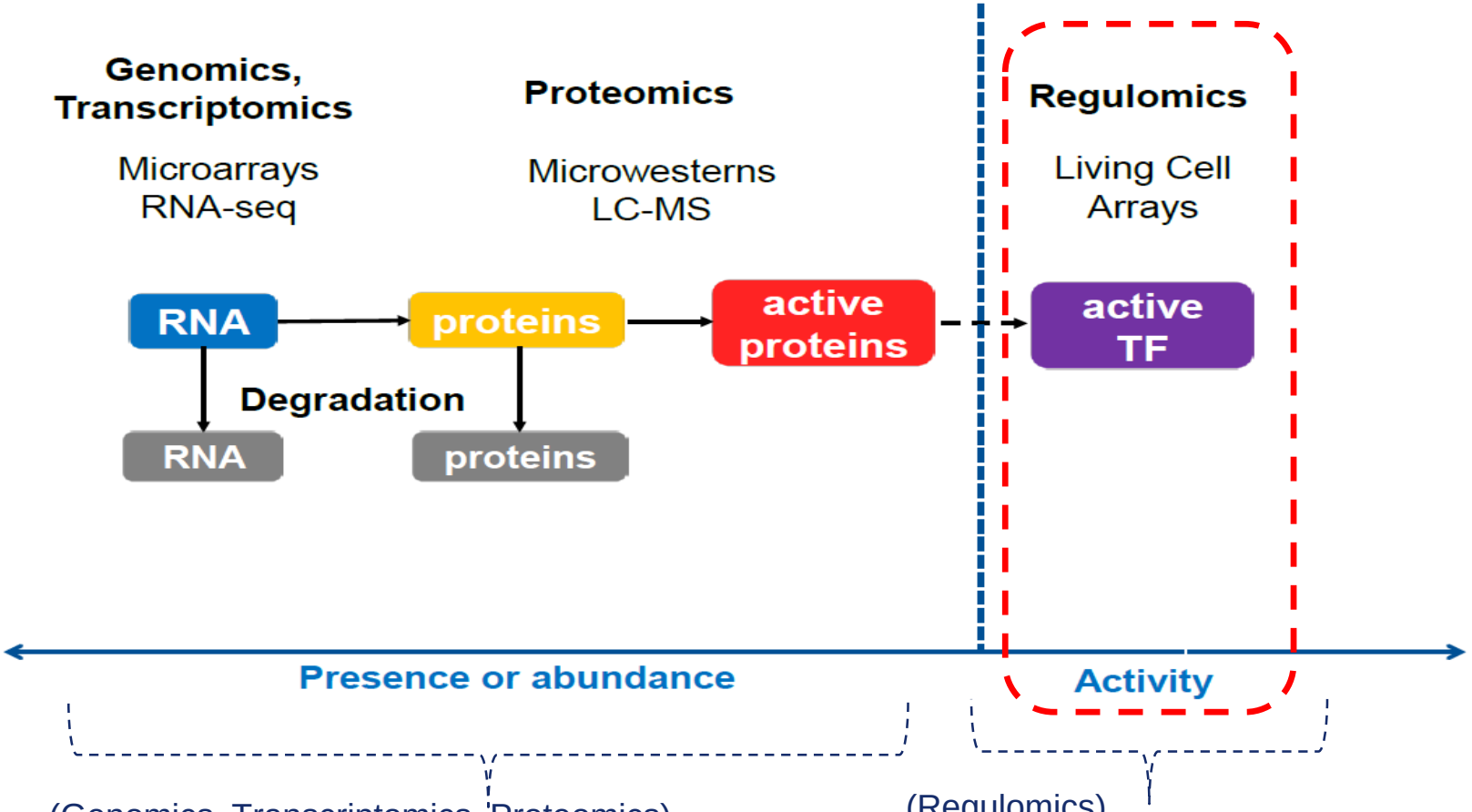
전사인자 네트워크 스크리닝 서비스

- NLCA 기술을 이용한 전사인자 네트워크와 약물 및 질환 작용점 (MOA) 분석

ebiogen

(주)이바이오젠

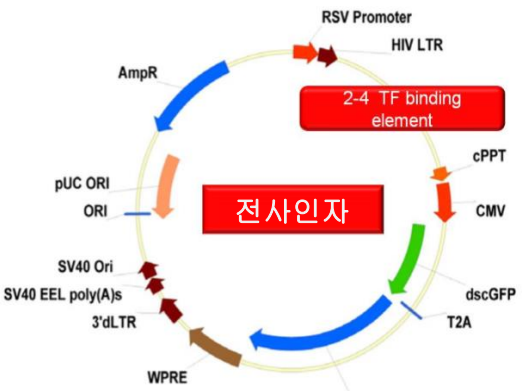
Not all molecules provide equal information

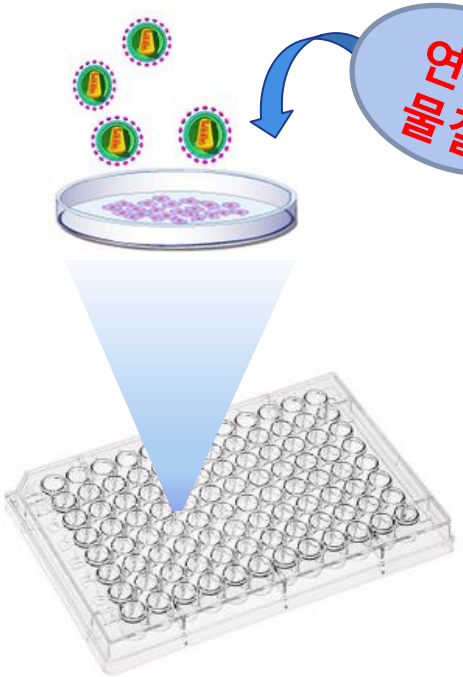


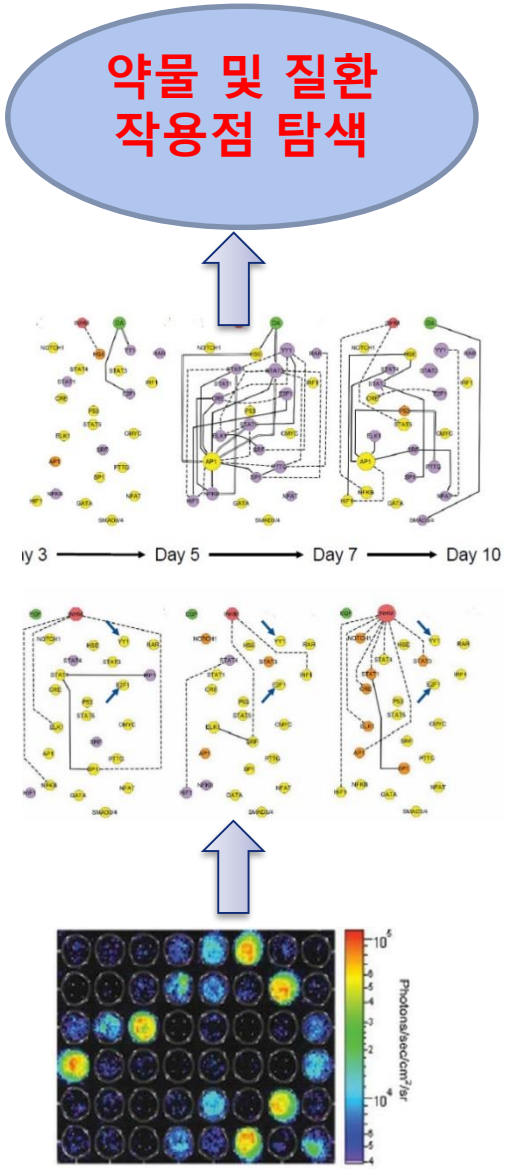
(Genomics, Transcriptomics, Proteomics)
- Lysis의 과정을 거치므로 기본적으로 관찰하고자 하는 한 시점에 molecule의 존재 또는 양만을 측정
- Activity 측정도 한 시점만을 측정

(Regulomics)
- Living cell array는 lysis의 과정 없으므로 실시간으로 다양한 시점을 관찰
- Molecule의 존재나 양이 아닌 조절자의 활성을 측정

NLCA (Network Living Cell Array)?

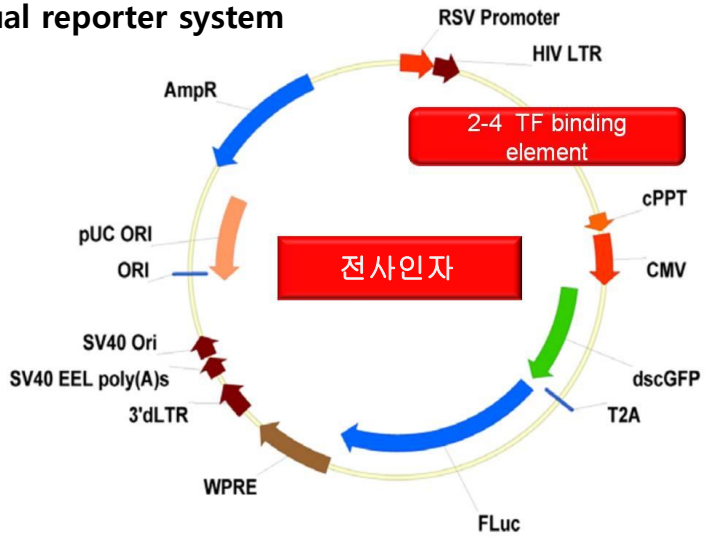




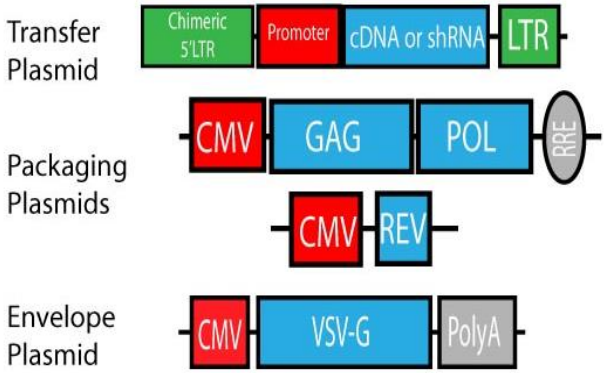


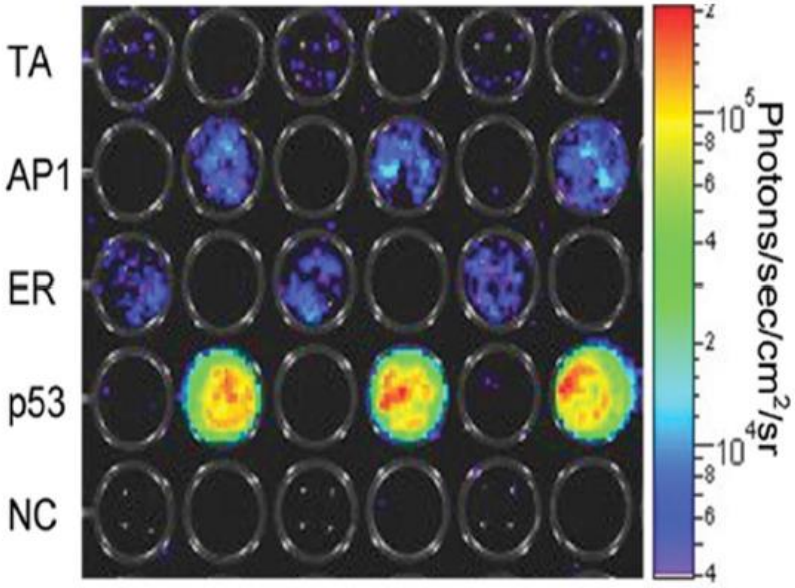
Living Cell Array (LCA) measures TF activity

Dual reporter system



3rd Geneeration Lentiviral Plasmids





Reports TF Activity

- Measure activity not abundance, TF has to be localized in the nucleus and has to bind to DNA
- Simultaneous dynamic real-time activity of multiple TFs in living cells (no cell lyse)
- Long term experiments, during tissue formation time scales
- 3D environment that better mimic physiological conditions
- Cost does not scale with time

List of transcription factor

List of transcription factor							
AP1	AP2	AP3	AP4	AR	ARNT1	Brachyury	cMyc
CRE	E2f(1)	Elk1	ER	ETS1	FOX03A	FOXA	Foxc2
GAS	GAS/ISRE	GATA	HIF1	Hnf1a	Hoxa1	HSE	HSTF
IRF1	ISRE	KLF4	LHX8	MEF1	NFkB	Notch1	p53
PAX1	PEA3	RAR	Runx1	Runx2	RXR	Smad	SNAIL
Sox	SP1	SRE	SRF	STAT3	TWIST-N	WT1	YY1
ZEB1							

NLCA 분석 프로그램

Bioinformatics
doi.10.1093/bioinformatics/xxxxxx
Advance Access Publication Date: Day Month Year
Manuscript Category

OXFORD

Systems biology

BTNET : Boosted Tree based gene regulatory network inference algorithm using time-course measurement data

Sungjoon Park [1,†], Jung Min Kim [4,†], Wonho Shin [2], Sungwon Han [5], Minji Jeon [1], Hyunjin Jang [3], Iksoon Jang [3,*] and Jaewoo Kang [1,2,*]

[1]Department of Computer Science and Engineering, Korea University, Seoul, Korea
[2]Interdisciplinary Graduate Program in Bioinformatics, Korea University, Seoul, Korea
[3]Division of Bioconvergence, Korea Basic Science Institute, Daejeon 305-333, Republic of Korea
[4]Genoplan Korea, Inc. and NAR Center, Inc., Seoul 06221, Republic of Korea
[5]School of Industrial Management Engineering, Korea University, Seoul, Republic of Korea

*To whom correspondence should be addressed.
†The authors wish it to be known that, in their opinion, the first two authors should be regarded as joint First Authors.

NLCA 실험분석 서비스

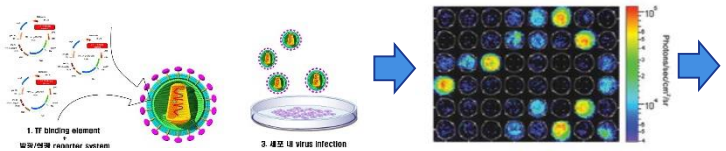
25-30개 전사인자 선별

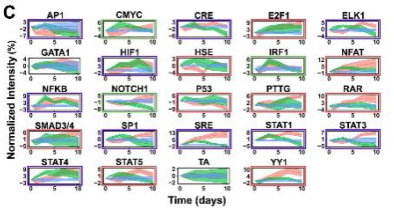
세포에 전사인자 감염

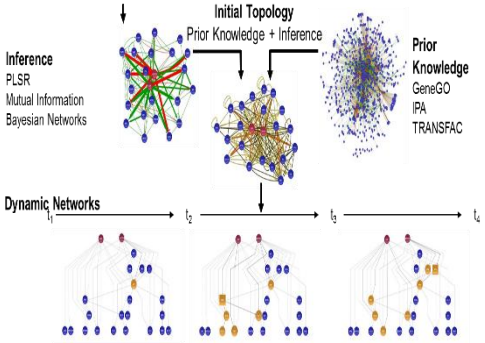
약물처리

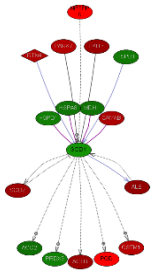
10일간 활성 측정

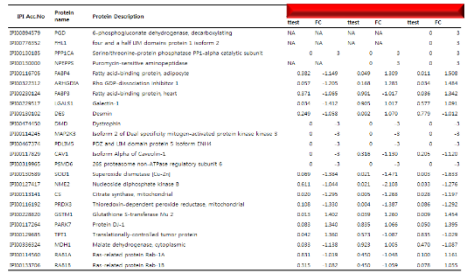
전사인자 활성 측정과 약물 및 질환작용점 분석

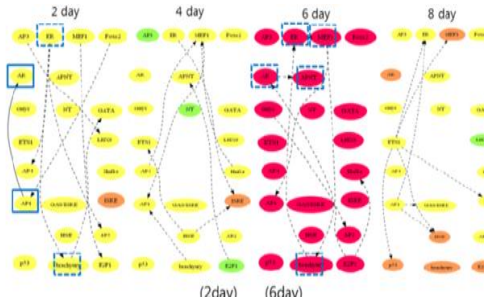












선정된 약물의 전사인자 네트워크 분석 결과

선별물질	2day	4day	6day	8day
SB1-1	AP1-AR		AR-APNT	
	ER-brachyury		brachyury-ER	
SB1-3	AR-AP1			
		APNT-E2f1		
		brachyury-LHX8		
			brachyury-Foxc2	

Order form (TF screening service)

* 연구자는 세포와 연구물질을 제공해 주셔야 합니다. (세포는 동결되어 저장된 상태로 제공)

• 세포정보

Species	☑ Human	☐ Mouse	☐ Other ( )
Cell type	☐ Primary cell	☑ Cell line	
Cell name	MH7A		
Culture condition	Media : DMEM		Antibiotics: 1% penicillin, streptomycin
	Serum: 10% FBS		CO_2: 5%
	Other:		

• 물질정보

	Name	Solvent	Volume	Conc.	Final conc.
1	MTX	DMSO	100ul	1mg/ml	1ug/ml
2					

• 측정시간

	Time interval	Measurement period	Add time
1	1 day	1 – 7 day	2
2			

• 전사인자정보 (☑ Selection)

☐ AP1	☐ AP2	☐ AP3	☐ AP4	☐ AR	☐ ARNT1	☐ Brachyury	☐ cMyc
☐ CRE	☐ E2f(1)	☐ Elk1	☑ ER	☐ ETS1	☐ FOX03A	☐ FOXA	☐ Foxc2
☐ GAS	☐ GAS/ISRE	☐ GATA	☐ HIF1	☑ Hnf1a	☑ Hoxa1	☐ HSE	☐ HSTF
☐ IRF1	☐ ISRE	☑ KLF4	☐ LHX8	☐ MEF1	☐ NFkB	☐ Notch1	☐ p53
☐ PAX1	☐ PEA3	☐ RAR	☐ Runx1	☑ Runx2	☐ RXR	☐ Smad	☐ SNAIL
☐ Sox	☐ SP1	☐ SRE	☐ SRF	☐ STAT3	☐ TWIST-N	☑ WT1	☐ YY1
☐ ZEB1							

* 주문양식 예시

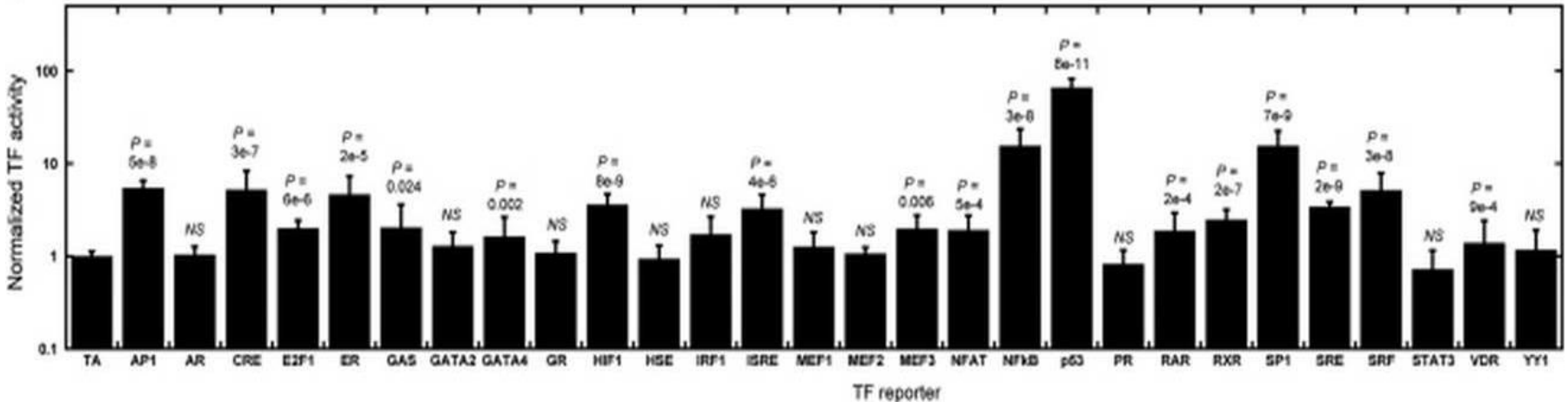
NLCA analysis process

Raw data (전사인자 활성 측정값)

Transcription factor

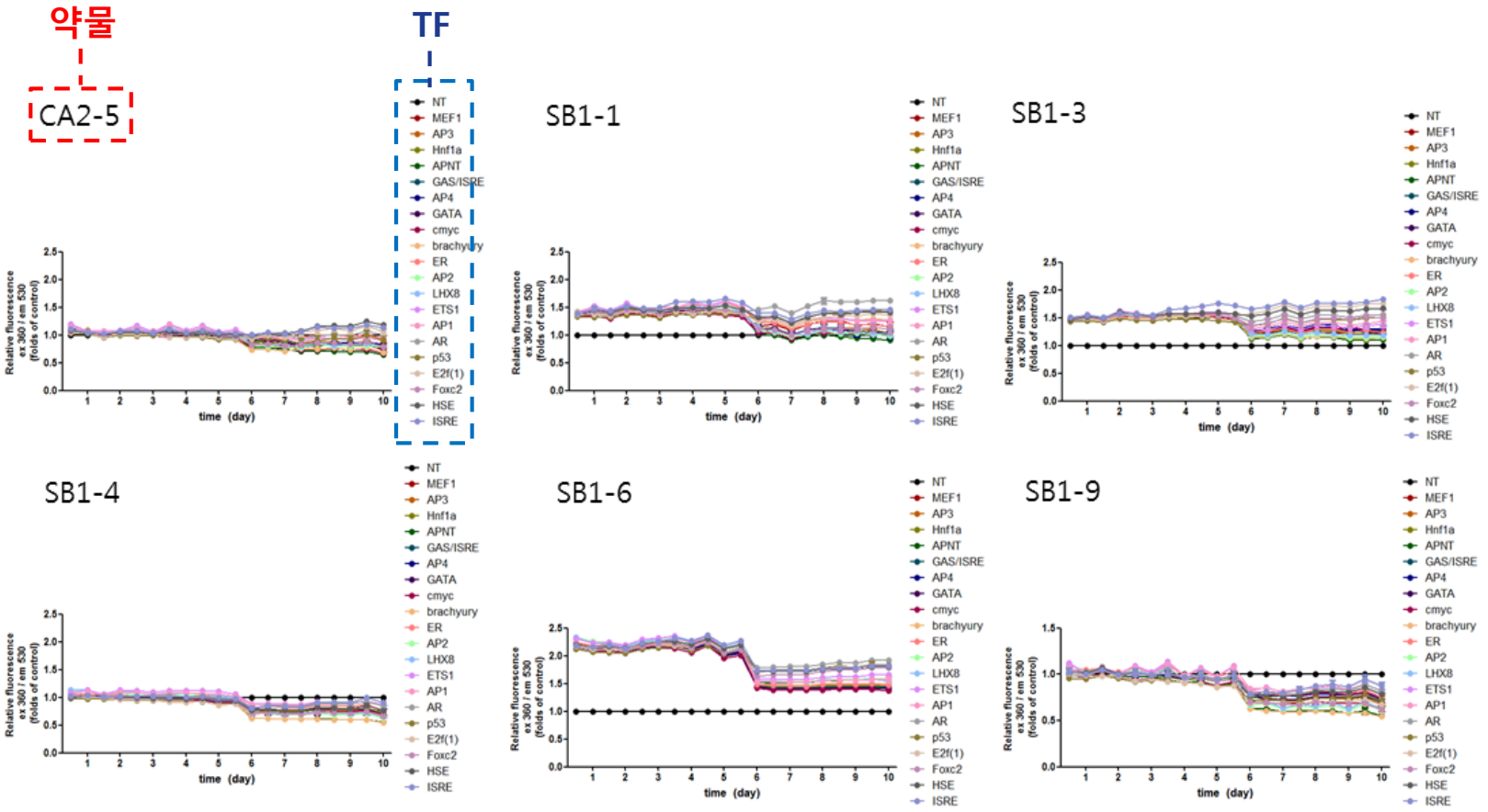
Time (days)

	0.5			1			2			3			4			5		
NT	28.3163	29.3853	27.8523	29.488	26.924	26.993	34.0367	34.9277	34.8547	41.1067	38.3687	42.5987	44.541	42.711	45.619	44.5567	43.9887	46.6257
Con	26.2903	26.5953	25.0503	23.385	25.529	22.926	27.7697	31.3227	26.9257	39.0287	41.0977	36.6977	47.356	49.762	47.582	54.1247	64.6227	56.7777
APNT	23.0823	26.7533	29.3393	21.211	25.3	26.348	23.2037	28.2787	31.7637	33.1747	37.8447	35.9447	38.759	41.169	40.308	45.3737	52.0267	53.1547
Brachyuri	18.638	21.792	19.888	19.5537	26.1977	33.2607	14.2973	19.1263	26.6383	19.9763	24.0093	21.8003	20.356	25.579	23.231	28.816	35.216	38.959
ap2	28.5253	28.6183	17.8713	28.2487	36.5897	35.2477	22.3753	27.0223	29.1043	26.1713	31.3403	29.1973	36.516	43.709	42.975	39.399	45.357	44.114
ap1	23.097	30.797	33.721	20.9567	25.4147	25.3637	18.2747	23.2857	24.7107	204.382	212.082	215.006	214.522	222.04	229.661	203.437	208.546	213.693
cmyc	22.616	23.689	20.953	21.595	28.05	26.227	24.2717	36.1067	41.0817	28.8207	32.6977	32.8057	33.672	39.009	37.646	35.9077	43.9377	43.5647
p53	32.315	33.757	37.18	32.2263	32.2133	35.5513	35.006	33.416	36.364	40.909	49.579	56.974	41.345	47.075	52.116	40.3527	49.0987	50.8497
ap4	23.5113	26.6993	24.1293	25.0603	33.1963	32.3413	23.9423	31.2113	26.2633	31.227	36.034	35.336	35.2143	40.0163	41.5313	39.5877	44.6927	46.1667
CRE	20.958	22.437	23.298	23.143	28.222	27.831	19.5417	28.2577	32.3077	20.3973	21.8763	22.7373	24.6933	30.5843	28.2123	26.908	36.155	39.614
#25	12.5903	14.2803	15.1863	20.3941	19.7711	20.9731	15.0117	13.0347	16.4707	-4.6138	-6.9068	-5.4558	14.2742	12.6732	17.0462	20.8929	176.029	177.352
AR	9.8083	9.5833	12.8253	6.7771	6.6961	8.9161	6.9477	7.0067	9.7507	-11.6248	-12.7068	-10.7538	13.1432	12.8622	16.4542	6.4049	163.567	166.444
#29	14.3683	14.1393	15.4553	10.2951	13.6881	17.7261	10.8977	14.5807	18.3847	-8.1868	-5.7048	-2.4808	11.2492	15.8512	19.2952	24.9709	185.558	188.725
#24	7.2993	7.6833	8.3413	6.6051	10.0521	12.8971	6.3377	8.3107	10.8637	-8.7548	-7.4568	-5.1008	10.5622	13.1712	16.9912	7.9819	167.744	170.459
#21	8.0153	8.6683	7.5293	3.5281	6.0811	7.2421	13.3737	15.6447	16.2877	-12.8248	-10.9448	-10.7858	11.4762	13.9102	16.9502	14.7069	172.56	173.438
#11	6.2343	8.8833	9.4843	1.7611	8.1031	9.6661	1.8297	8.1677	8.8997	-13.8618	-6.5418	-7.0438	5.2652	12.7232	13.9812	5.1309	166.405	168.562
#27	8.3193	9.9643	11.4983	9.2621	9.5331	12.5971	18.3837	20.5297	25.1327	-3.5848	-3.4298	0.2002	19.2072	22.3222	26.0182	22.3869	180.105	183.993



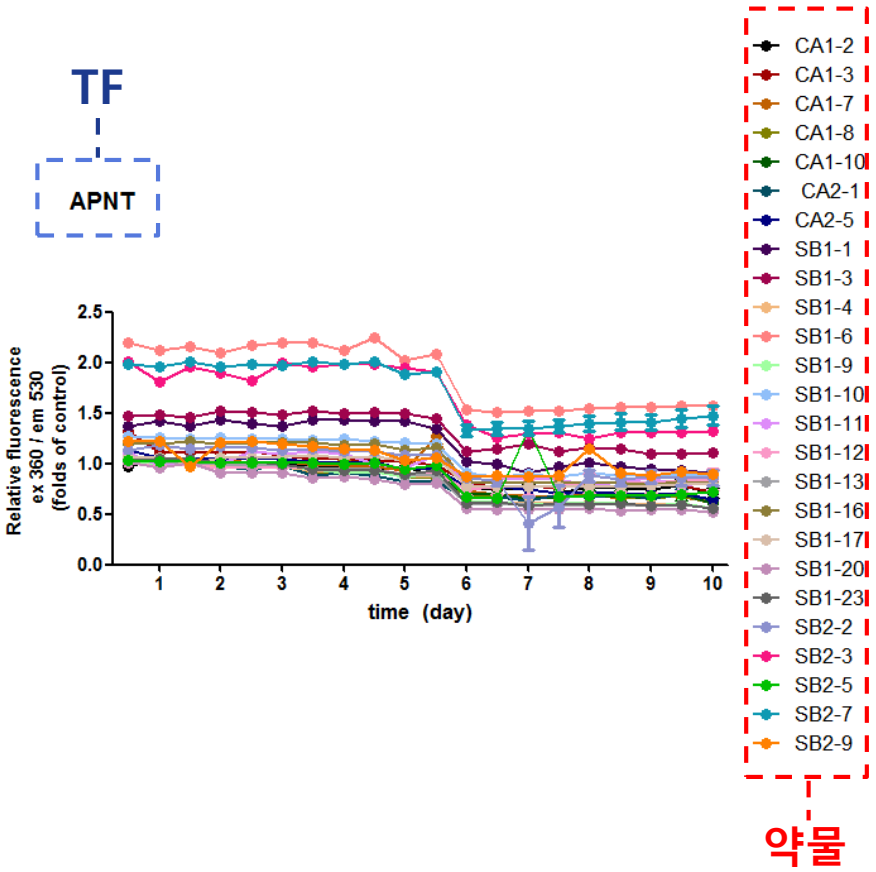
NLCA analysis process

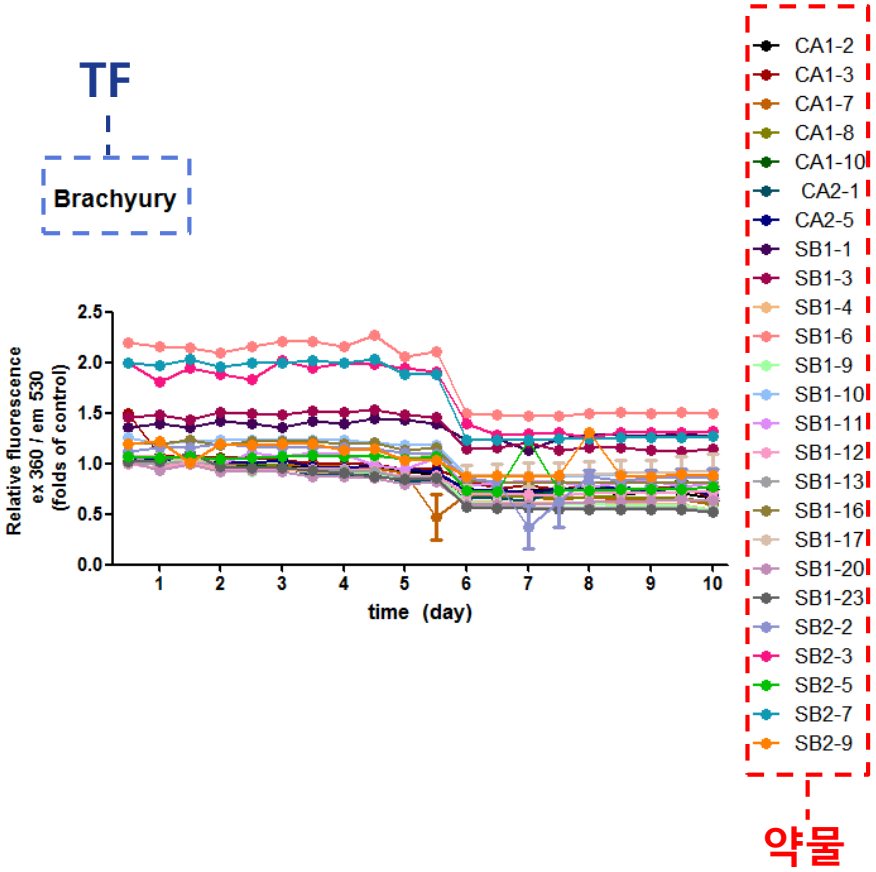
- 전사인자 활성 측정을 통한 **long-term** 생체 내 실시간 전사인자 발현분석



NLCA analysis process

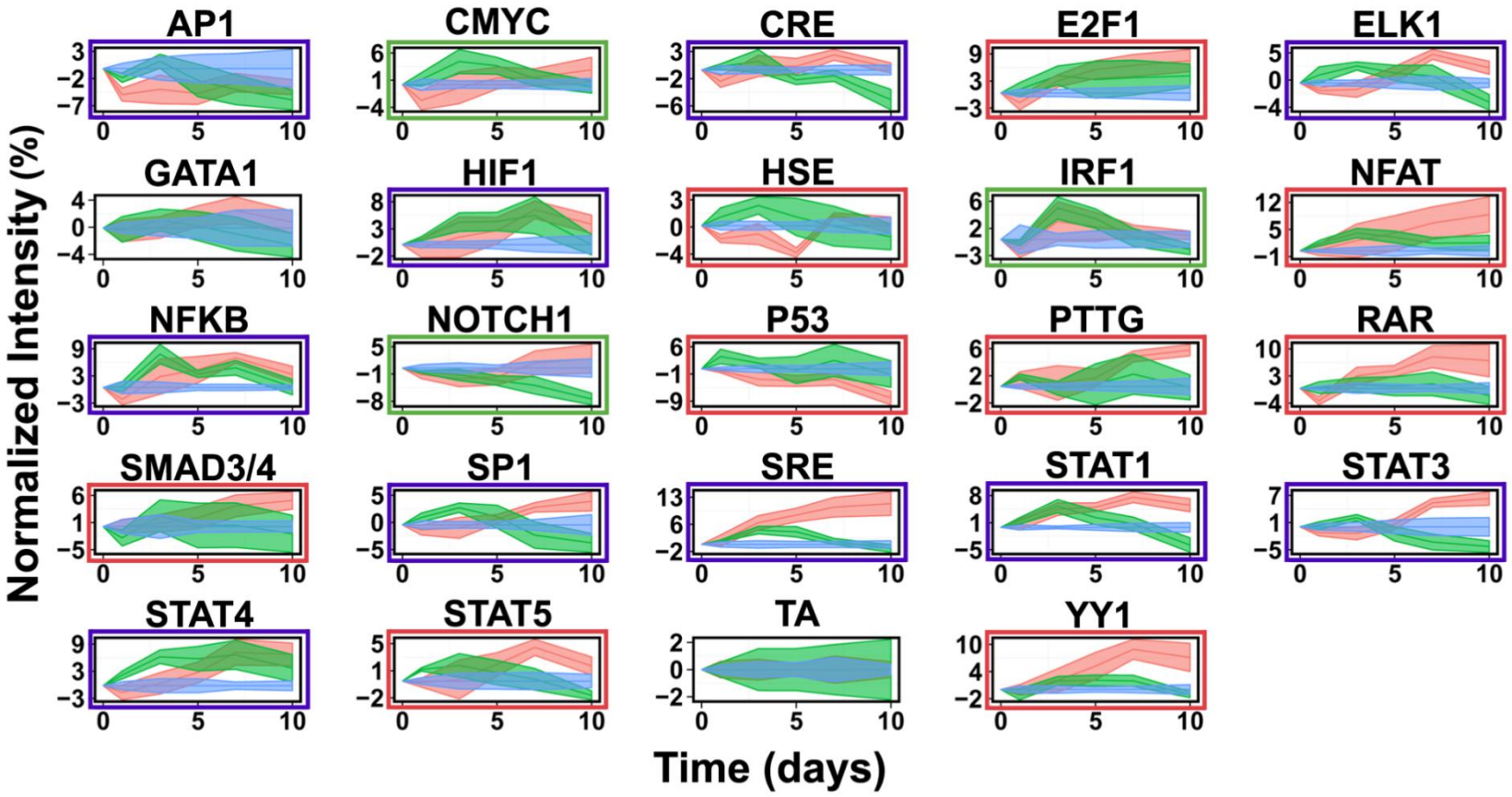
- 전사인자 활성 측정을 통한 **long-term** 생체 내 실시간 전사인자 발현분석





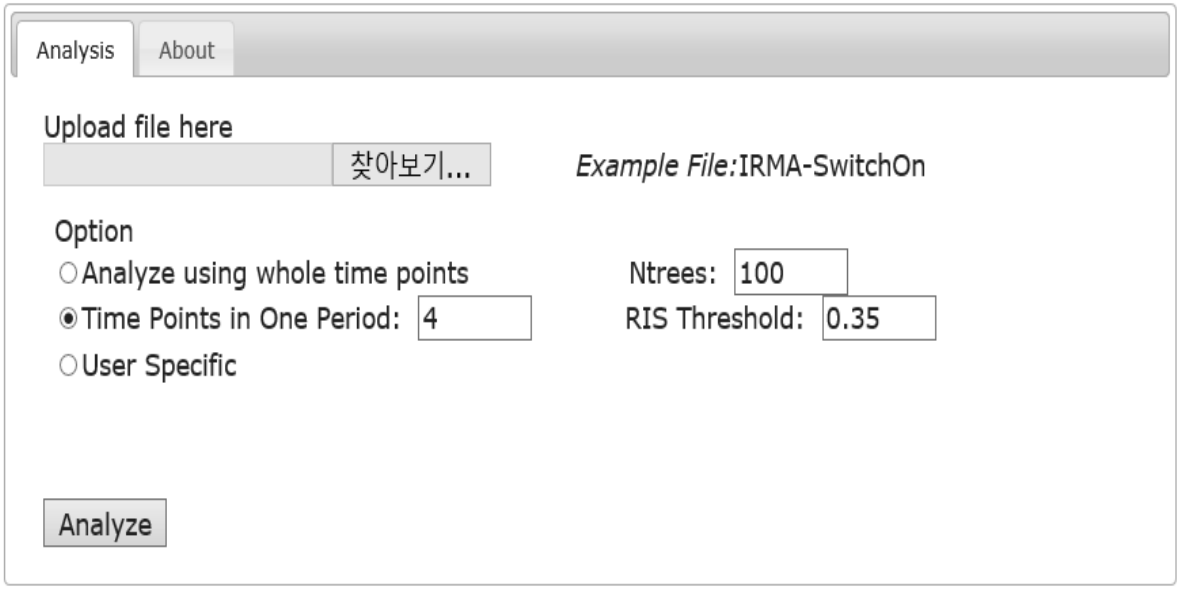
NLCA analysis process

- 전사인자 활성 측정을 통한 **long-term** 생체 내 실시간 전사인자 발현분석



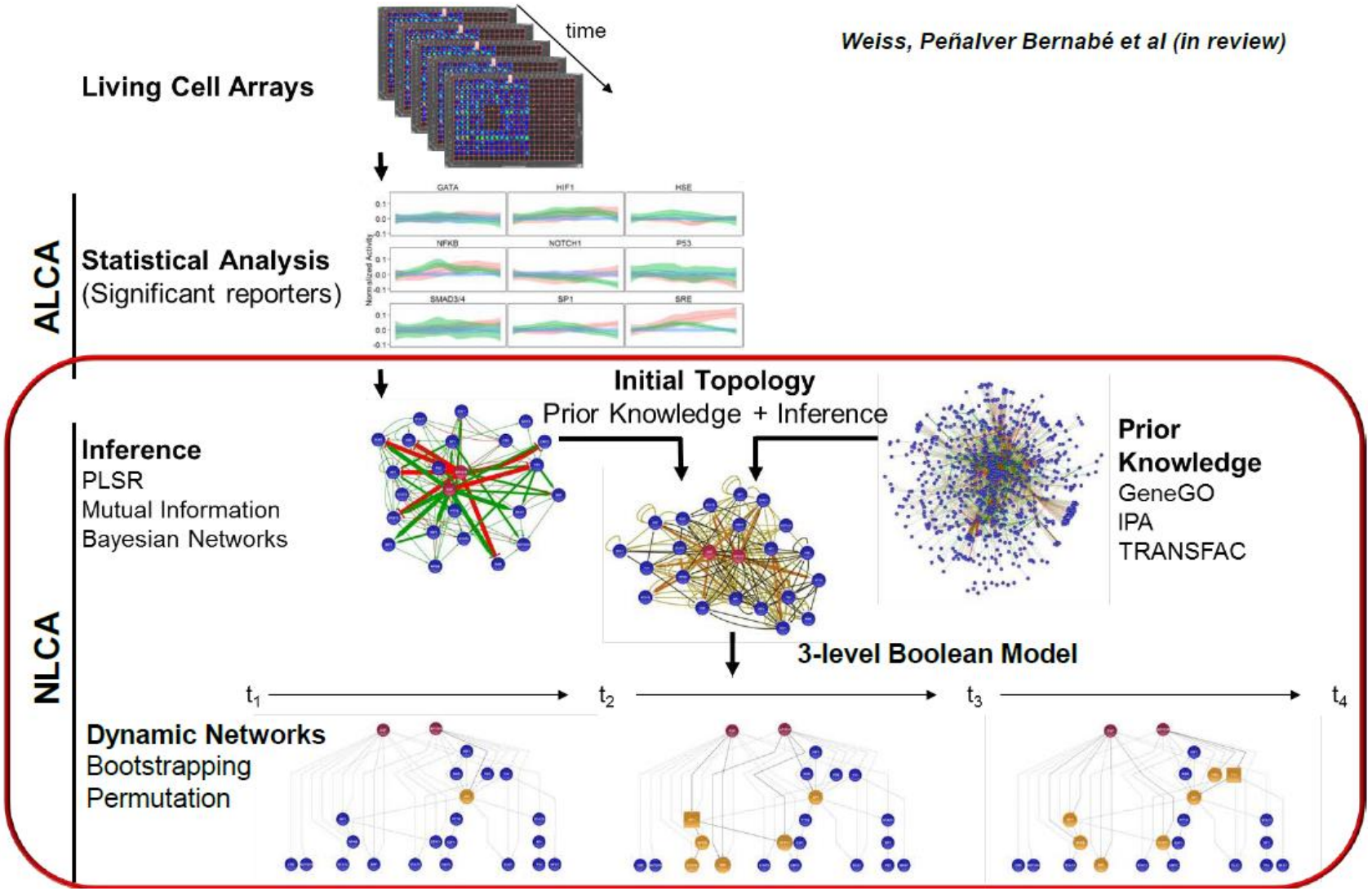
NLCA analysis process

iBTNET *An online tool for inferring gene regulatory network using boosted tree from time-course measurement data*



*Best viewed in the latest version of Chrome (31+), Safari (5.1+), or IE (11+, w/ the compatibility option turned off). JavaScript and Flash required.

Living Cell Array (LCA) Pipeline in R



How does the LCA network look like?

Up-regulated

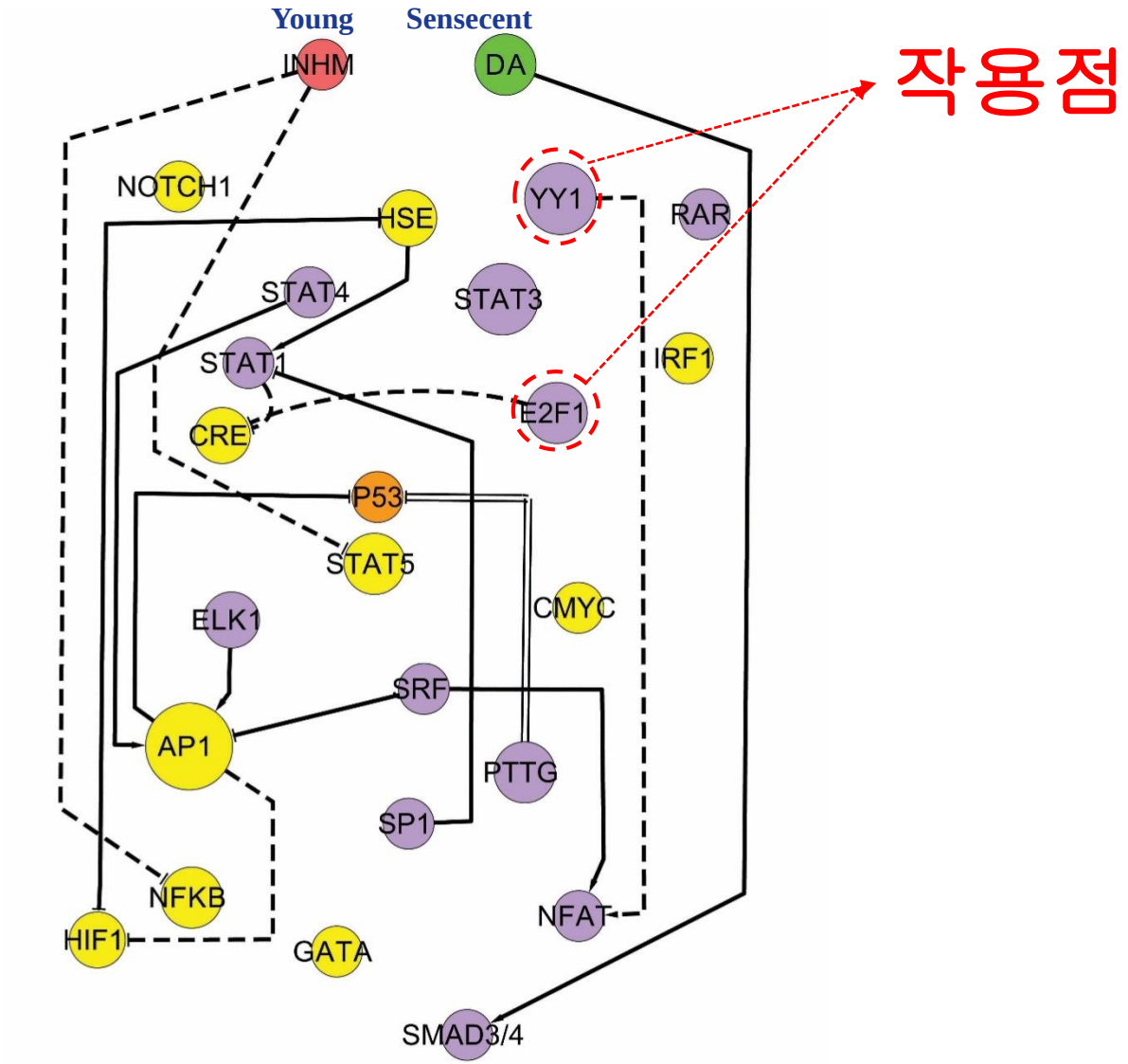
No change

Down-regulated

Prior knowledge

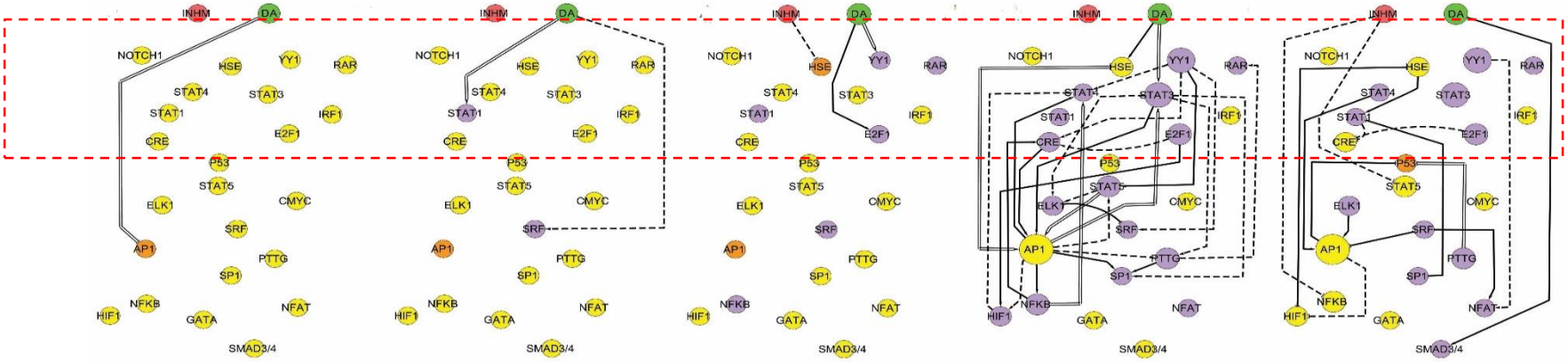
Inference methods

Both



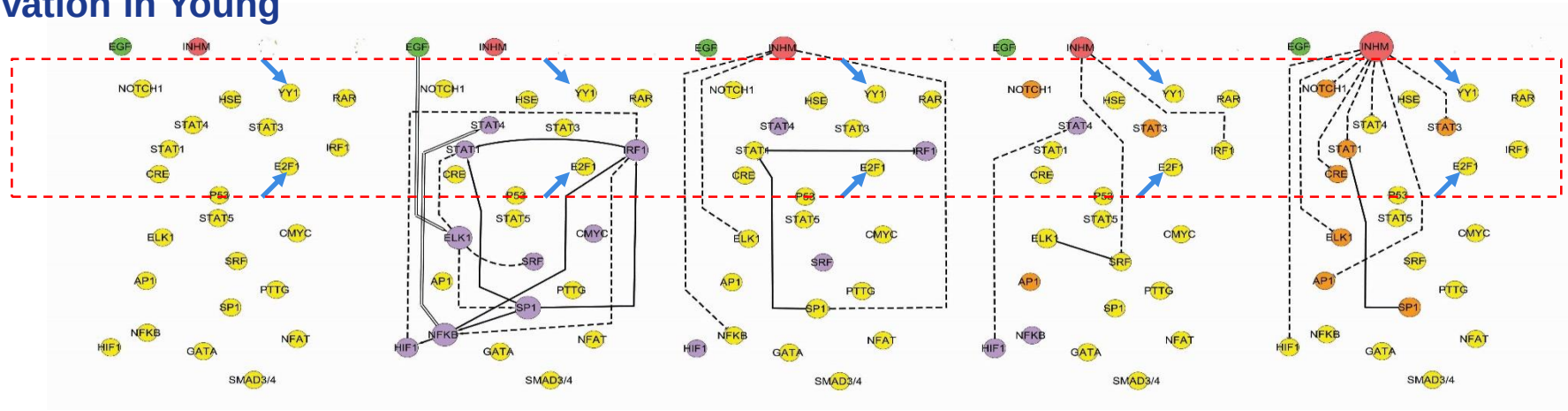
Different phenotypes, different dynamic networks

activation in Senescent



Day 0 → Day 1 → Day 3 → Day 5 → Day 7 → Day 10

activation in Young



(Senescent 와 Young 에서의 차이나는 작용점)

- Young에서 YY1과 E2F1은 1일부터 10일까지에서 활성되지 않고 있슴
- Senescent에서YY1과 E2F1은 다른 TF에 영향을 주는 시작부분의 TF 임

고객을 최우선으로 하고
직원이 즐겁게 일할 수 있는
국내 최고의 바이오 기업으로
성장해 나가겠습니다.

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BioResearch & HealthCare Creator

(주)이바이오젠

TEL : 02-3141-0791

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