.00	0.05	0.09	0.05	0.09
PRDM14	0.90	0.90	0.90	0.90	0.03	0.00	0.90	0.90	0.90	0.90
Pu.1	0.00	0.11	0.00	0.11	0.00	0.00	0.11	0.00	0.11	0.00
Runx1	0.12	0.93	0.12	0.93	0.14	0.00	0.93	0.12	0.93	0.12
Runx2	0.03	0.05	0.03	0.05	0.00	0.00	0.05	0.03	0.05	0.03
Sox2	0.94	0.95	0.94	0.95	0.06	0.10	0.95	0.94	0.95	0.94
Sox4	0.86	0.90	0.86	0.90	0.87	0.02	0.90	0.86	0.90	0.86
Sox7	0.00	0.11	0.00	0.11	0.92	0.00	0.11	0.00	0.11	0.00
Sox9	0.94	0.10	0.94	0.10	0.12	0.12	0.10	0.94	0.10	0.94
PPARγ	0.04	0.05	0.04	0.05	0.00	0.00	0.05	0.04	0.05	0.04
GR	0.00	0.00	0.00	0.00	0.11	0.02	0.00	0.00	0.00	0.00
NR4A	0.89	0.94	0.89	0.94	0.11	0.00	0.94	0.89	0.94	0.89
RARs	0.05	0.05	0.05	0.05	0.11	0.87	0.05	0.05	0.05	0.05

	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10
NR2F2	0.94	0.96	0.94	0.96	0.87	0.03	0.96	0.94	0.96	0.94
G-CSFR	0.00	0.01	0.00	0.01	0.03	0.00	0.01	0.00	0.01	0.00
IL-1	0.09	0.09	0.09	0.09	0.03	0.01	0.09	0.09	0.09	0.09
IL-10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
IL-3	0.03	0.89	0.03	0.89	0.04	0.00	0.89	0.03	0.89	0.03
IL-6	0.10	0.10	0.10	0.10	0.11	0.12	0.10	0.10	0.10	0.10
iκB	0.05	0.05	0.05	0.05	0.05	0.02	0.05	0.05	0.05	0.05
NF-κB	0.06	0.05	0.06	0.05	0.11	0.00	0.05	0.06	0.05	0.06
Stat3	0.95	0.96	0.95	0.96	0.14	0.00	0.96	0.95	0.96	0.95
Stat5	0.85	0.10	0.85	0.10	0.11	0.00	0.10	0.85	0.10	0.85
TGF-β	0.04	0.05	0.04	0.05	0.12	0.12	0.05	0.04	0.05	0.04
TNF-α	0.01	0.01	0.01	0.01	0.01	0.00	0.01	0.01	0.01	0.01
BMP	0.05	0.05	0.05	0.05	0.00	0.00	0.05	0.05	0.05	0.05
CCK	0.96	0.96	0.96	0.96	0.87	0.02	0.96	0.96	0.96	0.96
EGFR	0.93	0.95	0.93	0.95	0.13	0.00	0.95	0.93	0.95	0.93
FGF2	0.89	0.00	0.89	0.00	0.00	0.00	0.00	0.89	0.00	0.89
FGF4/8	0.87	0.87	0.87	0.87	0.00	0.02	0.87	0.87	0.87	0.87
FGF7	0.01	0.01	0.01	0.01	0.00	0.00	0.01	0.01	0.01	0.01
FGF9	0.89	0.01	0.89	0.01	0.02	0.02	0.01	0.89	0.01	0.89
FGFR2	0.11	0.00	0.11	0.00	0.00	0.00	0.00	0.11	0.00	0.11
FGFR3	0.88	0.00	0.88	0.00	0.00	0.00	0.00	0.88	0.00	0.88
FGFR4	0.93	0.87	0.93	0.87	0.00	0.00	0.87	0.93	0.87	0.93
Gast	0.89	0.95	0.89	0.95	0.02	0.03	0.95	0.89	0.95	0.89
HGF	0.90	0.95	0.90	0.95	0.83	0.00	0.95	0.90	0.95	0.90
IR	0.87	0.93	0.87	0.93	0.02	0.02	0.93	0.87	0.93	0.87
VEGF	0.10	0.11	0.10	0.11	0.82	0.00	0.11	0.10	0.11	0.10
Akt	0.97	0.98	0.97	0.98	0.14	0.09	0.98	0.97	0.98	0.97
AP2	0.94	0.94	0.94	0.94	0.87	0.87	0.94	0.94	0.94	0.94
c-Jun	0.12	0.97	0.12	0.97	0.85	0.01	0.97	0.12	0.97	0.12
HIF	0.96	0.96	0.96	0.96	0.06	0.00	0.96	0.96	0.96	0.96
MAPK	0.95	0.94	0.95	0.94	0.14	0.00	0.94	0.95	0.94	0.95
Mkp2	0.89	0.00	0.89	0.00	0.00	0.00	0.00	0.89	0.00	0.89
PKA	0.94	0.95	0.94	0.95	0.06	0.00	0.95	0.94	0.95	0.94
PTEN	0.09	0.09	0.09	0.09	0.83	0.94	0.09	0.09	0.09	0.09
p53	0.05	0.05	0.05	0.05	0.12	0.95	0.05	0.05	0.05	0.05
E-Cadherin	0.02	0.02	0.02	0.02	0.87	0.91	0.02	0.02	0.02	0.02
HSPG2	0.00	0.00	0.00	0.00	0.02	0.02	0.00	0.00	0.00	0.00
Integrin	0.06	0.06	0.06	0.06	0.11	0.00	0.06	0.06	0.06	0.06
Notch	0.06	0.10	0.06	0.10	0.05	0.00	0.10	0.06	0.10	0.06
NGAL	0.02	0.89	0.02	0.89	0.02	0.00	0.89	0.02	0.89	0.02
NOG	0.92	0.94	0.92	0.94	0.02	0.03	0.94	0.92	0.94	0.92
OPN	0.02	0.89	0.02	0.89	0.04	0.02	0.89	0.02	0.89	0.02
SHH	0.88	0.89	0.88	0.89	0.03	0.12	0.89	0.88	0.89	0.88
Wnt	0.10	0.95	0.10	0.95	0.04	0.02	0.95	0.10	0.95	0.10

This table has the original data for Fig. 2. They are calculated using equations listed in Sect. II A 1 with parameter $n = 3$ and $a = 10$ by two methods: a) *Newtonian iteration method* for solving fixed point including attractors as well as saddle points and other unstable fixed points and b) *Euler method* for calculating trajectories of differential equations. They generate identical result. 9 of the 10 attractors are obtained while calculating with 10,000 random initial positions. The 10th attractor can be calculated using perturbation around unstable fixed points. We further run the program with 100,000 and 1,000,000 initial positions, acquiring identical 10 attractors.

Table S4. Recurrence of attractors using different forms of equations. Alternative equation (a). All attractors are obtained. Here E1 denotes the results from Table S3; E2 denotes the results from the alternative equation (a).

	S1		S2		S3		S4		S5		S6		S7		S8		S9		S10	
	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1
Cyclin D/Cdk4,6	0.49	0.93	0.50	0.93	0.24	0.88	0.25	0.89	0.00	0.00	0.00	0.00	0.50	0.93	0.49	0.93	0.25	0.89	0.24	0.88
Cyclin E/Cdk2	0.49	0.85	0.49	0.84	0.00	0.01	0.00	0.01	0.00	0.00	0.00	0.00	0.49	0.84	0.49	0.85	0.00	0.01	0.00	0.01
E2F	0.49	0.86	0.49	0.86	0.00	0.01	0.00	0.01	0.00	0.00	0.00	0.00	0.49	0.86	0.49	0.86	0.00	0.01	0.00	0.01
Myc	0.00	0.10	0.00	0.10	0.00	0.10	0.00	0.10	0.00	0.00	0.00	0.00	0.00	0.10	0.00	0.10	0.00	0.10	0.00	0.10
p21	0.00	0.09	0.00	0.09	0.00	0.09	0.00	0.09	0.25	0.90	0.24	0.93	0.00	0.09	0.00	0.09	0.00	0.09	0.00	0.09
p27	0.00	0.09	0.00	0.09	0.00	0.09	0.00	0.09	0.40	0.90	0.40	0.93	0.00	0.09	0.00	0.09	0.00	0.09	0.00	0.09
pRb	0.98	0.93	0.98	0.93	0.44	0.87	0.44	0.88	0.00	0.00	0.00	0.00	0.98	0.93	0.98	0.93	0.44	0.88	0.44	0.87
Ras	0.47	0.95	0.50	0.96	0.47	0.95	0.50	0.96	0.20	0.89	0.00	0.00	0.50	0.96	0.47	0.95	0.50	0.96	0.47	0.95
Bad	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Bax	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.07	0.99	0.94	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Bcl-2	0.00	0.01	0.00	0.02	0.00	0.01	0.00	0.02	0.20	0.82	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Bcl-xL	0.56	0.93	0.33	0.90	0.56	0.93	0.33	0.90	0.00	0.05	0.00	0.00	0.03	0.13	0.05	0.13	0.03	0.13	0.05	0.13
Bim	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05	1.00	0.95	1.00	0.99	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05
Caspase 3	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.23	0.85	0.22	0.85	0.23	0.85	0.22	0.85
Cytochrome C	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.10	0.28	0.84	0.26	0.83	0.28	0.84	0.26	0.83
Fas	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
XIAP	0.39	0.95	0.38	0.95	0.39	0.95	0.38	0.95	0.01	0.09	0.19	0.86	0.01	0.07	0.01	0.07	0.01	0.07	0.01	0.07
C/EBPα	0.00	0.02	0.00	0.03	0.00	0.02	0.00	0.03	0.02	0.11	0.00	0.02	0.00	0.03	0.00	0.02	0.00	0.03	0.00	0.02
C/EBPβ	0.66	0.94	0.64	0.93	0.66	0.94	0.64	0.93	0.04	0.13	0.01	0.12	0.64	0.93	0.66	0.94	0.64	0.93	0.66	0.94
Cdx2	0.00	0.04	0.00	0.05	0.00	0.04	0.00	0.05	0.29	0.88	0.00	0.02	0.00	0.05	0.00	0.04	0.00	0.05	0.00	0.04
Foxa1	0.05	0.12	0.02	0.11	0.05	0.12	0.02	0.11	0.02	0.11	0.96	0.95	0.02	0.11	0.05	0.12	0.02	0.11	0.05	0.12
Foxa2	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05	0.01	0.03	0.33	0.86	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05
Gata1/2	0.00	0.10	0.00	0.09	0.00	0.10	0.00	0.09	0.05	0.07	0.00	0.00	0.00	0.09	0.00	0.10	0.00	0.09	0.00	0.10
Gata4/6	0.00	0.05	0.00	0.04	0.00	0.05	0.00	0.04	0.10	0.13	0.00	0.00	0.00	0.04	0.00	0.05	0.00	0.04	0.00	0.05
Hes1	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.02	0.00	0.02	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.00
Hey2	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.00
HNF1	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.01	0.49	0.86	0.00	0.01	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.00
HNF4α	0.00	0.02	0.00	0.02	0.00	0.02	0.00	0.02	0.57	0.87	0.00	0.09	0.00	0.02	0.00	0.02	0.00	0.02	0.00	0.02
Hoxa10	0.53	0.92	0.00	0.01	0.53	0.92	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.53	0.92	0.00	0.01	0.53	0.92
Hoxa3	0.00	0.00	0.01	0.10	0.00	0.00	0.01	0.10	0.19	0.84	0.33	0.87	0.01	0.10	0.00	0.00	0.01	0.10	0.00	0.00
Hoxa5	0.32	0.87	0.00	0.00	0.32	0.87	0.00	0.00	0.30	0.85	0.33	0.87	0.00	0.00	0.32	0.87	0.00	0.00	0.32	0.87
Hoxa9	0.24	0.86	0.00	0.02	0.24	0.86	0.00	0.02	0.00	0.03	0.00	0.00	0.00	0.02	0.24	0.86	0.00	0.02	0.24	0.86
PGC-1	0.01	0.09	0.00	0.05	0.01	0.09	0.00	0.05	0.01	0.00	0.00	0.00	0.00	0.05	0.01	0.09	0.00	0.05	0.01	0.09
PRDM14	0.98	0.90	0.98	0.90	0.98	0.90	0.98	0.90	0.00	0.03	0.00	0.00	0.98	0.90	0.98	0.90	0.98	0.90	0.98	0.90
Pu.1	0.00	0.00	0.03	0.11	0.00	0.00	0.03	0.11	0.00	0.00	0.00	0.00	0.03	0.11	0.00	0.00	0.03	0.11	0.00	0.00
Runx1	0.03	0.12	0.33	0.93	0.03	0.12	0.33	0.93	0.03	0.14	0.00	0.00	0.33	0.93	0.03	0.12	0.33	0.93	0.03	0.12
Runx2	0.00	0.03	0.00	0.05	0.00	0.03	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.03	0.00	0.05	0.00	0.03
Sox2	0.49	0.94	0.74	0.95	0.49	0.94	0.74	0.95	0.01	0.06	0.02	0.10	0.74	0.95	0.49	0.94	0.74	0.95	0.49	0.94
Sox4	0.18	0.86	0.24	0.90	0.18	0.86	0.24	0.90	0.24	0.87	0.00	0.02	0.24	0.90	0.18	0.86	0.24	0.90	0.18	0.86
Sox7	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.11	0.38	0.92	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.11	0.00	0.00
Sox9	0.49	0.94	0.00	0.10	0.49	0.94	0.00	0.10	0.04	0.12	0.00	0.12	0.00	0.10	0.49	0.94	0.00	0.10	0.49	0.94
PPARγ	0.01	0.04	0.00	0.05	0.01	0.04	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.05	0.01	0.04	0.00	0.05	0.01	0.04
GR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.11	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
NR4A	0.33	0.89	0.65	0.94	0.33	0.89	0.65	0.94	0.00	0.11	0.00	0.00	0.65	0.94	0.33	0.89	0.65	0.94	0.33	0.89
RARs	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05	0.04	0.11	0.47	0.87	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05
NR2F2	0.32	0.94	0.47	0.96	0.32	0.94	0.47	0.96	0.22	0.87	0.00	0.03	0.47	0.96	0.32	0.94	0.47	0.96	0.32	0.94
G-CSFR	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.03	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.00
IL-1	0.00	0.09	0.00	0.09	0.00	0.09	0.00	0.09	0.01	0.03	0.00	0.01	0.00	0.09	0.00	0.09	0.00	0.09	0.00	0.09
IL-10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
IL-3	0.00	0.03	0.32	0.89	0.00	0.03	0.32	0.89	0.02	0.04	0.00	0.00	0.32	0.89	0.00	0.03	0.32	0.89	0.00	0.03
IL-6	0.00	0.10	0.00	0.10	0.00	0.10	0.00	0.10	0.00	0.11	0.00	0.12	0.00	0.10	0.00	0.10	0.00	0.10	0.00	0.10
iκB	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05	0.01	0.05	0.00	0.02	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05
NF-κB	0.00	0.06	0.00	0.05	0.00	0.06	0.00	0.05	0.01	0.11	0.00	0.00	0.00	0.05	0.00	0.06	0.00	0.05	0.00	0.06
Stat3	0.49	0.95	0.49	0.96	0.49	0.95	0.49	0.96	0.01	0.14	0.00	0.00	0.49	0.96	0.49	0.95	0.49	0.96	0.49	0.95
Stat5	0.17	0.85	0.01	0.10	0.17	0.85	0.01	0.10	0.00	0.11	0.00	0.00	0.01	0.10	0.17	0.85	0.01	0.10	0.17	0.85
TGF-β	0.00	0.04	0.00	0.05	0.00	0.04	0.00	0.05	0.01	0.12	0.00	0.12	0.00	0.05	0.00	0.04	0.00	0.05	0.00	0.04
TNF-α	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.00	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01
BMP	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05
CCK	0.47	0.96	0.49	0.96	0.47	0.96	0.49	0.96	0.21	0.87	0.00	0.02	0.49	0.96	0.47	0.96	0.49	0.96	0.47	0.96
EGFR	0.44	0.93	0.71	0.95	0.44	0.93	0.71	0.95	0.01	0.13	0.00	0.00	0.71	0.95	0.44	0.93	0.71	0.95	0.44	0.93
FGF2	0.49	0.89	0.00	0.00	0.49	0.89	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.49	0.89	0.00	0.00	0.49	0.89
FGF4/8	0.95	0.87	0.95	0.87	0.95	0.87	0.95	0.87	0.00	0.00	0.00	0.02	0.95	0.87	0.95	0.87	0.95	0.87	0.95	0.87
FGF7	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01
FGF9	0.98	0.89	0.00	0.01	0.98	0.89	0.00	0.01	0.02	0.02	0.00	0.02	0.00	0.01	0.98	0.89	0.00	0.01	0.98	0.89
FGFR2	0.00	0.11	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.11
FGFR3	1.00	0.88	0.00	0.00	1.00	0.88	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.88	0.00	0.00	1.00	0.88
FGFR4	1.00	0.93	0.50	0.87	1.00	0.93	0.50	0.87	0.00	0.00	0.00	0.00	0.50	0.87	1.00	0.93	0.50	0.87	1.00	0.93
Gast	0.33	0.89	0.66	0.95	0.33	0.89	0.66	0.95	0.00	0.02	0.00	0.03	0.66	0.95	0.33	0.89	0.66	0.95	0.33	0.89
HGF	0.33	0.90	0.66	0.95	0.33	0.90	0.66	0.95	0.17	0.83	0.00	0.00	0.66	0.95	0.33	0.90	0.66	0.95	0.33	0.90
IR	0.24	0.87	0.48	0.93	0.24	0.87	0.48	0.93	0.00	0.02	0.00	0.02	0.48	0.93	0.24	0.87	0.48	0.93	0.24	0.87
VEGF	0.00	0.10	0.02	0.11	0.00	0.10	0.02	0.11	0.15	0.82	0.00	0.00	0.02	0.11	0.00	0.10	0.02	0.11	0.00	0.10
Akt	0.52	0.97	0.63	0.98	0.52	0.97	0.63	0.98	0.01	0.14	0.00	0.09	0.63	0.98	0.52	0.97	0.63	0.98	0.52	0.97
AP2	0.65	0.94	0.66	0.94	0.65	0.94	0.66	0.94	0.30	0.87	0.33	0.87	0.66	0.94	0.65	0.94	0.66	0.94	0.65	0.94
c-Jun	0.00	0.12	0.65	0.97	0.00	0.12	0.65	0.97	0.13	0.85	0.00	0.01	0.65	0.97	0.00	0.12	0.65	0.97	0.00	0.12
HIF	0.97	0.96	0.99	0.96	0.97	0.96	0.99	0.96	0.00	0.06	0.00	0.00	0.99	0.96	0.97	0.96	0.99	0.96	0.97	0.96
MAPK	0.42	0.95	0.28	0.94	0.42	0.95	0.28	0.94	0.01	0.14	0.00	0.00	0.28	0.94	0.42	0.95	0.28	0.94	0.42	0.95
Mkp2	0.99	0.89	0.00	0.00	0.99	0.89	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.99	0.89	0.00	0.00	0.99	0.89
PKA	0.65	0.94	0.66	0.95	0.65	0.94	0.66	0.95	0.00	0.06	0.00	0.00	0.66	0.95	0.65	0.94	0.66	0.95	0.65	0.94
PTEN	0.00	0.09	0.00	0.09	0.00	0.09	0.00	0.09	0.31	0.83	0.65	0.94	0.00	0.09	0.00	0.09	0.00	0.09	0.00	0.09
p53	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05	0.03	0.12	0.58	0.95	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05
E-Cadherin	0.00	0.02	0.00	0.02	0.00	0.02	0.00	0.02	0.57	0.87	0.58	0.91	0.00	0.02	0.00	0.02	0.00	0.02	0.00	0.02
HSPG2	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Integrin	0.00	0.06	0.00	0.06	0.00	0.06	0.00	0.06	0.02	0.11	0.00	0.00	0.00	0.06	0.00	0.06	0.00	0.06	0.00	0.06
Notch	0.00	0.06	0.00	0.10	0.00	0.06	0.00	0.10	0.00	0.05	0.00	0.00	0.00	0.10	0.00	0.06	0.00	0.10	0.00	0.06
NGAL	0.01	0.02	0.47	0.89	0.01	0.02	0.47	0.89	0.01	0.02	0.00	0.00	0.47	0.89	0.01	0.02	0.47	0.89	0.01	0.02
NOG	0.65	0.92	0.64	0.94	0.65	0.92	0.64	0.94	0.01	0.02	0.00	0.03	0.64	0.94	0.65	0.92	0.64	0.94	0.65	0.92
OPN	0.00	0.02	0.32	0.89	0.00	0.02	0.32	0.89	0.01	0.04	0.00	0.02	0.32	0.89	0.00	0.02	0.32	0.89	0.00	0.02
SHH	0.35	0.88	0.33	0.89	0.35	0.88	0.33	0.89	0.00	0.03	0.01	0.12	0.33	0.89	0.35	0.88	0.33	0.89	0.35	0.88
Wnt	0.00	0.10	0.43	0.95	0.00	0.10	0.43	0.95	0.00	0.04	0.00	0.02	0.43	0.95	0.00	0.10	0.43	0.95	0.00	0.10

Table S5. Recurrence of attractors using different forms of equations. Alternative equation (b). 8 attractors are exactly obtained. The differentiated states S5 and S6 under this equation form are merged and become a limit cycle attractor. The average value along one period is listed here.

	S1	S2	S3	S4	S5, S6	S7	S8	S9	S10
Cyclin D/Cdk4,6	0.99	0.99	0.96	0.96	0.00	0.99	0.99	0.96	0.96
Cyclin E/Cdk2	0.91	0.91	0.00	0.00	0.00	0.91	0.91	0.00	0.00
E2F	0.95	0.95	0.00	0.00	0.00	0.95	0.95	0.00	0.00
Myc	0.05	0.05	0.05	0.05	0.00	0.05	0.05	0.05	0.05
p21	0.04	0.04	0.04	0.04	0.97	0.04	0.04	0.04	0.04
p27	0.04	0.04	0.04	0.04	0.98	0.04	0.04	0.04	0.04
pRb	0.99	0.99	0.95	0.95	0.00	0.99	0.99	0.95	0.95
Ras	1.00	1.00	1.00	1.00	0.98	1.00	1.00	1.00	1.00
Bad	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Bax	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
Bcl-2	0.00	0.00	0.00	0.00	0.64	0.00	0.00	0.00	0.00
Bcl-xL	0.99	0.96	0.99	0.96	0.44	0.05	0.06	0.05	0.06
Bim	0.01	0.01	0.01	0.01	0.98	0.01	0.01	0.01	0.01
Caspase 3	0.00	0.00	0.00	0.00	0.00	0.94	0.94	0.94	0.94
Cytochrome C	0.00	0.00	0.00	0.00	0.00	0.93	0.93	0.93	0.93
Fas	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
XIAP	0.99	0.99	0.99	0.99	0.55	0.01	0.01	0.01	0.01
C/EBPα	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
C/EBPβ	0.99	0.99	0.99	0.99	0.05	0.99	0.99	0.99	0.99
Cdx2	0.00	0.01	0.00	0.01	0.94	0.01	0.00	0.01	0.00
Foxa1	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Foxa2	0.01	0.01	0.01	0.01	0.37	0.01	0.01	0.01	0.01
Gata1/2	0.04	0.04	0.04	0.04	0.02	0.04	0.04	0.04	0.04
Gata4/6	0.01	0.00	0.01	0.00	0.05	0.00	0.01	0.00	0.01
Hes1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hey2	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
HNF1	0.00	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.00
HNF4α	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00
Hoxa10	0.99	0.01	0.99	0.01	0.03	0.01	0.99	0.01	0.99
Hoxa3	0.00	0.05	0.00	0.05	0.97	0.05	0.00	0.05	0.00
Hoxa5	0.95	0.00	0.95	0.00	0.97	0.00	0.95	0.00	0.95
Hoxa9	0.95	0.02	0.95	0.02	0.38	0.02	0.95	0.02	0.95
PGC-1	0.04	0.01	0.04	0.01	0.00	0.01	0.04	0.01	0.04
PRDM14	0.95	0.95	0.95	0.95	0.00	0.95	0.95	0.95	0.95
Pu.1	0.00	0.05	0.00	0.05	0.00	0.05	0.00	0.05	0.00
Runx1	0.05	0.98	0.05	0.98	0.03	0.98	0.05	0.98	0.05
Runx2	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01	0.00
Sox2	0.99	1.00	0.99	1.00	0.01	1.00	0.99	1.00	0.99
Sox4	0.95	0.96	0.95	0.96	0.98	0.96	0.95	0.96	0.95
Sox7	0.00	0.05	0.00	0.05	0.98	0.05	0.00	0.05	0.00
Sox9	0.97	0.04	0.97	0.04	0.03	0.04	0.97	0.04	0.97
PPARγ	0.00	0.01	0.00	0.01	0.00	0.01	0.00	0.01	0.00
GR	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00
NR4A	0.96	0.99	0.96	0.99	0.37	0.99	0.96	0.99	0.96
RARs	0.01	0.01	0.01	0.01	0.33	0.01	0.01	0.01	0.01
NR2F2	0.99	1.00	0.99	1.00	0.55	1.00	0.99	1.00	0.99
G-CSFR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
IL-1	0.05	0.05	0.05	0.05	0.01	0.05	0.05	0.05	0.05
IL-10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
IL-3	0.01	0.95	0.01	0.95	0.01	0.95	0.01	0.95	0.01
IL-6	0.05	0.05	0.05	0.05	0.23	0.05	0.05	0.05	0.05
iκB	0.01	0.01	0.01	0.01	0.50	0.01	0.01	0.01	0.01
NF-κB	0.01	0.01	0.01	0.01	0.02	0.01	0.01	0.01	0.01
Stat3	0.99	0.98	0.99	0.98	0.03	0.98	0.99	0.98	0.99
Stat5	0.96	0.05	0.96	0.05	0.32	0.05	0.96	0.05	0.96
TGF-β	0.00	0.01	0.00	0.01	0.03	0.01	0.00	0.01	0.00
TNF-α	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
BMP	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
CCK	1.00	1.00	1.00	1.00	0.96	1.00	1.00	1.00	1.00
EGFR	0.99	1.00	0.99	1.00	0.06	1.00	0.99	1.00	0.99
FGF2	0.95	0.00	0.95	0.00	0.00	0.00	0.95	0.00	0.95
FGF4/8	0.95	0.94	0.95	0.94	0.00	0.94	0.95	0.94	0.95
FGF7	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
FGF9	0.95	0.00	0.95	0.00	0.00	0.00	0.95	0.00	0.95
FGFR2	0.05	0.00	0.05	0.00	0.00	0.00	0.05	0.00	0.05
FGFR3	0.94	0.00	0.94	0.00	0.00	0.00	0.94	0.00	0.94
FGFR4	0.99	0.94	0.99	0.94	0.00	0.94	0.99	0.94	0.99
Gast	0.96	0.99	0.96	0.99	0.00	0.99	0.96	0.99	0.96
HGF	0.96	0.99	0.96	0.99	0.98	0.99	0.96	0.99	0.96
IR	0.95	0.99	0.95	0.99	0.00	0.99	0.95	0.99	0.95
VEGF	0.04	0.04	0.04	0.04	0.57	0.04	0.04	0.04	0.04
Akt	1.00	1.00	1.00	1.00	0.06	1.00	1.00	1.00	1.00
AP2	0.99	0.99	0.99	0.99	0.93	0.99	0.99	0.99	0.99
c-Jun	0.05	1.00	0.05	1.00	0.96	1.00	0.05	1.00	0.05
HIF	1.00	1.00	1.00	1.00	0.52	1.00	1.00	1.00	1.00
MAPK	1.00	0.99	1.00	0.99	0.05	0.99	1.00	0.99	1.00
Mkp2	0.95	0.00	0.95	0.00	0.00	0.00	0.95	0.00	0.95
PKA	0.99	0.99	0.99	0.99	0.05	0.99	0.99	0.99	0.99
PTEN	0.05	0.05	0.05	0.05	0.94	0.05	0.05	0.05	0.05
p53	0.01	0.01	0.01	0.01	0.04	0.01	0.01	0.01	0.01
E-Cadherin	0.00	0.00	0.00	0.00	0.24	0.00	0.00	0.00	0.00
HSPG2	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Integrin	0.01	0.01	0.01	0.01	0.03	0.01	0.01	0.01	0.01
Notch	0.01	0.05	0.01	0.05	0.01	0.05	0.01	0.05	0.01
NGAL	0.00	0.95	0.00	0.95	0.00	0.95	0.00	0.95	0.00
NOG	0.99	0.99	0.99	0.99	0.00	0.99	0.99	0.99	0.99
OPN	0.00	0.95	0.00	0.95	0.00	0.95	0.00	0.95	0.00
SHH	0.95	0.96	0.95	0.96	0.01	0.96	0.95	0.96	0.95
Wnt	0.05	0.98	0.05	0.98	0.00	0.98	0.05	0.98	0.05

Table S6. Attractors: Boolean dynamics *vs.* differential equations. Inside each slot is comparison of corresponding attractors obtained separately from Boolean dynamics (left) and differential equations (right). All attractors from differential equations except S6 are obtained by Boolean dynamics. The comparison result demonstrates that our differential equations generate consistent results with Boolean network modeling.

	S1		S2		S3		S4		S5		S7		S8		S9		S10	
	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1	E2	E1
Cyclin D/Cdk4,6	1	0.93	1	0.93	1	0.88	1	0.89	0	0.00	1	0.93	1	0.93	1	0.89	1	0.88
Cyclin E/Cdk2	1	0.85	1	0.84	0	0.01	0	0.01	0	0.00	1	0.84	1	0.85	0	0.01	0	0.01
E2F	1	0.86	1	0.86	0	0.01	0	0.01	0	0.00	1	0.86	1	0.86	0	0.01	0	0.01
Myc	0	0.10	0	0.10	0	0.10	0	0.10	0	0.00	0	0.10	0	0.10	0	0.10	0	0.10
p21	0	0.09	0	0.09	0	0.09	0	0.09	1	0.90	0	0.09	0	0.09	0	0.09	0	0.09
p27	0	0.09	0	0.09	0	0.09	0	0.09	1	0.90	0	0.09	0	0.09	0	0.09	0	0.09
pRb	1	0.93	1	0.93	1	0.87	1	0.88	0	0.00	1	0.93	1	0.93	1	0.88	1	0.87
Ras	1	0.95	1	0.96	1	0.95	1	0.96	1	0.89	1	0.96	1	0.95	1	0.96	1	0.95
Bad	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Bax	0	0.00	0	0.00	0	0.00	0	0.00	0	0.07	0	0.00	0	0.00	0	0.00	0	0.00
Bcl-2	0	0.01	0	0.02	0	0.01	0	0.02	1	0.82	0	0.00	0	0.00	0	0.00	0	0.00
Bcl-xL	1	0.93	1	0.90	1	0.93	1	0.90	0	0.05	0	0.13	0	0.13	0	0.13	0	0.13
Bim	0	0.05	0	0.05	0	0.05	0	0.05	1	0.95	0	0.05	0	0.05	0	0.05	0	0.05
Caspase 3	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	0.85	1	0.85	1	0.85	1	0.85
Cytochrome C	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	1	0.84	1	0.83	1	0.84	1	0.83
Fas	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
XIAP	1	0.95	1	0.95	1	0.95	1	0.95	0	0.09	0	0.07	0	0.07	0	0.07	0	0.07
C/EBPα	0	0.02	0	0.03	0	0.02	0	0.03	0	0.11	0	0.03	0	0.02	0	0.03	0	0.02
C/EBPβ	1	0.94	1	0.93	1	0.94	1	0.93	0	0.13	1	0.93	1	0.94	1	0.93	1	0.94
Cdx2	0	0.04	0	0.05	0	0.04	0	0.05	1	0.88	0	0.05	0	0.04	0	0.05	0	0.04
Foxa1	0	0.12	0	0.11	0	0.12	0	0.11	0	0.11	0	0.11	0	0.12	0	0.11	0	0.12
Foxa2	0	0.05	0	0.05	0	0.05	0	0.05	0	0.03	0	0.05	0	0.05	0	0.05	0	0.05
Gata1/2	0	0.10	0	0.09	0	0.10	0	0.09	0	0.07	0	0.09	0	0.10	0	0.09	0	0.10
Gata4/6	0	0.05	0	0.04	0	0.05	0	0.04	0	0.13	0	0.04	0	0.05	0	0.04	0	0.05
Hes1	0	0.00	0	0.01	0	0.00	0	0.01	0	0.02	0	0.01	0	0.00	0	0.01	0	0.00
Hey2	0	0.00	0	0.01	0	0.00	0	0.01	0	0.00	0	0.01	0	0.00	0	0.01	0	0.00
HNF1	0	0.00	0	0.01	0	0.00	0	0.01	1	0.86	0	0.01	0	0.00	0	0.01	0	0.00
HNF4α	0	0.02	0	0.02	0	0.02	0	0.02	1	0.87	0	0.02	0	0.02	0	0.02	0	0.02
Hoxa10	1	0.92	0	0.01	1	0.92	0	0.01	0	0.00	0	0.01	1	0.92	0	0.01	1	0.92
Hoxa3	0	0.00	0	0.10	0	0.00	0	0.10	1	0.84	0	0.10	0	0.00	0	0.10	0	0.00
Hoxa5	1	0.87	0	0.00	1	0.87	0	0.00	1	0.85	0	0.00	1	0.87	0	0.00	1	0.87
Hoxa9	1	0.86	0	0.02	1	0.86	0	0.02	0	0.03	0	0.02	1	0.86	0	0.02	1	0.86
PGC-1	0	0.09	0	0.05	0	0.09	0	0.05	0	0.00	0	0.05	0	0.09	0	0.05	0	0.09
PRDM14	1	0.90	1	0.90	1	0.90	1	0.90	0	0.03	1	0.90	1	0.90	1	0.90	1	0.90
Pu.1	0	0.00	0	0.11	0	0.00	0	0.11	0	0.00	0	0.11	0	0.00	0	0.11	0	0.00
Runx1	0	0.12	1	0.93	0	0.12	1	0.93	0	0.14	1	0.93	0	0.12	1	0.93	0	0.12
Runx2	0	0.03	0	0.05	0	0.03	0	0.05	0	0.00	0	0.05	0	0.03	0	0.05	0	0.03
Sox2	1	0.94	1	0.95	1	0.94	1	0.95	0	0.06	1	0.95	1	0.94	1	0.95	1	0.94
Sox4	1	0.86	1	0.90	1	0.86	1	0.90	1	0.87	1	0.90	1	0.86	1	0.90	1	0.86
Sox7	0	0.00	0	0.11	0	0.00	0	0.11	1	0.92	0	0.11	0	0.00	0	0.11	0	0.00
Sox9	1	0.94	0	0.10	1	0.94	0	0.10	0	0.12	0	0.10	1	0.94	0	0.10	1	0.94
PPARγ	0	0.04	0	0.05	0	0.04	0	0.05	0	0.00	0	0.05	0	0.04	0	0.05	0	0.04
GR	0	0.00	0	0.00	0	0.00	0	0.00	0	0.11	0	0.00	0	0.00	0	0.00	0	0.00
NR4A	1	0.89	1	0.94	1	0.89	1	0.94	0	0.11	1	0.94	1	0.89	1	0.94	1	0.89
RARs	0	0.05	0	0.05	0	0.05	0	0.05	0	0.11	0	0.05	0	0.05	0	0.05	0	0.05
NR2F2	1	0.94	1	0.96	1	0.94	1	0.96	1	0.87	1	0.96	1	0.94	1	0.96	1	0.94
G-CSFR	0	0.00	0	0.01	0	0.00	0	0.01	0	0.03	0	0.01	0	0.00	0	0.01	0	0.00
IL-1	0	0.09	0	0.09	0	0.09	0	0.09	0	0.03	0	0.09	0	0.09	0	0.09	0	0.09
IL-10	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
IL-3	0	0.03	1	0.89	0	0.03	1	0.89	0	0.04	1	0.89	0	0.03	1	0.89	0	0.03
IL-6	0	0.10	0	0.10	0	0.10	0	0.10	0	0.11	0	0.10	0	0.10	0	0.10	0	0.10
iκB	0	0.05	0	0.05	0	0.05	0	0.05	0	0.05	0	0.05	0	0.05	0	0.05	0	0.05
NF-κB	0	0.06	0	0.05	0	0.06	0	0.05	0	0.11	0	0.05	0	0.06	0	0.05	0	0.06
Stat3	1	0.95	1	0.96	1	0.95	1	0.96	0	0.14	1	0.96	1	0.95	1	0.96	1	0.95
Stat5	1	0.85	0	0.10	1	0.85	0	0.10	0	0.11	0	0.10	1	0.85	0	0.10	1	0.85
TGF-β	0	0.04	0	0.05	0	0.04	0	0.05	0	0.12	0	0.05	0	0.04	0	0.05	0	0.04
TNF-α	0	0.01	0	0.01	0	0.01	0	0.01	0	0.01	0	0.01	0	0.01	0	0.01	0	0.01
BMP	0	0.05	0	0.05	0	0.05	0	0.05	0	0.00	0	0.05	0	0.05	0	0.05	0	0.05
CCK	1	0.96	1	0.96	1	0.96	1	0.96	1	0.87	1	0.96	1	0.96	1	0.96	1	0.96
EGFR	1	0.93	1	0.95	1	0.93	1	0.95	0	0.13	1	0.95	1	0.93	1	0.95	1	0.93
FGF2	1	0.89	0	0.00	1	0.89	0	0.00	0	0.00	0	0.00	1	0.89	0	0.00	1	0.89
FGF4/8	1	0.87	1	0.87	1	0.87	1	0.87	0	0.00	1	0.87	1	0.87	1	0.87	1	0.87
FGF7	0	0.01	0	0.01	0	0.01	0	0.01	0	0.00	0	0.01	0	0.01	0	0.01	0	0.01
FGF9	1	0.89	0	0.01	1	0.89	0	0.01	0	0.02	0	0.01	1	0.89	0	0.01	1	0.89
FGFR2	0	0.11	0	0.00	0	0.11	0	0.00	0	0.00	0	0.00	0	0.11	0	0.00	0	0.11
FGFR3	1	0.88	0	0.00	1	0.88	0	0.00	0	0.00	0	0.00	1	0.88	0	0.00	1	0.88
FGFR4	1	0.93	1	0.87	1	0.93	1	0.87	0	0.00	1	0.87	1	0.93	1	0.87	1	0.93
Gast	1	0.89	1	0.95	1	0.89	1	0.95	0	0.02	1	0.95	1	0.89	1	0.95	1	0.89
HGF	1	0.90	1	0.95	1	0.90	1	0.95	1	0.83	1	0.95	1	0.90	1	0.95	1	0.90
IR	1	0.87	1	0.93	1	0.87	1	0.93	0	0.02	1	0.93	1	0.87	1	0.93	1	0.87
VEGF	0	0.10	0	0.11	0	0.10	0	0.11	1	0.82	0	0.11	0	0.10	0	0.11	0	0.10
Akt	1	0.97	1	0.98	1	0.97	1	0.98	0	0.14	1	0.98	1	0.97	1	0.98	1	0.97
AP2	1	0.94	1	0.94	1	0.94	1	0.94	1	0.87	1	0.94	1	0.94	1	0.94	1	0.94
c-Jun	0	0.12	1	0.97	0	0.12	1	0.97	1	0.85	1	0.97	0	0.12	1	0.97	0	0.12
HIF	1	0.96	1	0.96	1	0.96	1	0.96	0	0.06	1	0.96	1	0.96	1	0.96	1	0.96
MAPK	1	0.95	1	0.94	1	0.95	1	0.94	0	0.14	1	0.94	1	0.95	1	0.94	1	0.95
Mkp2	1	0.89	0	0.00	1	0.89	0	0.00	0	0.00	0	0.00	1	0.89	0	0.00	1	0.89
PKA	1	0.94	1	0.95	1	0.94	1	0.95	0	0.06	1	0.95	1	0.94	1	0.95	1	0.94
PTEN	0	0.09	0	0.09	0	0.09	0	0.09	1	0.83	0	0.09	0	0.09	0	0.09	0	0.09
p53	0	0.05	0	0.05	0	0.05	0	0.05	0	0.12	0	0.05	0	0.05	0	0.05	0	0.05
E-Cadherin	0	0.02	0	0.02	0	0.02	0	0.02	1	0.87	0	0.02	0	0.02	0	0.02	0	0.02
HSPG2	0	0.00	0	0.00	0	0.00	0	0.00	0	0.02	0	0.00	0	0.00	0	0.00	0	0.00
Integrin	0	0.06	0	0.06	0	0.06	0	0.06	0	0.11	0	0.06	0	0.06	0	0.06	0	0.06
Notch	0	0.06	0	0.10	0	0.06	0	0.10	0	0.05	0	0.10	0	0.06	0	0.10	0	0.06
NGAL	0	0.02	1	0.89	0	0.02	1	0.89	0	0.02	1	0.89	0	0.02	1	0.89	0	0.02
NOG	1	0.92	1	0.94	1	0.92	1	0.94	0	0.02	1	0.94	1	0.92	1	0.94	1	0.92
OPN	0	0.02	1	0.89	0	0.02	1	0.89	0	0.04	1	0.89	0	0.02	1	0.89	0	0.02
SHH	1	0.88	1	0.89	1	0.88	1	0.89	0	0.03	1	0.89	1	0.88	1	0.89	1	0.88
Wnt	0	0.10	1	0.95	0	0.10	1	0.95	0	0.04	1	0.95	0	0.10	1	0.95	0	0.10

Table S7. Unstable fixed points from differential equations. We obtain 21 unstable fixed points where 14 of them are saddle points. Among them, 12 saddle points and 6 other unstable fixed points together with 8 attractors form a face-centered cubic type topological structure in the phase space. In addition, there is an unstable point at the body-center as well. These 21 unstable points are first obtained while calculating with 100,000 random initial positions using *Newtonian iteration method*. We further run the program with 1,000,000 and more initial positions, acquiring an identical result.

	U1	U2	U3	U4	U5	U6	U7	U8	U9	U10	U11	U12	U13	U14	U15	U16	U17	U18	U19	U20	U21
Cyclin D/Cdk4,6	0.90	0.87	0.89	0.92	0.93	0.89	0.02	0.88	0.93	0.00	0.90	0.87	0.92	0.89	0.88	0.90	0.87	0.92	0.89	0.88	0.88
Cyclin E/Cdk2	0.41	0.01	0.01	0.84	0.84	0.41	0.00	0.01	0.85	0.00	0.41	0.01	0.84	0.41	0.40	0.41	0.01	0.84	0.41	0.40	0.40
E2F	0.41	0.01	0.01	0.86	0.86	0.41	0.00	0.01	0.86	0.00	0.41	0.01	0.86	0.41	0.41	0.41	0.01	0.86	0.41	0.41	0.41
Myc	0.10	0.10	0.10	0.10	0.10	0.10	0.02	0.10	0.10	0.01	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
p21	0.09	0.09	0.09	0.09	0.09	0.09	0.74	0.09	0.09	0.91	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09
p27	0.09	0.09	0.09	0.09	0.09	0.09	0.72	0.09	0.09	0.93	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09
pRb	0.89	0.87	0.88	0.93	0.93	0.89	0.00	0.87	0.93	0.00	0.89	0.87	0.93	0.89	0.88	0.89	0.87	0.93	0.89	0.88	0.88
Ras	0.96	0.95	0.96	0.95	0.96	0.95	0.80	0.95	0.95	0.03	0.96	0.95	0.95	0.95	0.95	0.96	0.95	0.95	0.95	0.95	0.95
Bad	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Bax	0.00	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.81	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Bcl-2	0.02	0.01	0.00	0.01	0.00	0.01	0.63	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Bcl-xL	0.90	0.89	0.28	0.89	0.28	0.93	0.27	0.28	0.28	0.00	0.13	0.13	0.13	0.13	0.89	0.28	0.28	0.28	0.28	0.13	0.28
Bim	0.05	0.05	0.05	0.05	0.05	0.05	0.82	0.05	0.05	0.99	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Caspase 3	0.00	0.00	0.61	0.00	0.61	0.00	0.00	0.62	0.62	0.00	0.85	0.85	0.85	0.85	0.00	0.61	0.61	0.61	0.62	0.85	0.61
Cytochrome C	0.00	0.00	0.57	0.00	0.57	0.00	0.00	0.58	0.58	0.10	0.84	0.84	0.84	0.83	0.00	0.57	0.57	0.57	0.58	0.84	0.57
Fas	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
XIAP	0.95	0.95	0.19	0.95	0.19	0.95	0.29	0.18	0.18	0.85	0.07	0.07	0.07	0.07	0.95	0.19	0.19	0.19	0.18	0.07	0.19
C/EBPα	0.03	0.03	0.03	0.03	0.03	0.02	0.15	0.02	0.02	0.05	0.03	0.03	0.03	0.02	0.03	0.03	0.03	0.03	0.02	0.03	0.03
C/EBPβ	0.93	0.94	0.93	0.94	0.93	0.94	0.15	0.94	0.94	0.11	0.93	0.94	0.94	0.94	0.94	0.93	0.94	0.94	0.94	0.94	0.94
Cdx2	0.05	0.04	0.05	0.04	0.05	0.04	0.68	0.04	0.04	0.37	0.05	0.04	0.04	0.04	0.04	0.05	0.04	0.04	0.04	0.04	0.04
Foxa1	0.11	0.40	0.11	0.40	0.11	0.12	0.11	0.12	0.12	0.82	0.11	0.40	0.40	0.12	0.40	0.11	0.40	0.40	0.12	0.40	0.40
Foxa2	0.05	0.05	0.05	0.05	0.05	0.05	0.13	0.05	0.05	0.85	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Gata1/2	0.09	0.20	0.09	0.20	0.09	0.10	0.10	0.10	0.10	0.24	0.09	0.20	0.20	0.10	0.20	0.09	0.20	0.20	0.10	0.20	0.20
Gata4/6	0.04	0.06	0.04	0.06	0.04	0.05	0.16	0.05	0.05	0.17	0.04	0.06	0.06	0.05	0.06	0.04	0.06	0.06	0.05	0.06	0.06
Hes1	0.01	0.01	0.01	0.01	0.01	0.00	0.13	0.00	0.00	0.02	0.01	0.01	0.01	0.00	0.01	0.01	0.01	0.01	0.00	0.01	0.01
Hey2	0.01	0.01	0.01	0.01	0.01	0.00	0.01	0.00	0.00	0.00	0.01	0.01	0.01	0.00	0.01	0.01	0.01	0.01	0.00	0.01	0.01
HNF1	0.01	0.01	0.01	0.01	0.01	0.00	0.57	0.00	0.00	0.03	0.01	0.01	0.01	0.00	0.01	0.01	0.01	0.01	0.00	0.01	0.01
HNF4α	0.02	0.02	0.02	0.02	0.02	0.02	0.52	0.02	0.02	0.14	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Hoxa10	0.01	0.68	0.01	0.68	0.01	0.92	0.05	0.92	0.92	0.00	0.01	0.68	0.68	0.92	0.68	0.01	0.68	0.68	0.92	0.68	0.68
Hoxa3	0.10	0.01	0.10	0.01	0.10	0.00	0.74	0.00	0.00	0.87	0.10	0.01	0.01	0.00	0.01	0.10	0.01	0.01	0.00	0.01	0.01
Hoxa5	0.00	0.39	0.00	0.39	0.00	0.87	0.73	0.87	0.87	0.87	0.00	0.39	0.39	0.87	0.39	0.00	0.39	0.39	0.87	0.39	0.39
Hoxa9	0.02	0.49	0.02	0.49	0.02	0.86	0.17	0.86	0.86	0.00	0.02	0.49	0.49	0.86	0.49	0.02	0.49	0.49	0.86	0.49	0.49
PGC-1	0.05	0.09	0.05	0.09	0.05	0.09	0.01	0.09	0.09	0.00	0.05	0.09	0.09	0.09	0.09	0.05	0.09	0.09	0.09	0.09	0.09
PRDM14	0.90	0.87	0.90	0.87	0.90	0.90	0.09	0.90	0.90	0.00	0.90	0.87	0.87	0.90	0.87	0.90	0.87	0.87	0.90	0.87	0.87
Pu.1	0.11	0.21	0.11	0.21	0.11	0.00	0.01	0.00	0.00	0.00	0.11	0.21	0.21	0.00	0.21	0.11	0.21	0.21	0.00	0.21	0.21
Runx1	0.93	0.45	0.93	0.45	0.93	0.12	0.17	0.12	0.12	0.07	0.93	0.45	0.45	0.12	0.45	0.93	0.45	0.45	0.12	0.45	0.45
Runx2	0.05	0.03	0.05	0.03	0.05	0.03	0.01	0.03	0.03	0.00	0.05	0.03	0.03	0.03	0.03	0.05	0.03	0.03	0.03	0.03	0.03
Sox2	0.95	0.93	0.95	0.93	0.95	0.94	0.10	0.94	0.94	0.09	0.95	0.93	0.93	0.94	0.93	0.95	0.93	0.93	0.94	0.93	0.93
Sox4	0.90	0.50	0.90	0.50	0.90	0.86	0.85	0.86	0.86	0.25	0.90	0.50	0.50	0.86	0.50	0.90	0.50	0.50	0.86	0.50	0.50
Sox7	0.11	0.01	0.11	0.01	0.11	0.00	0.87	0.00	0.00	0.30	0.11	0.01	0.01	0.00	0.01	0.11	0.01	0.01	0.00	0.01	0.01
Sox9	0.10	0.90	0.10	0.90	0.10	0.94	0.15	0.94	0.94	0.12	0.10	0.90	0.90	0.94	0.90	0.10	0.90	0.90	0.94	0.90	0.90
PPARγ	0.05	0.05	0.05	0.05	0.05	0.04	0.02	0.04	0.04	0.00	0.05	0.05	0.05	0.04	0.05	0.05	0.05	0.05	0.04	0.05	0.05
GR	0.00	0.00	0.00	0.00	0.00	0.00	0.18	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
NR4A	0.94	0.89	0.94	0.89	0.94	0.89	0.29	0.89	0.89	0.00	0.94	0.89	0.89	0.89	0.89	0.94	0.89	0.89	0.89	0.89	0.89
RARs	0.05	0.05	0.05	0.05	0.05	0.05	0.22	0.05	0.05	0.85	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
NR2F2	0.96	0.94	0.96	0.94	0.96	0.94	0.62	0.94	0.94	0.12	0.96	0.94	0.94	0.94	0.94	0.96	0.94	0.94	0.94	0.94	0.94
G-CSFR	0.01	0.08	0.01	0.08	0.01	0.00	0.08	0.00	0.00	0.00	0.01	0.08	0.08	0.00	0.08	0.01	0.08	0.08	0.00	0.08	0.08
IL-1	0.09	0.09	0.09	0.09	0.09	0.09	0.10	0.09	0.09	0.02	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09
IL-10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
IL-3	0.89	0.50	0.89	0.50	0.89	0.03	0.08	0.03	0.03	0.13	0.89	0.50	0.50	0.03	0.50	0.89	0.50	0.50	0.03	0.50	0.50
IL-6	0.10	0.10	0.10	0.10	0.10	0.10	0.32	0.10	0.10	0.12	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
iκB	0.05	0.05	0.05	0.05	0.05	0.05	0.28	0.05	0.05	0.02	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
NF-κB	0.05	0.06	0.05	0.06	0.05	0.06	0.19	0.06	0.06	0.05	0.05	0.06	0.06	0.06	0.06	0.05	0.06	0.06	0.06	0.06	0.06
Stat3	0.96	0.89	0.96	0.89	0.96	0.95	0.22	0.95	0.95	0.03	0.96	0.89	0.89	0.95	0.89	0.96	0.89	0.89	0.95	0.89	0.89
Stat5	0.10	0.46	0.10	0.46	0.10	0.85	0.28	0.85	0.85	0.02	0.10	0.46	0.46	0.85	0.46	0.10	0.46	0.46	0.85	0.46	0.46
TGF-β	0.05	0.05	0.05	0.05	0.05	0.04	0.24	0.04	0.04	0.13	0.05	0.05	0.05	0.04	0.05	0.05	0.05	0.05	0.04	0.05	0.05
TNF-α	0.01	0.01	0.01	0.01	0.01	0.01	0.07	0.01	0.01	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
BMP	0.05	0.05	0.05	0.05	0.05	0.05	0.03	0.05	0.05	0.04	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
CCK	0.96	0.96	0.96	0.96	0.96	0.96	0.76	0.96	0.96	0.37	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96	0.96
EGFR	0.95	0.90	0.95	0.90	0.95	0.93	0.21	0.93	0.93	0.02	0.95	0.90	0.90	0.93	0.90	0.95	0.90	0.90	0.93	0.90	0.90
FGF2	0.00	0.76	0.00	0.76	0.00	0.89	0.02	0.89	0.89	0.00	0.00	0.76	0.76	0.89	0.76	0.00	0.76	0.76	0.89	0.76	0.76
FGF4/8	0.87	0.87	0.87	0.87	0.87	0.87	0.02	0.87	0.87	0.02	0.87	0.87	0.87	0.87	0.87	0.87	0.87	0.87	0.87	0.87	0.87
FGF7	0.01	0.01	0.01	0.01	0.01	0.01	0.03	0.01	0.01	0.00	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
FGF9	0.01	0.88	0.01	0.88	0.01	0.89	0.03	0.89	0.89	0.02	0.01	0.88	0.88	0.89	0.88	0.01	0.88	0.88	0.89	0.88	0.88
FGFR2	0.00	0.11	0.00	0.11	0.00	0.11	0.00	0.11	0.11	0.00	0.00	0.11	0.11	0.11	0.11	0.00	0.11	0.11	0.11	0.11	0.11
FGFR3	0.00	0.87	0.00	0.87	0.00	0.88	0.00	0.88	0.88	0.00	0.00	0.87	0.87	0.88	0.87	0.00	0.87	0.87	0.88	0.87	0.87
FGFR4	0.87	0.93	0.87	0.93	0.87	0.93	0.00	0.93	0.93	0.00	0.87	0.93	0.93	0.93	0.93	0.87	0.93	0.93	0.93	0.93	0.93
Gast	0.95	0.89	0.95	0.89	0.95	0.89	0.13	0.89	0.89	0.08	0.95	0.89	0.89	0.89	0.89	0.95	0.89	0.89	0.89	0.89	0.89
HGF	0.95	0.90	0.95	0.90	0.95	0.90	0.69	0.90	0.90	0.29	0.95	0.90	0.90	0.90	0.90	0.95	0.90	0.90	0.90	0.90	0.90
IR	0.93	0.87	0.93	0.87	0.93	0.87	0.05	0.87	0.87	0.07	0.93	0.87	0.87	0.87	0.87	0.93	0.87	0.87	0.87	0.87	0.87
VEGF	0.11	0.10	0.11	0.10	0.11	0.10	0.64	0.10	0.10	0.01	0.11	0.10	0.10	0.10	0.10	0.11	0.10	0.10	0.10	0.10	0.10
Akt	0.98	0.97	0.98	0.97	0.98	0.97	0.23	0.97	0.97	0.10	0.98	0.97	0.97	0.97	0.97	0.98	0.97	0.97	0.97	0.97	0.97
AP2	0.94	0.94	0.94	0.94	0.94	0.94	0.72	0.94	0.94	0.86	0.94	0.94	0.94	0.94	0.94	0.94	0.94	0.94	0.94	0.94	0.94
c-Jun	0.97	0.18	0.97	0.18	0.97	0.12	0.76	0.12	0.12	0.35	0.97	0.18	0.18	0.12	0.18	0.97	0.18	0.18	0.12	0.18	0.18
HIF	0.96	0.95	0.96	0.95	0.96	0.96	0.32	0.96	0.96	0.00	0.96	0.95	0.95	0.96	0.95	0.96	0.95	0.95	0.96	0.95	0.95
MAPK	0.94	0.94	0.94	0.94	0.94	0.95	0.21	0.95	0.95	0.00	0.94	0.94	0.94	0.95	0.94	0.94	0.94	0.94	0.95	0.94	0.94
Mkp2	0.00	0.76	0.00	0.76	0.00	0.89	0.00	0.89	0.89	0.00	0.00	0.76	0.76	0.89	0.76	0.00	0.76	0.76	0.89	0.76	0.76
PKA	0.95	0.94	0.95	0.94	0.95	0.94	0.26	0.94	0.94	0.00	0.95	0.94	0.94	0.94	0.94	0.95	0.94	0.94	0.94	0.94	0.94
PTEN	0.09	0.11	0.09	0.11	0.09	0.09	0.67	0.09	0.09	0.92	0.09	0.11	0.11	0.09	0.11	0.09	0.11	0.11	0.09	0.11	0.11
p53	0.05	0.08	0.05	0.08	0.05	0.05	0.12	0.05	0.05	0.82	0.05	0.08	0.08	0.05	0.08	0.05	0.08	0.08	0.05	0.08	0.08
E-Cadherin	0.02	0.02	0.02	0.02	0.02	0.02	0.49	0.02	0.02	0.91	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
HSPG2	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Integrin	0.06	0.06	0.06	0.06	0.06	0.06	0.12	0.06	0.06	0.00	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06
Notch	0.10	0.10	0.10	0.10	0.10	0.06	0.10	0.06	0.06	0.02	0.10	0.10	0.10	0.06	0.10	0.10	0.10	0.10	0.06	0.10	0.10
NGAL	0.89	0.48	0.89	0.48	0.89	0.02	0.05	0.02	0.02	0.00	0.89	0.48	0.48	0.02	0.48	0.89	0.48	0.48	0.02	0.48	0.48
NOG	0.94	0.92	0.94	0.92	0.94	0.92	0.05	0.92	0.92	0.08	0.94	0.92	0.92	0.92	0.92	0.94	0.92	0.92	0.92	0.92	0.92
OPN	0.89	0.48	0.89	0.48	0.89	0.02	0.15	0.02	0.02	0.02	0.89	0.48	0.48	0.02	0.48	0.89	0.48	0.48	0.02	0.48	0.48
SHH	0.89	0.88	0.89	0.88	0.89	0.88	0.13	0.88	0.88	0.12	0.89	0.88	0.88	0.88	0.88	0.89	0.88	0.88	0.88	0.88	0.88
Wnt	0.95	0.12	0.95	0.12	0.95	0.10	0.07	0.10	0.10	0.17	0.95	0.12	0.12	0.10	0.12	0.95	0.12	0.12	0.10	0.12	0.12

	Saddle U1	Saddle U2	Saddle U3	Saddle U4	Saddle U5	Saddle U6	Saddle U7	Saddle U8	Saddle U9	Saddle U10	Saddle U11	Saddle U12	Saddle U13	Saddle U14	U15	U16	U17	U18	U19	U20	U21
Connected Stable Points & Times (Total 1000 perturbations)	S1 515 S2 485	S1 486 S3 514	S1 483 S7 517	S2 534 S4 466	S2 488 S8 512	S3 516 S4 484	S3 491 S5 509	S3 505 S10 495	S4 486 S9 514	S5 481 S6 519	S7 493 S8 507	S7 464 S10 536	S8 497 S9 503	S9 539 S10 461	S1 264 S2 258 S3 229 S4 249	S1 240 S2 247 S7 253 S8 260	S1 244 S3 248 S7 254 S10 254	S2 227 S4 264 S8 241 S9 268	S3 266 S4 228 S9 252 S10 254	S7 265 S8 261 S9 252 S10 222	S1 113 S2 99 S3 130 S4 143 S7 133 S8 132 S9 112 S10 138