

# Bioinformatics screening regarding herbal components that targetedly regulate the function of tumour- associated macrophages

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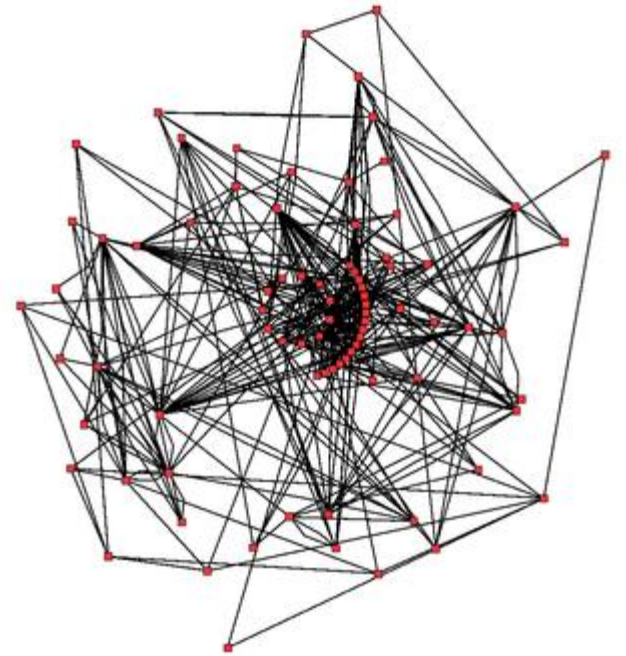
Konkuk University

# Network Biology

- Gene society라 할 수 있는 cellular system
- 동일한 유전자도 어떤 gene set과 상호작용 하는지에 의해 이질적인 기능을 나타낼 수 있음 -> pleiotropy
- 네트워크의 개발과 그 생물학적 응용에 집중하는 연구분야를 network biology

# 유전자 네트워크의 종류와 모델링 기법

- system을 node와 edge로 모델링
- node는 component, edge는 relationship
  - ① protein-protein interaction network
  - ② transcriptional regulatory network
  - ③ functional gene network



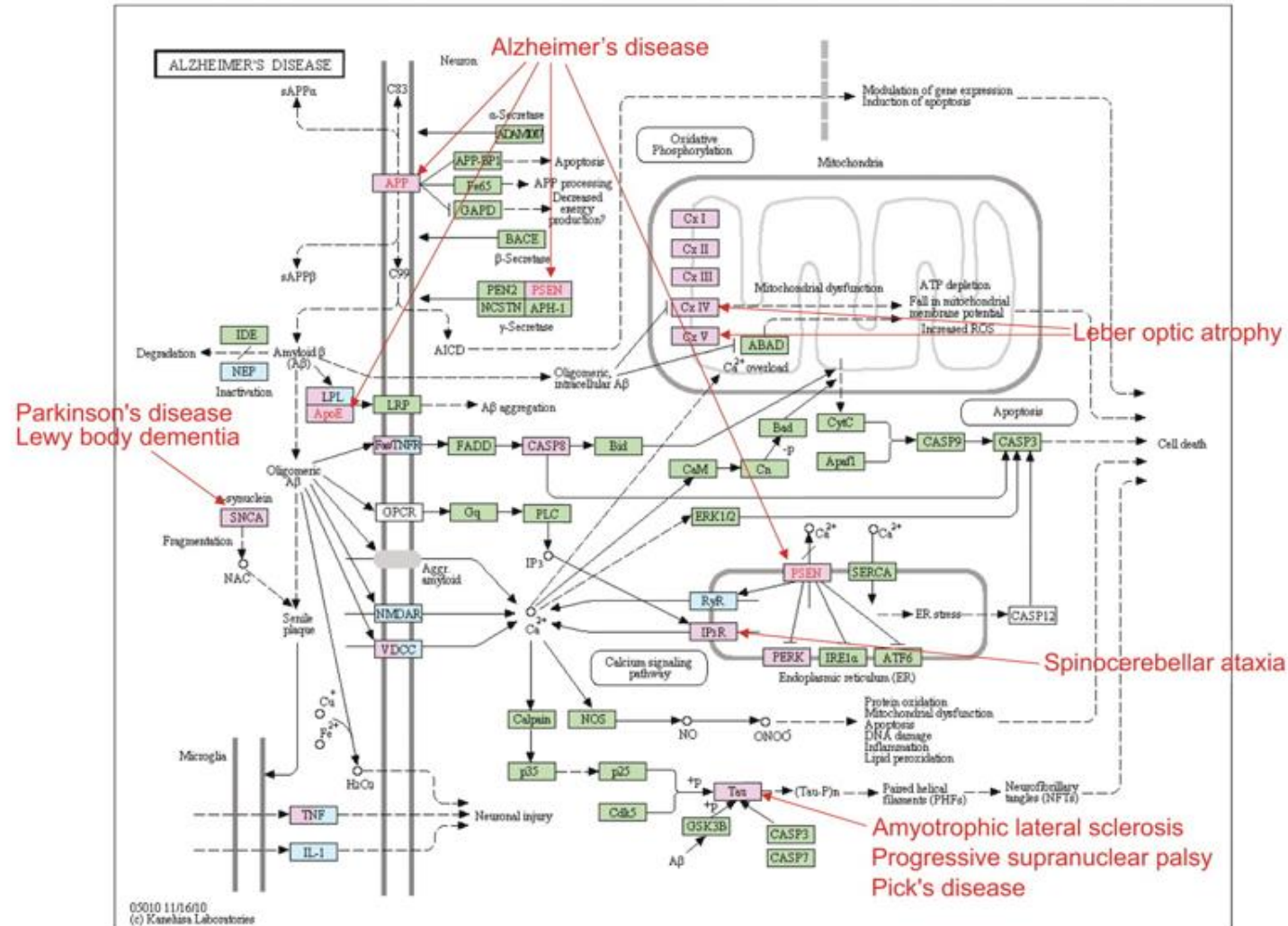
# functional gene network 생물학적 응용기법

1. gene의 새로운 기능 예측
2. gene의 기능상실이 개체 형질에 가져올 결과 예측
3. essential gene의 예측
4. disease causal gene과 그들의 modulator 예측



# Knowledge base extension

Disease/drug mapping is the process to map all known disease genes (pink) and all known drug targets (light blue) against all KEGG pathway maps.



Minoru Kanehisa et al. Nucl. Acids Res. 2011;nar.gkr988

# Introduction

- Tumour-associated macrophages(TAMs) are the most common type of inflammatory cells in tumour stroma.
- Conventional cancer treatments include **surgery, radiotherapy and chemotherapy**, but the use of these treatments is greatly limited due to poor prognoses and severe side-effects.
- Traditional Chinese medicinal herbs are being employed as new anticancer drugs.
- In the present study, they used modular analysis bioinformatics techniques to screen for **the differentially expressed genes in TAMs** that play a role in their core functional groups.

# Materials and methods

- Screening for differentially expressed genes in TAMs.
- Establishing and analyzing the modules of the differentially expressed genes.
- Screening for traditional Chinese medicine components that regulate the functional modules.
- Literature review and the generation of a regulatory network connecting herbal components and modules.
- Statistical analysis.



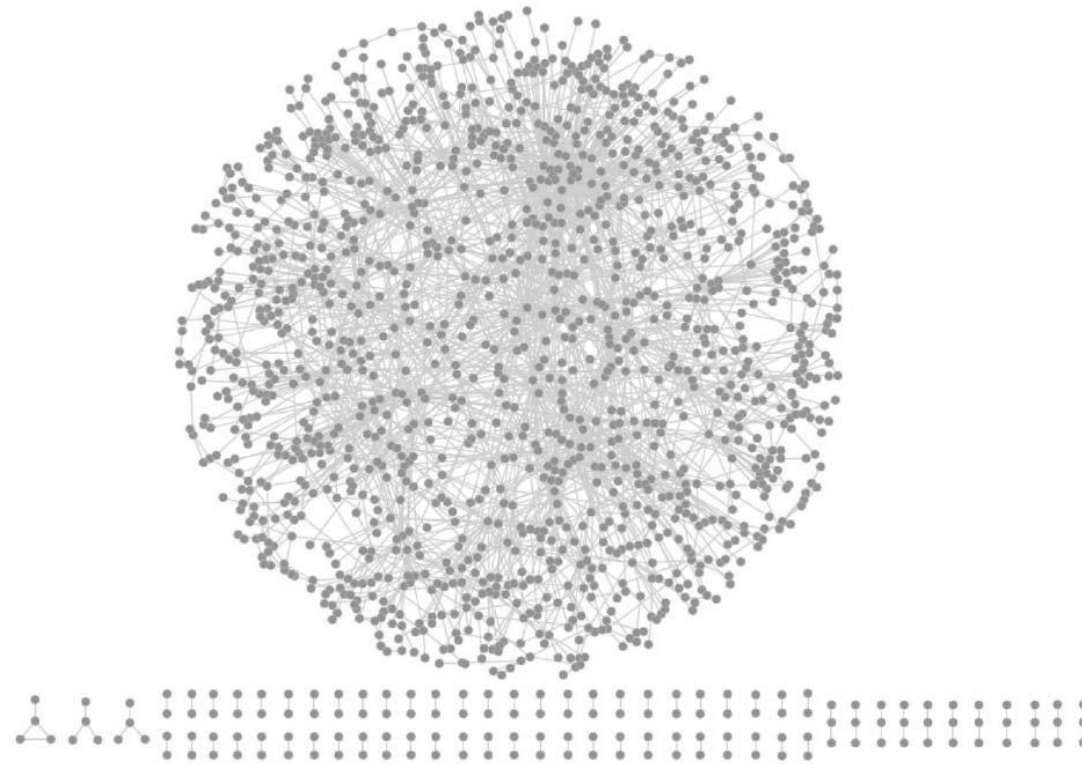
# Summary of 4 data series

Series	Array platform	Samples	Experiment design	Group
GSE38283 Expression data from normal brain/glioma associated macrophages	GPL1261 Affymetrix mouse genome 430 2.0 array	GSM937959	Macrophages from normal brain, Rep 1	Control
		GSM937960	Macrophages from normal brain, Rep 2	Control
		GSM937961	Macrophages from normal brain, Rep 3	Control
		GSM937962	Macrophages from G1261, Rep 1	TAM
		GSM937963	Macrophages from G1261, Rep 2	TAM
		GSM937964	Macrophages from G1261, Rep 3	TAM
		GSM937965	Macrophages from G1261, Rep 4	TAM
GSE18804 Expression data from <i>in vitro</i> -induced non-hypoxic TAMs	GPL6246 Affymetrix mouse gene 1.0 ST array	GSM466436	Macrophage unconditioned, Rep 1	Control
		GSM466437	Macrophage unconditioned, Rep 2	Control
		GSM466438	Macrophage unconditioned, Rep 3	Control
		GSM466439	TAMs_human glioblastoma-conditioned, Rep 1	TAM
		GSM466440	TAMs_human glioblastoma-conditioned, Rep 2	TAM
		GSM466441	TAMs_human glioblastoma-conditioned, Rep 3	TAM
		GSM466442	TAMs_human colorectal adenocarcinoma- conditioned, Rep 1	TAM
		GSM466443	TAMs_human colorectal adenocarcinoma- conditioned, Rep 2	TAM
GSE18404 High-density gene expression analysis of TAMs from mouse mammary tumours	GPL9298 Nimbelgen mouse 35K array	GSM458919	TAM, Rep 1	TAM
		GSM458920	TAM, Rep 2	TAM
		GSM458921	TAM, Rep 3	TAM
		GSM458922	TAM, Rep 4	TAM
		GSM458923	Splenic Macrophage, Rep 1	Control
		GSM458924	Splenic Macrophage, Rep 2	Control
		GSM458925	Splenic Macrophage, Rep 3	Control
		GSM458926	Splenic Macrophage, Rep 4	Control
GSE36047 Macrophages in invadopodia formation	GPL13252 Agilent-027114 human 8x60 k microarray	GSM879917	Macrophage cultured for 6 h	Control
		GSM879918	Macrophage cocultured with tumour cells (DU-145) for 6 h	TAM

# Screening the gene modules.

Among the 4 groups of TAM expression profiles, a total of 4,753 differentially expressed genes were identified.

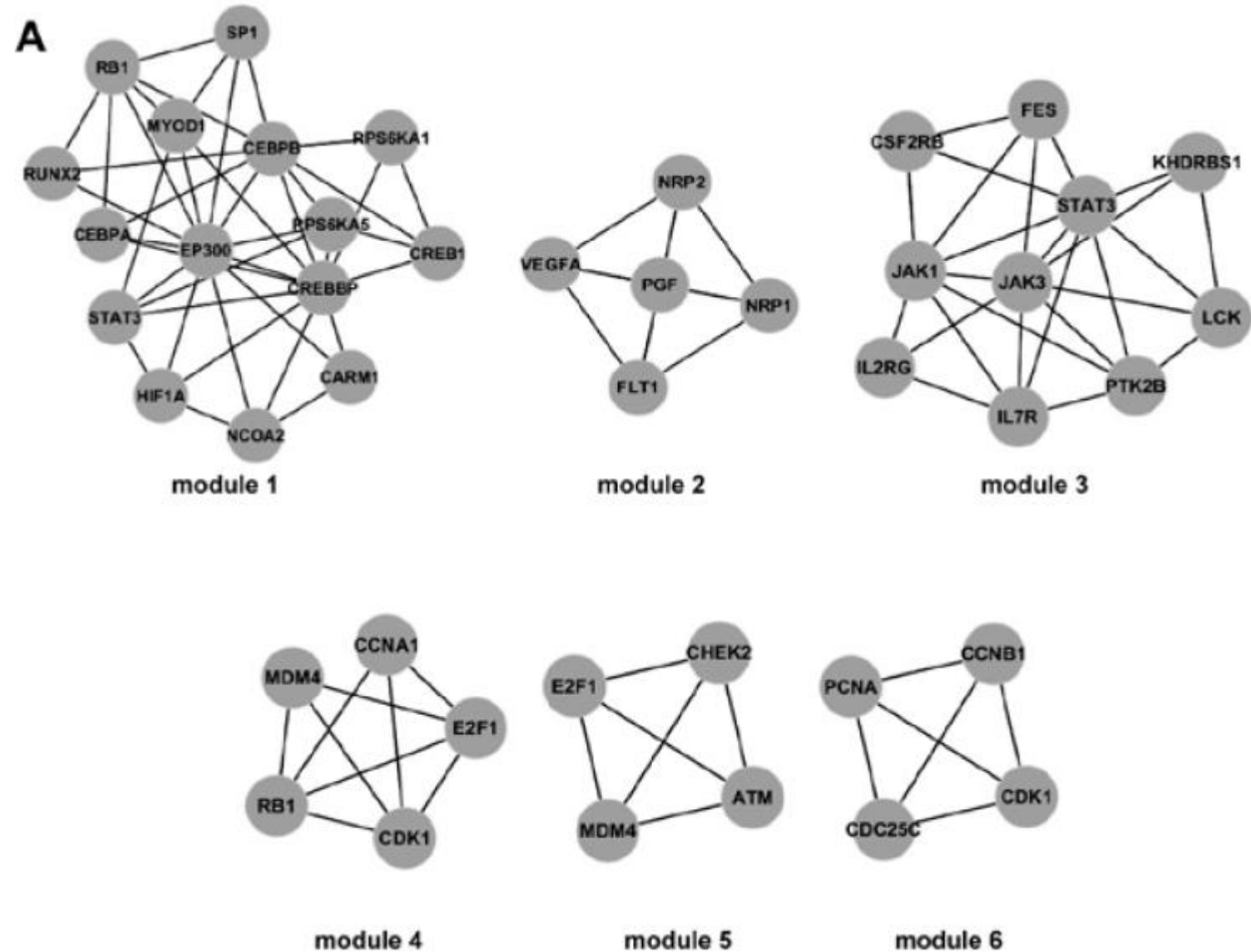
PPI network - 2,407 edges and 1,501 nodes.



# Screening the gene modules.

CFinder software was used to identify modules within the sub-networks.

$k = 4$ , 6 modules were identified that had a total of 46 genes.

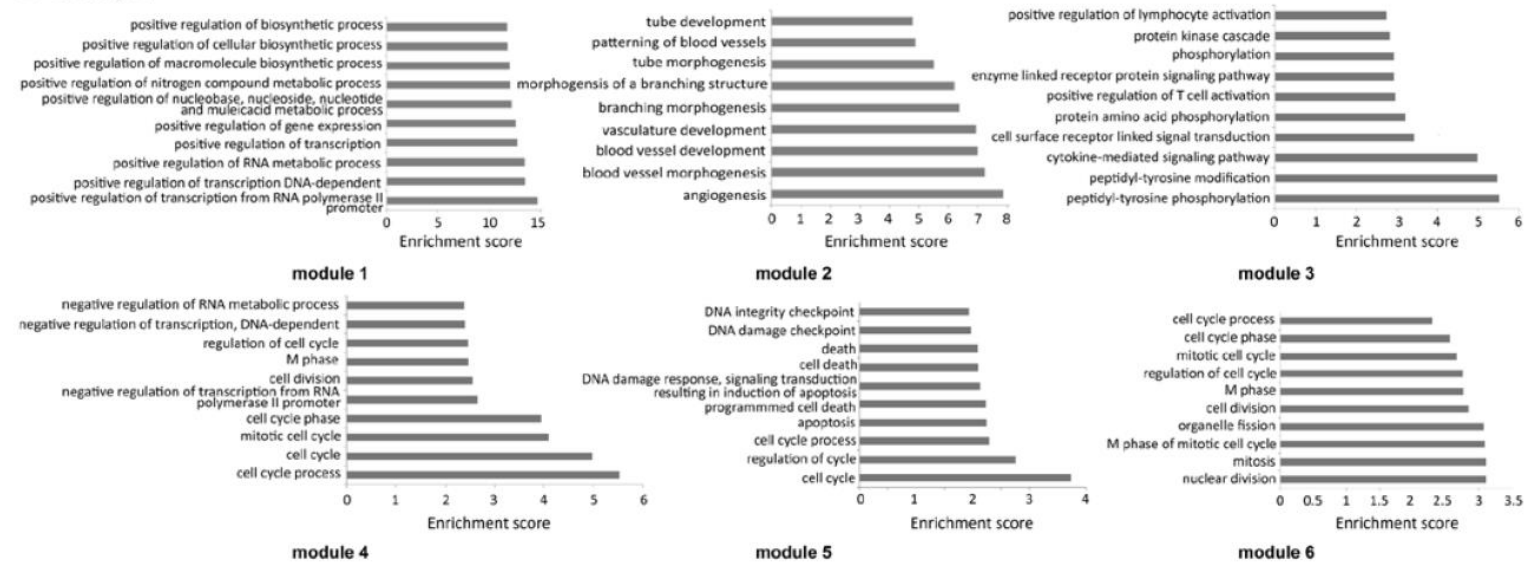


## Functional analyses of the gene modules.

DAVID software was used to conduct a GO\_BP analysis of each module.

The top 10 scores were plotted as a bar chart.

### B GO analysis:

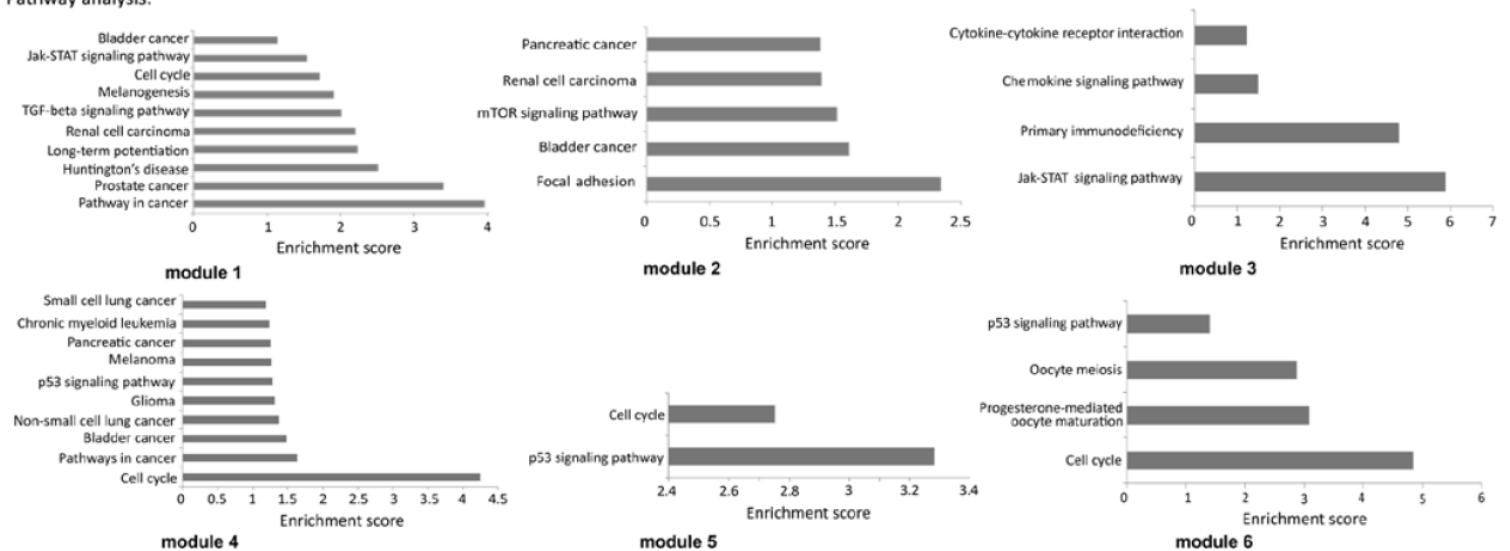


## Functional analyses of the gene modules.

DAVID software was also used to perform a pathway analysis of each module.

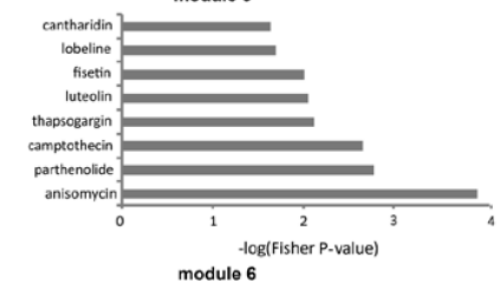
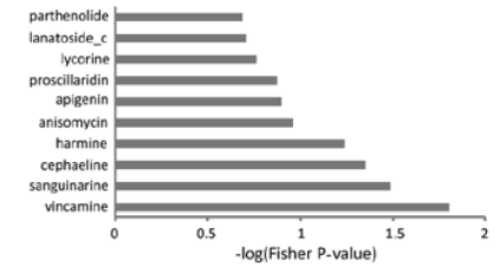
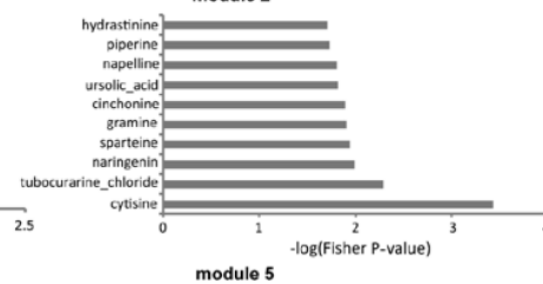
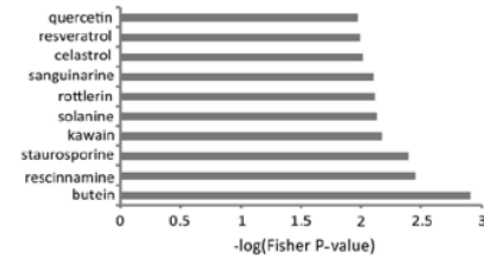
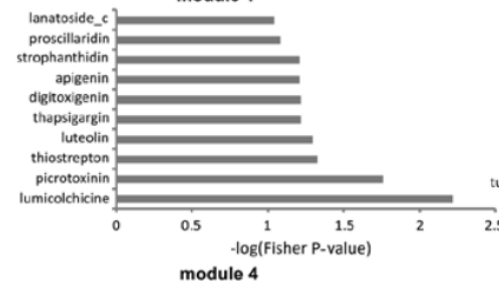
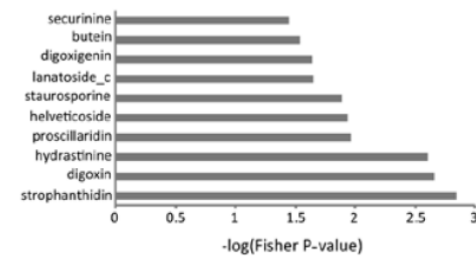
The top 10 scores were plotted as a bar chart.

### C Pathway analysis:



## Herbal components that regulate the gene modules.

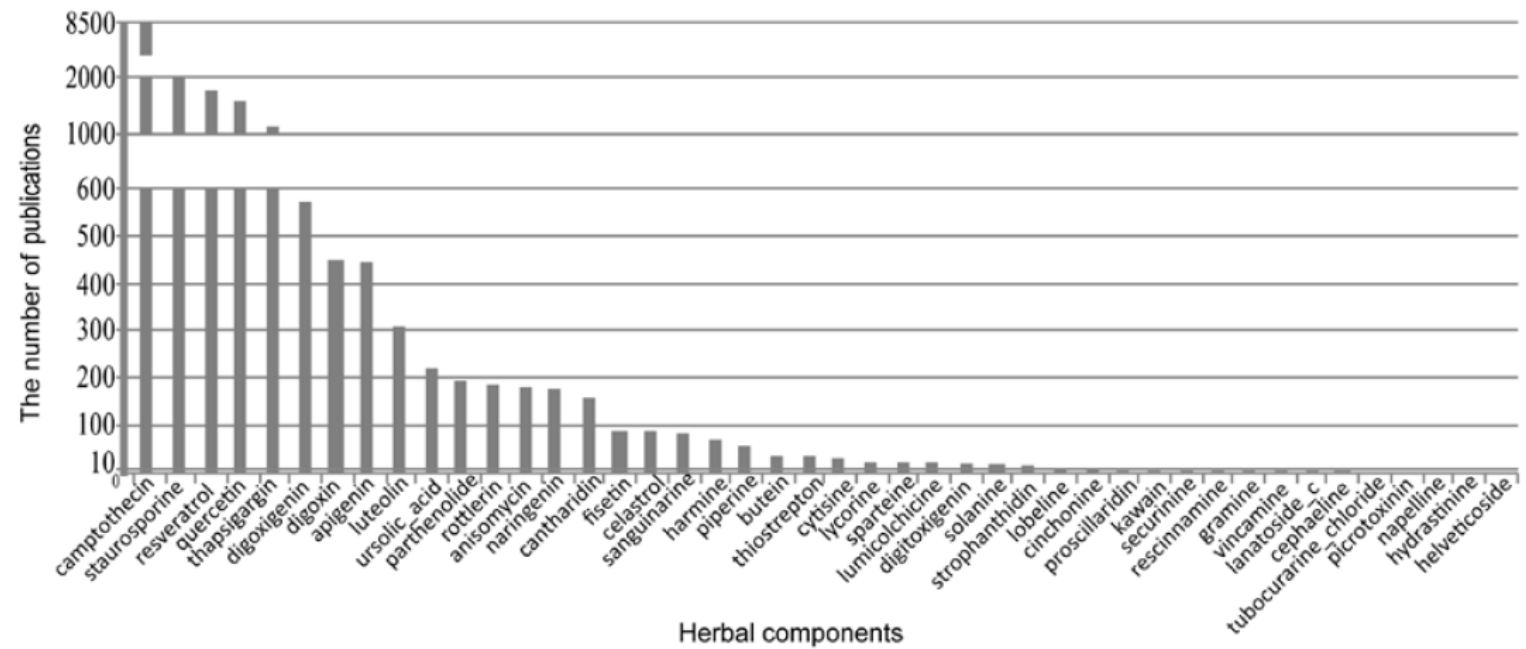
The genes from each module were mapped with the differentially expressed genes found from the c-map database, allowing us to determine the relationships between the genes in each module and the tested small molecules.



# Potential new anticancer drugs.

Potential new anticancer drugs that regulate the genes in the 6 core modules were identified through literature review.

the 44 determined herbal small molecules





# Article

## Creating a regulatory network connecting the herbal components and the modules.

Combined with the 44 herbal components and the 6 modules and the results of the literature review.

