

About OMICS Group

OMICS Group is an amalgamation of [Open Access publications](#) and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 500 online open access [scholarly journals](#) in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 500 [International conferences](#) annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

About OMICS International Conferences

OMICS International is a pioneer and leading science event organizer, which publishes around 500 open access journals and conducts over 500 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

.

Integrative Image and RNA-seq Data Analysis

Momiao Xiong

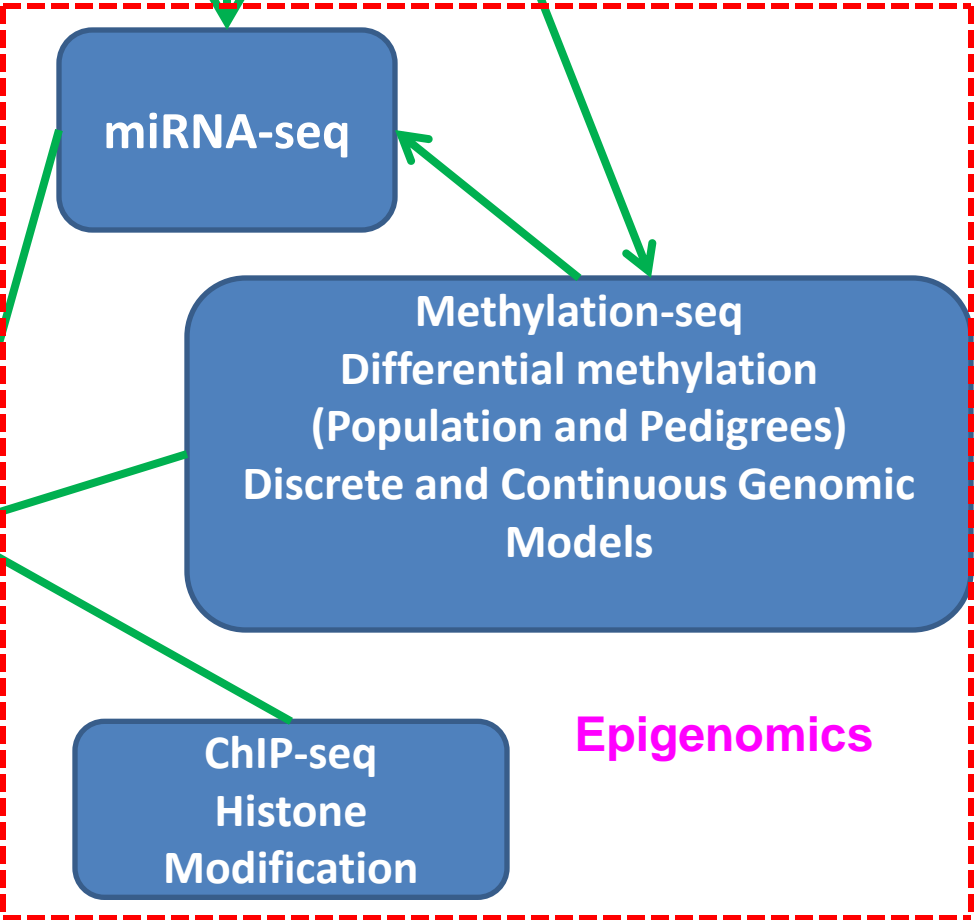
University Of Texas School of
Public Health

***Transcriptome analysis:
Unveiling the Layers of
Expressions***

Resequencing and De novo sequencing
Association Studies (Population and Pedigrees)
Discrete and Continuous Genomic Models

Imaging
Disease Subtype
Image-RNA

Differential Expression, Co-expression Networks, Allele specific expression
(Population and Pedigrees)
Disease risk and drug response prediction
Discrete and Continuous Genomic Models



eQTL

miRNA-seq

Image – Genetics

DTI

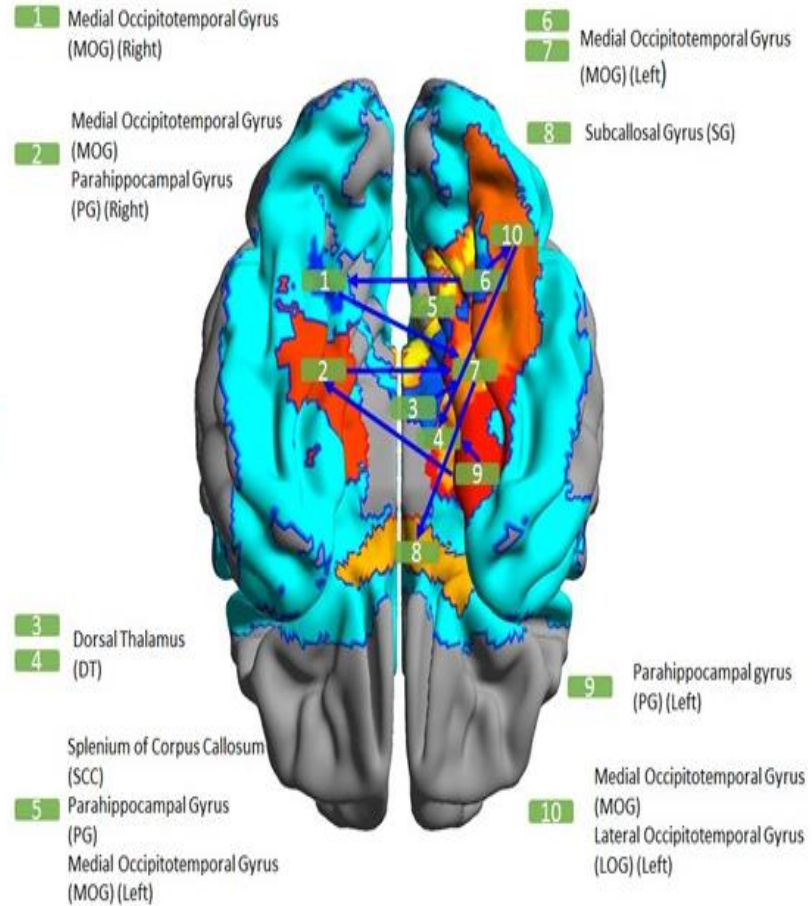
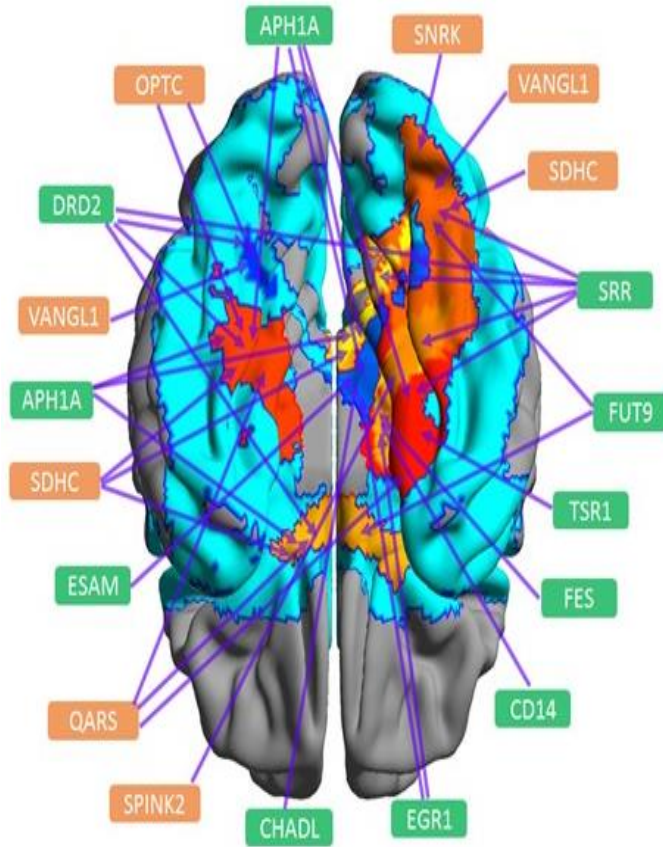
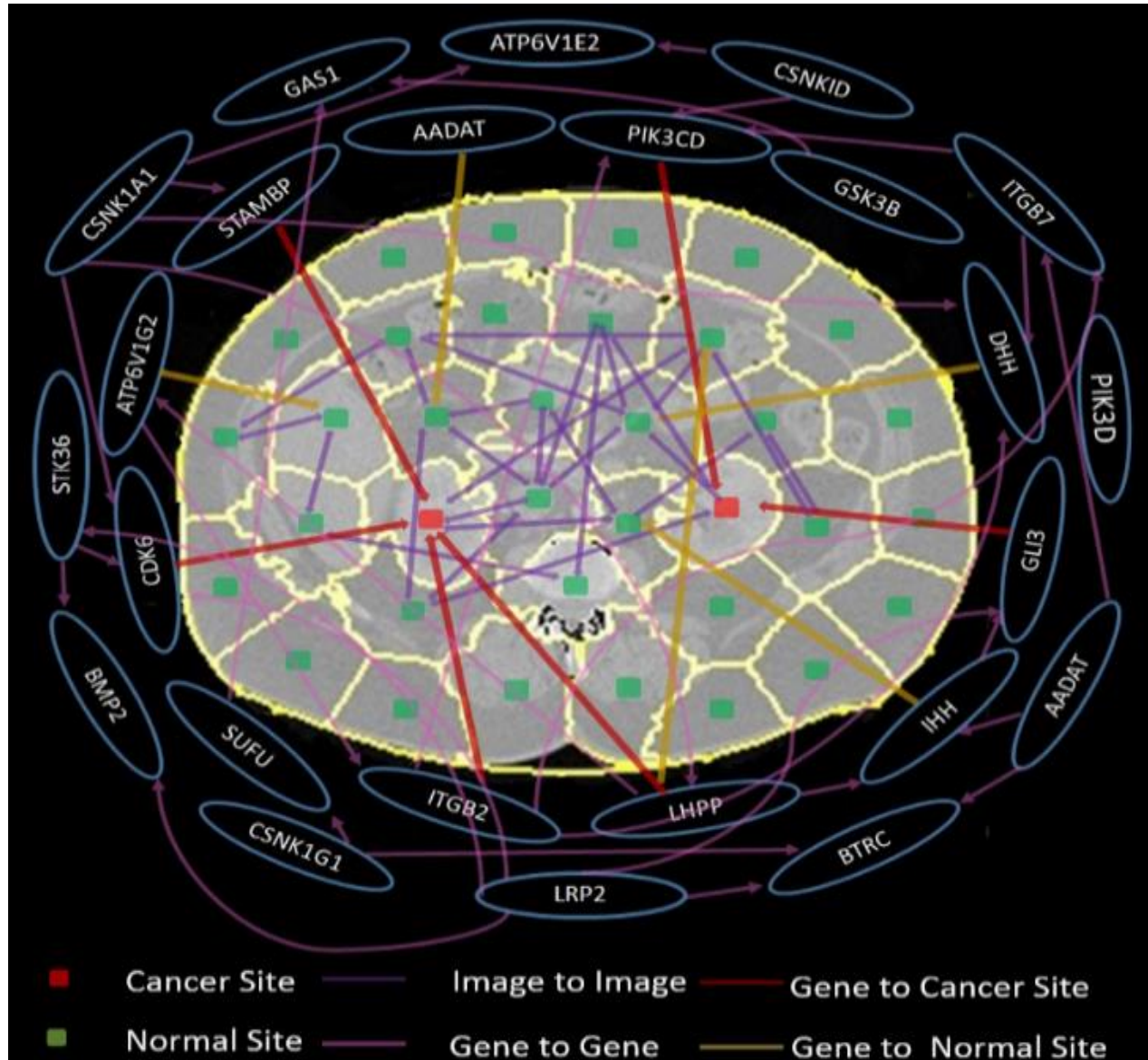
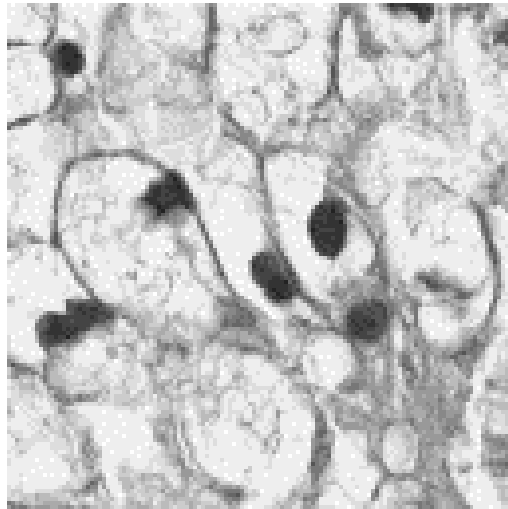


Image – Gene Expressions

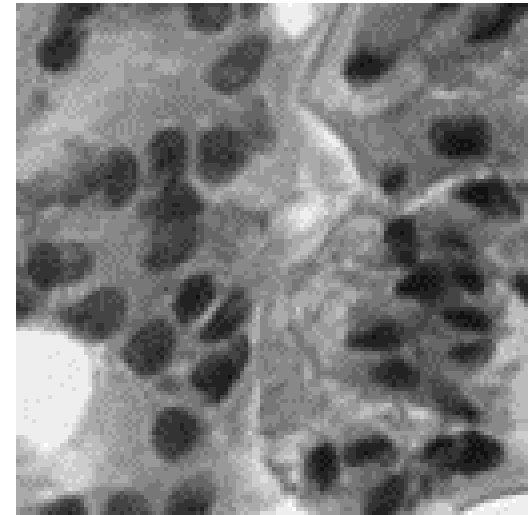
CT



Kidney Normal and Tumor Image

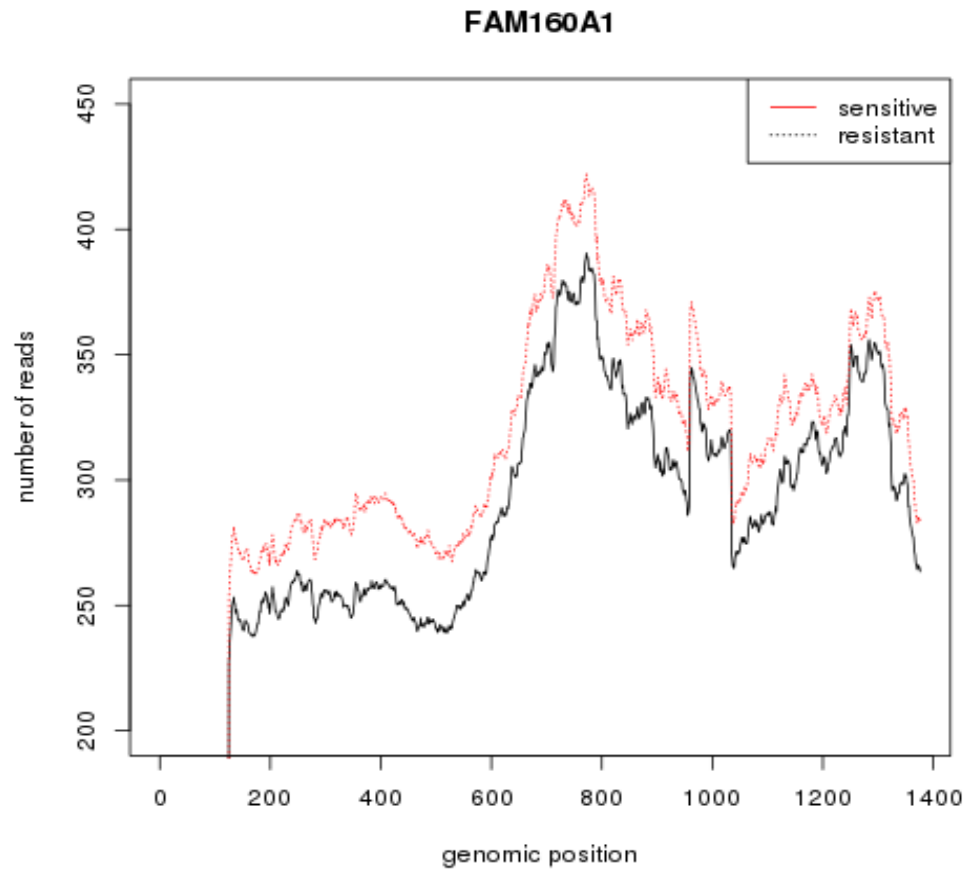


Kidney Tumor



Kidney Normal

RNA-seq Data (Ovarian Cancer)



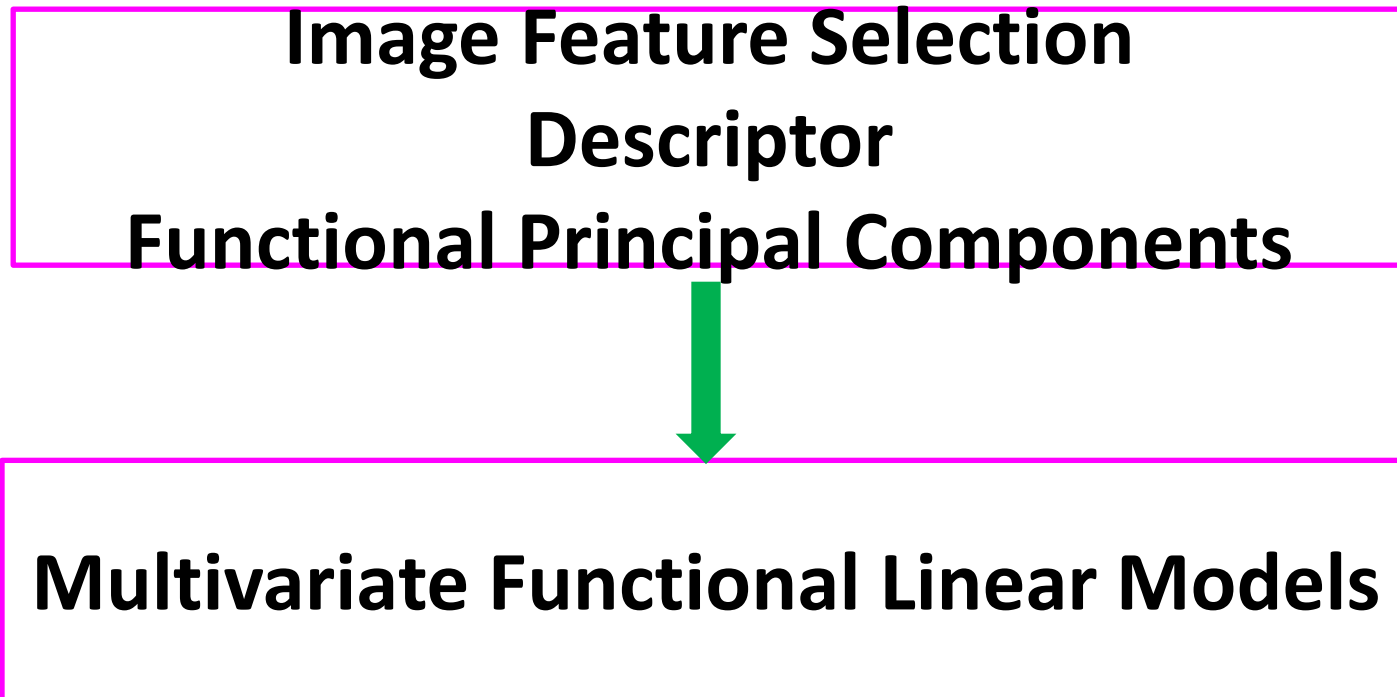
Methods for Imaging-Genetic Data Analysis

- **Single Variate Regression Analysis**
 - Summary Statistics for imaging data
 - Signal in pixel or voxel for imaging data
- **Multivariate Analyses**
 - (Liu J, Calhoun VD. A review of multivariate analyses in imaging genetics. Front Neuroinform. 8:29).
 - PCA, multifactor dimensionality reduction, independent component analysis (ICA), and clustering.
- **Sparse Canonical Correlation Analysis**
 - voxel-based morphometry
 - Chi EC, Allen GI, Zhou H, Kohannim O, Lange K, Thompson PM. IMAGING GENETICS VIA SPARSE CANONICAL CORRELATION ANALYSIS. Proc IEEE Int Symp Biomed Imaging. 2013:740-743.

Limitations

- **Imaging data reduction methods do not consider imaging signal space variation.**
- **Current methods for RNA-seq data analysis ignore genomic positional level variation and allele specific variation**

Procedures of Image-RNA-seq Data Analysis



Two dimensional Functional Principle Component Analysis

$$f = \int_S \int_T \beta(s, t) x(s, t) ds dt$$

a weight function

centered random function

$$\begin{aligned} \max & \int_S \int_T \int_S \int_T \beta(s_1, t_1) R(s_1, t_1, s_2, t_2) \beta(s_2, t_2) ds_1 dt_1 ds_2 dt_2 \\ \text{s.t.} & \int_S \int_T \beta^2(s, t) ds dt = 1. \end{aligned}$$

covariance function

$$\int_S \int_T R(s_1, t_1, s_2, t_2) \beta(s_2, t_2) ds_2 dt_2 = \lambda \beta(s_1, t_1)$$

integral equation

Functional Expansion

$$x_i(t, s) = \sum_{j=1}^J \xi_{ij} \beta_j(s, t), i = 1, \dots, N,$$

Random Functions

Eigenfunctions

$$\xi_{ij} = \int_S \int_T x_i(t, s) \beta_j(s, t) ds dt.$$

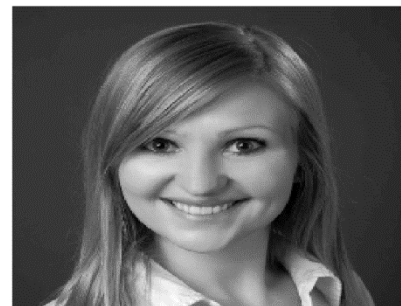
Functional Principal Component Score

Comparison Between FPCA Scores and Fourier Coefficients



- (a) Original Images
- (b) Reconstruction of the images with **6 FPCA** scores
- (c) Reconstruction of the images with first **16129 Fourier coefficients.**

Reconstructed Image by FPCA



Six FPC

CT PANC Normal

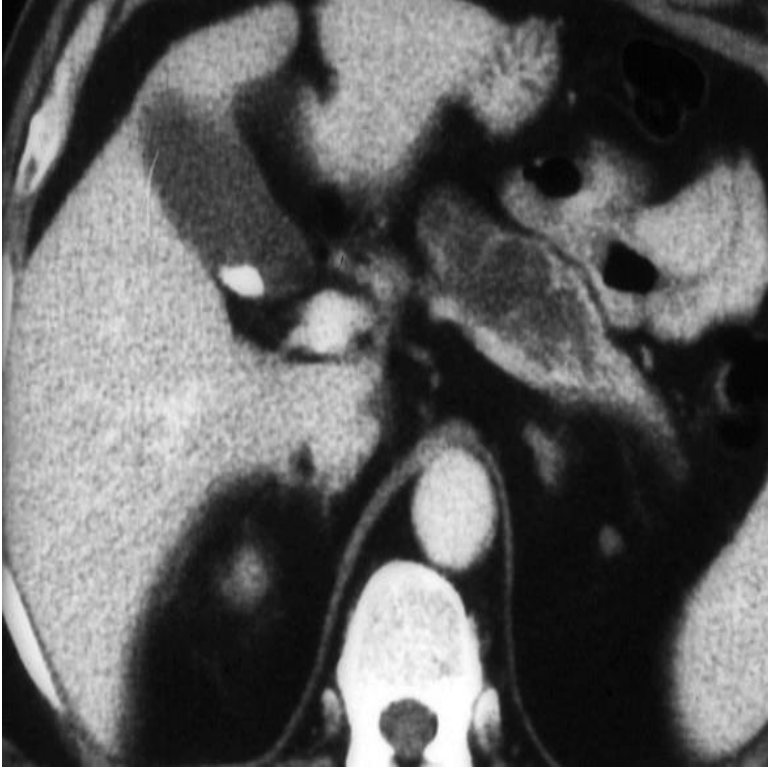


Original Image

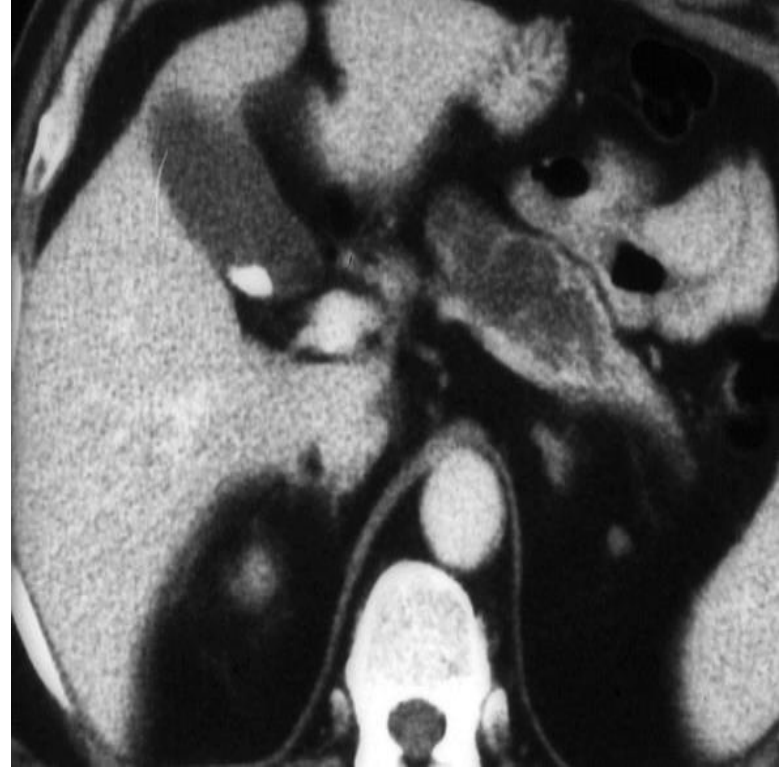


Reconstruction Image

IPMN



Original Image



Reconstruction Image

PANC Adenoma Ca Advanced



Original Image



Reconstruction Image from FPCA

Multivariate Functional Linear Models

Model:

K -th trait (FPC score)

RNA-seq profile
(number of reads)

$$y_{ik} = \alpha_{0k} + \int_T \alpha_k(t) x_i(t) dt + \varepsilon_{ik},$$

i-th individual

genetic additive effect

Genomic Position

Eigenfunctional Expansion



$$x_i(t) = \sum_{j=1}^{\infty} \xi_{ij} \phi_j(t)$$



$$y_{ik} = \int_T \alpha_k(t) \sum_{j=1}^{\infty} \xi_{ij} \phi_j(t) dt + \varepsilon_{ik}$$

$$= \sum_{j=1}^{\infty} \xi_{ij} \int_T \alpha_k(t) \phi_j(t) dt + \varepsilon_{ik}$$

$$= \sum_{j=1}^{\infty} \xi_{ij} \alpha_{kj} + \varepsilon_{ik}, i = 1, \dots, n, k = 1, \dots, K,$$

$$\alpha_{kj} = \int_T \alpha_k(t) \phi_j(t) dt$$

Reduced Multivariate Model

$$Y = [Y_1, \dots, Y_K] = \begin{bmatrix} Y_{11} & \cdots & Y_{1K} \\ \vdots & \ddots & \vdots \\ Y_{n1} & \cdots & Y_{nK} \end{bmatrix}, \quad \xi = \begin{bmatrix} \xi_{11} & \cdots & \xi_{1J} \\ \vdots & \ddots & \vdots \\ \xi_{n1} & \cdots & \xi_{nJ} \end{bmatrix}, \quad \alpha_k = \begin{bmatrix} \alpha_{k1} \\ \vdots \\ \alpha_{kJ} \end{bmatrix}, \quad \alpha = [\alpha_1, \dots, \alpha_K]$$

$$\varepsilon = \begin{bmatrix} \varepsilon_{11} & \cdots & \varepsilon_{1K} \\ \cdots & \cdots & \cdots \\ \varepsilon_{n1} & \cdots & \varepsilon_{nK} \end{bmatrix}$$



$$Y = \xi\alpha + \varepsilon$$

$$\hat{\alpha} = \underline{(\xi^T \xi)^{-1} \xi^T} (Y - \bar{Y})$$

$$\hat{\Sigma} = \frac{1}{n} (Y - \xi\hat{\alpha})^T (Y - \xi\hat{\alpha})$$

$$A$$

$$\text{vec}(\hat{\alpha}) = (A \otimes I) \text{vec}(Y - \bar{Y})$$


Test Statistic

$$\begin{aligned}\Lambda &= \text{var}(\text{vec}(\hat{\alpha})) = (I_k \otimes A)(\Sigma \otimes I_n)(I_k \otimes A^T) \\ &= \Sigma \otimes (AA^T)\end{aligned}$$

Null Hypothesis

$$\alpha_k(t) = 0, \forall t \in [a, b], k = 1, \dots, K, \quad H_0 : \alpha = 0$$

$$T = \hat{\alpha}^T \Lambda^{-1} \hat{\alpha}$$


$$\chi_{(KJ)}^2$$



Number of traits

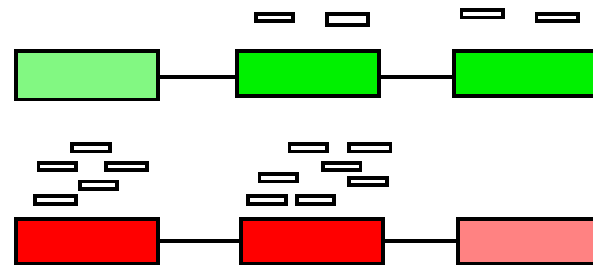
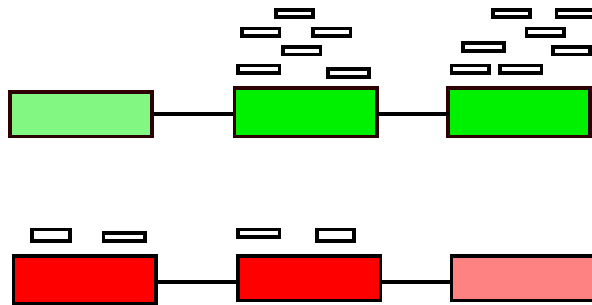


Number of components in expansion

Position matters

Control

Treatment

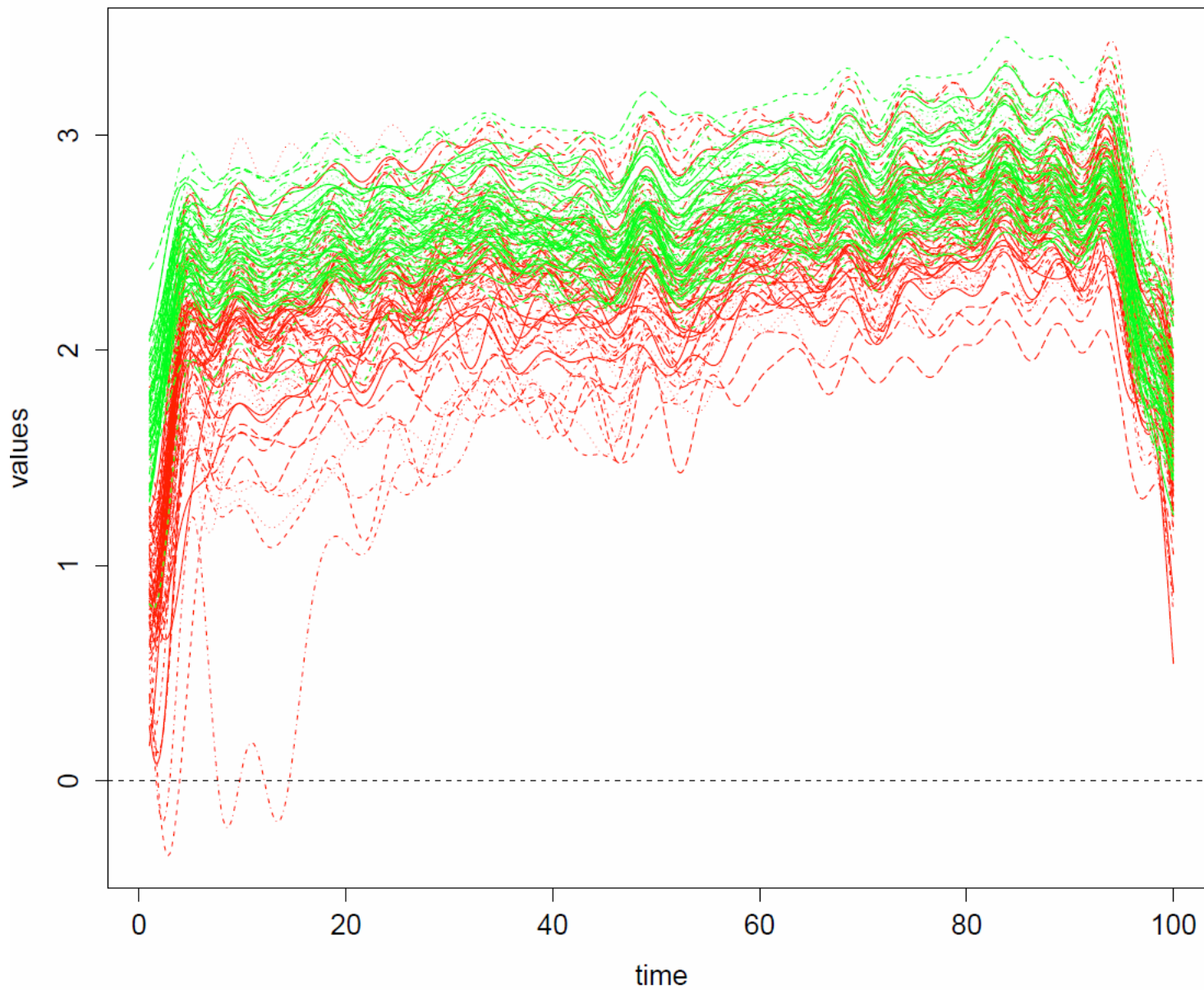


Isoform1

Isoform2

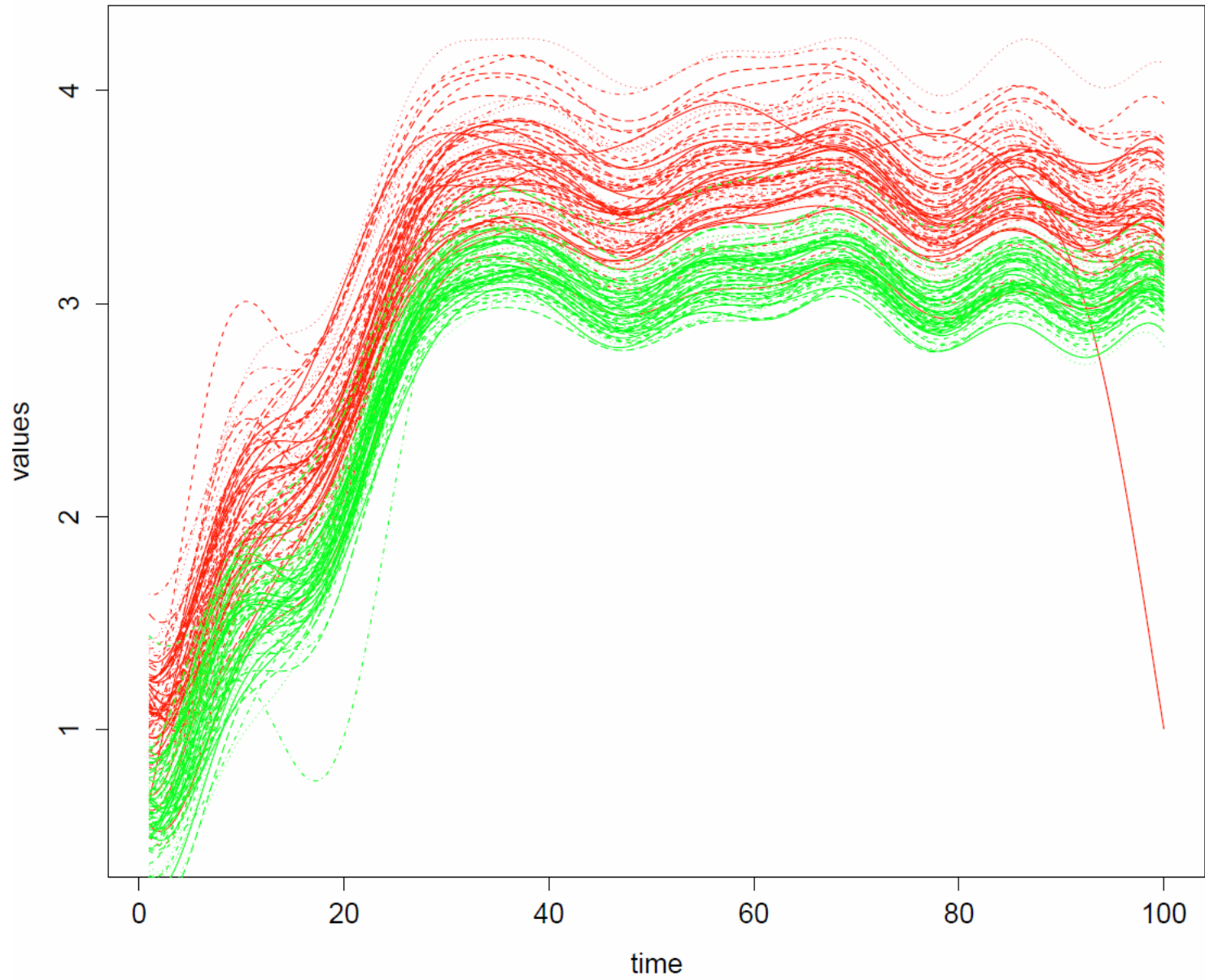
- Bad idea to treat all reads equally, ignoring their genomic positions. Therefore, they **cannot detect** differentially expressed gene.

RBBP8

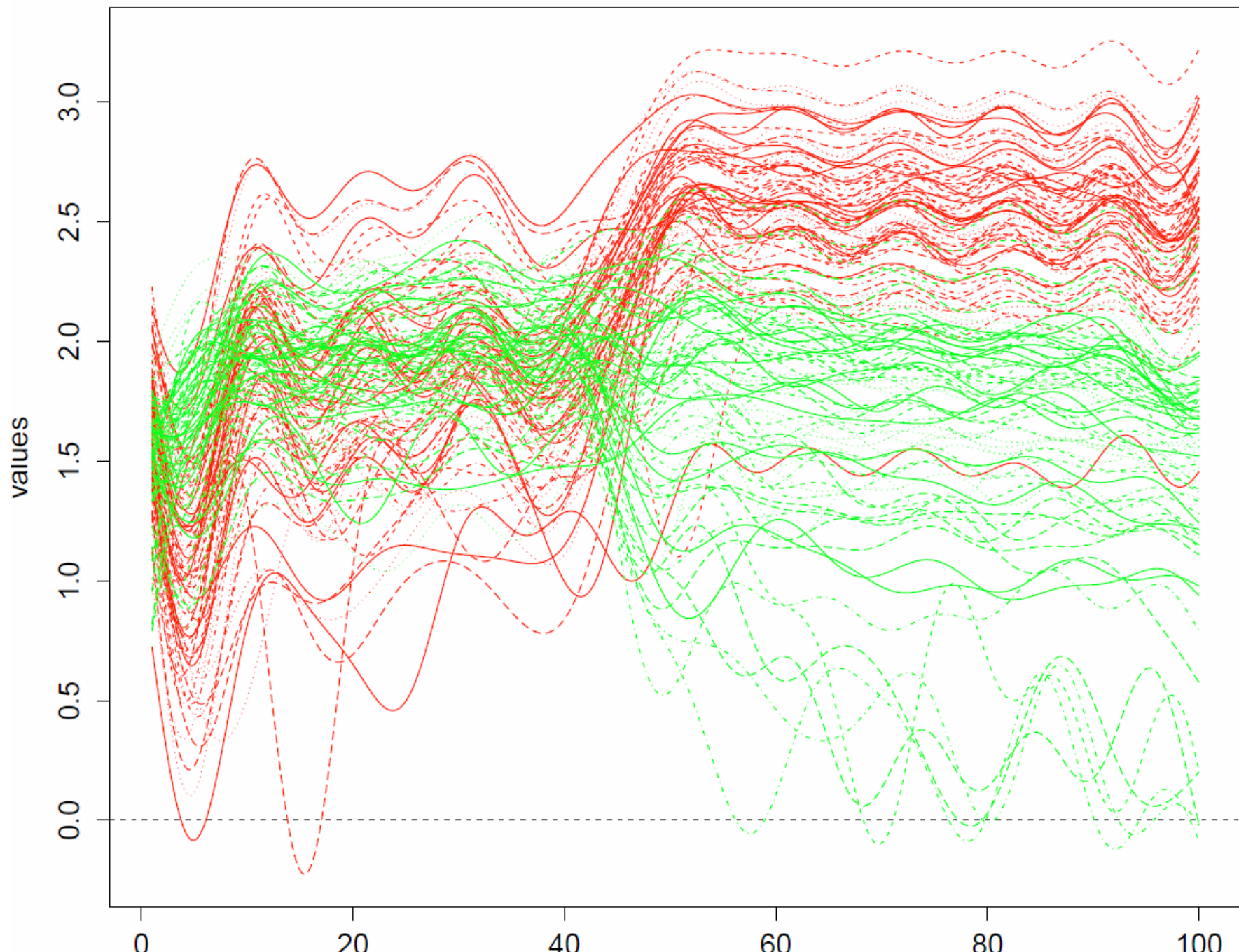


Green:
Normal
Red: Tumor

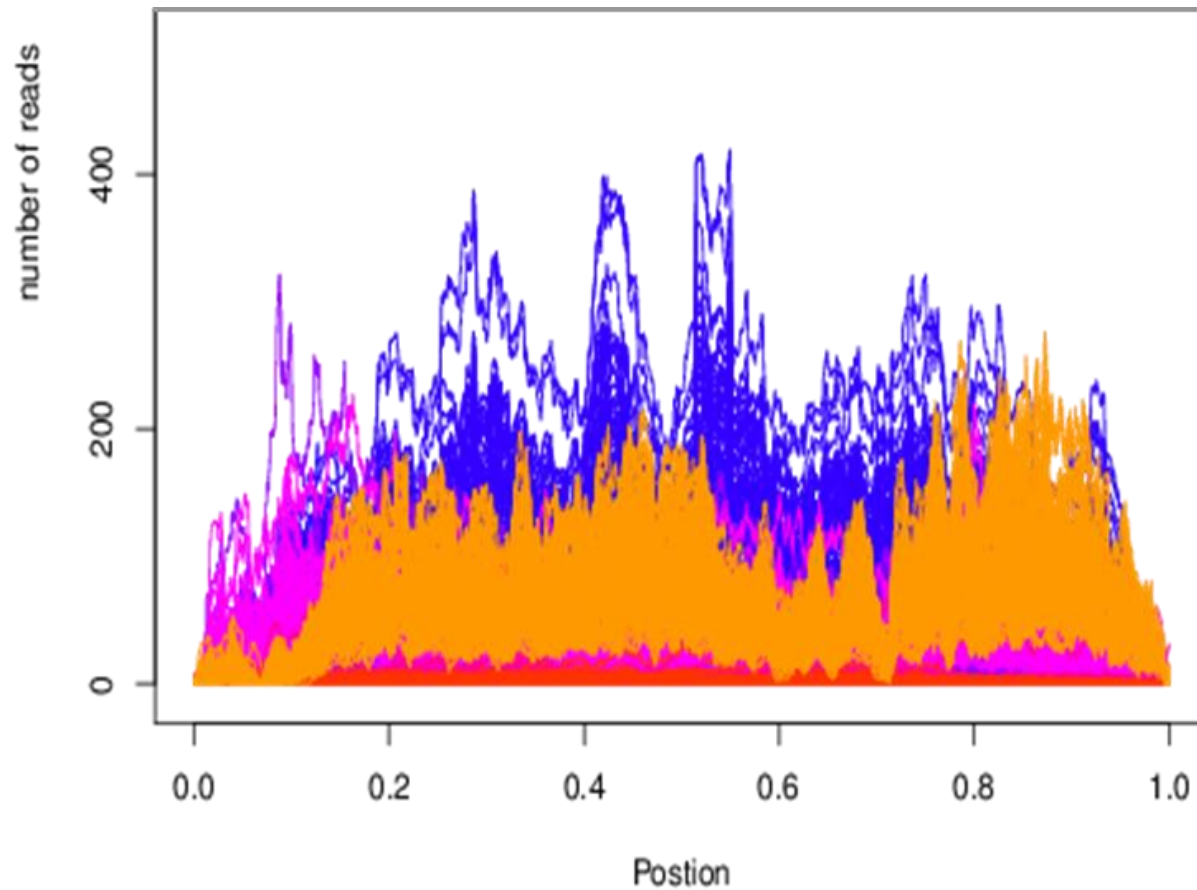
SEC61G



C18ORF56

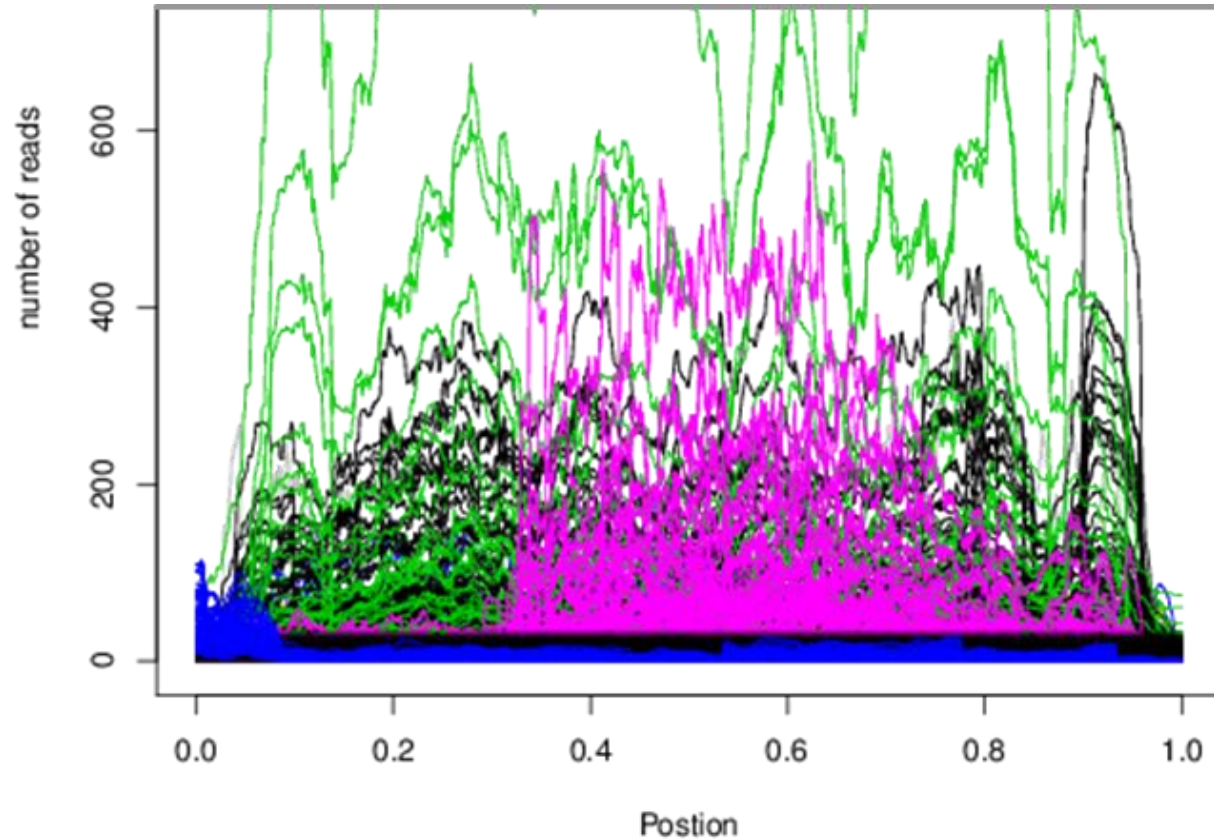


RNA-seq Data Cluster Analysis using FPCA



RNA-seq Data

Cluster Analysis using Level 3



Application

Ovarian Cancer

(TCGA Data)

- Histology Images
- Total Samples: 176
- Drug Sensitive: 106
- Drug Resistant: 76

All these images are sampled and resized to the dimension of $128*128 = 16,384$

Number of Genes: 13,357

Significance of P-value=3.74E-06

Total Number of Significant Genes: 21

QQ-Plot of OV RNA-seq Association Test

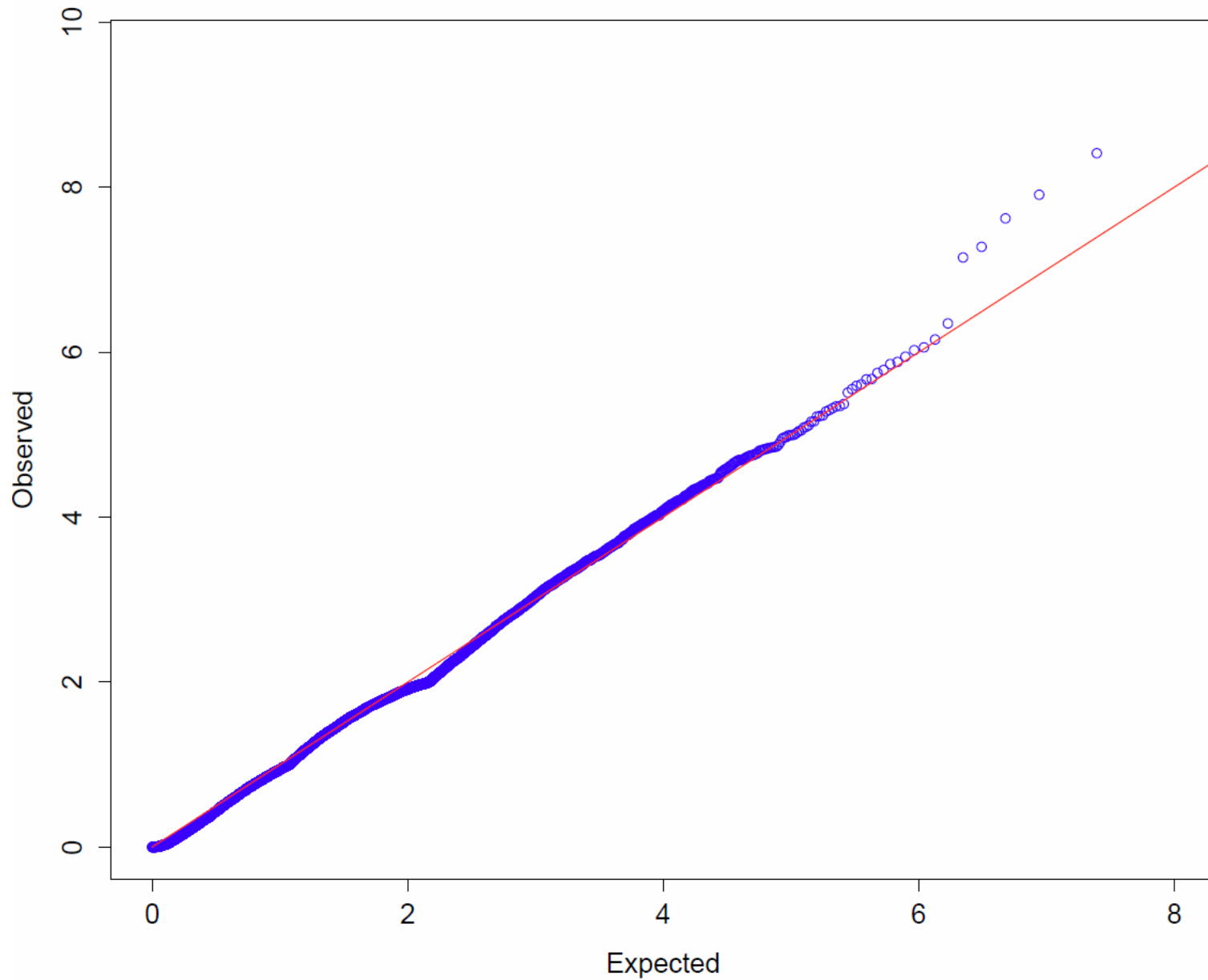


Table 1. List of 21 RNA-seq significantly associated with image.

Gene	P-value			Gene	P-value		
	MFLM		Regression		MFLM		Regression
	FPCA	Descriptor	Level 3		FPCA	Descriptor	Level 3
ZNF805	2.31E-10	4.34E-01	9.33E-01	PHKA1	1.31E-06	2.80E-02	7.15E-01
LOC653501	3.86E-09	2.49E-02	9.04E-01	PTPRG	1.39E-06	9.50E-01	6.58E-01
TMEM170B	1.23E-08	6.18E-03	9.11E-01	IFT88	1.64E-06	1.09E-05	8.11E-01
DRP2	2.38E-08	9.76E-02	5.89E-01	PARD3B	1.78E-06	8.89E-01	4.49E-01
OR6V1	5.27E-08	2.07E-03	1.76E-01	LIMD1	2.11E-06	4.69E-01	8.71E-01
GPR113	7.09E-08	3.67E-07	5.70E-01	FAM73A	2.13E-06	3.97E-03	9.28E-01
ZNF484	4.47E-07	6.77E-03	9.34E-01	CAPN14	2.45E-06	1.78E-02	4.80E-01
DNAL1	7.00E-07	6.64E-03	8.59E-01	CPEB3	2.55E-06	2.62E-02	9.88E-01
ITGA10	8.72E-07	2.01E-01	6.41E-01	CDCA2	2.80E-06	9.73E-01	3.74E-01
NBEAL1	9.43E-07	7.67E-03	7.12E-01	PUS3	3.08E-06	7.81E-01	9.22E-01
C16orf52	1.13E-06	2.10E-02	9.06E-01				

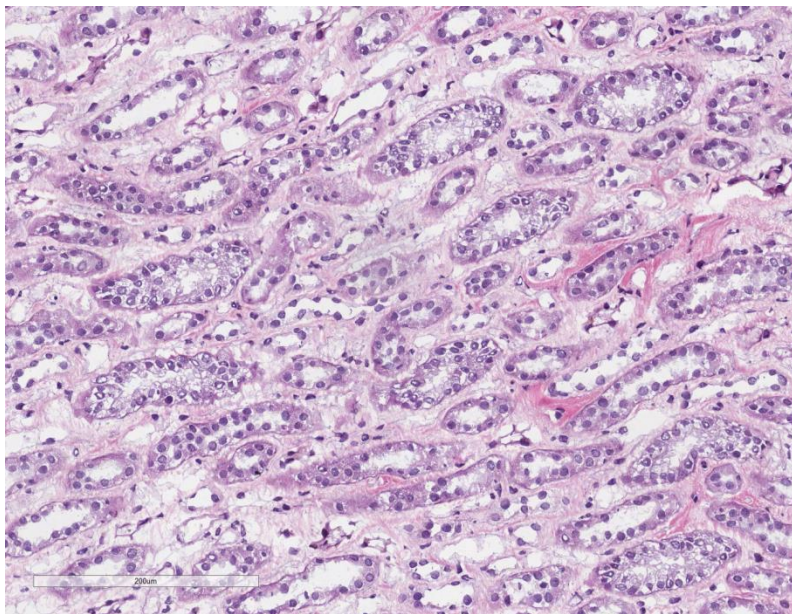
Real Data Analysis

Kidney Renal Clear Cell Carcinoma (KIRC)

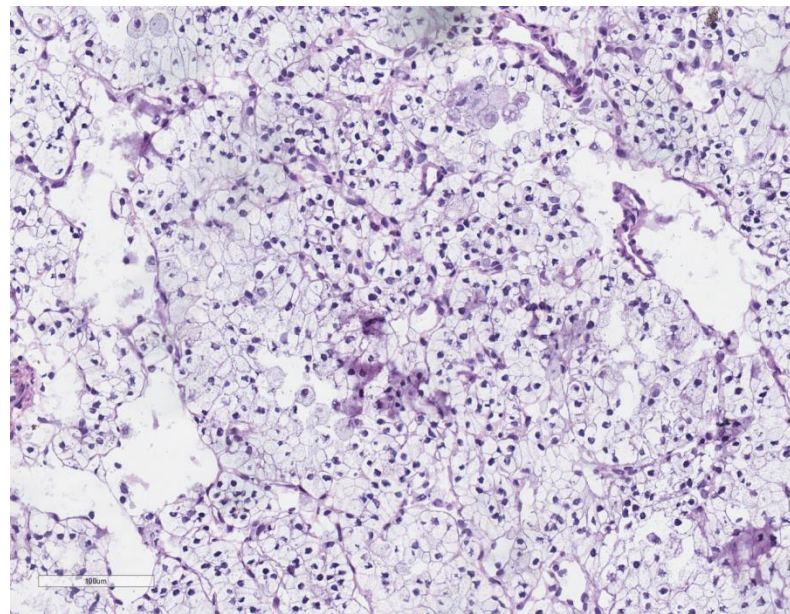
Total Images: 188

Case: 121, Control: 67

Normal



Tumor



kidney cancer (KIRC)

- Images: **188**
- Cancer: **121**
- Normal: **67**
- Number of Genes: **16,774**
- P-value (significance)= **2.98E-06**
- Number of Significant Genes=**84**

FPCA

Test Set

Training Set

	Sensitivity	Specificity	Accuracy	Sensitivity	Specificity	Accuracy	Num of FPCA
CV1	0.9200	0.6190	0.7826	0.8333	0.8043	0.8239	3
CV2	0.9091	0.7000	0.8438	0.8990	0.7719	0.8526	11
CV3	0.8800	0.9091	0.8889	0.8646	0.7857	0.8355	5
CV4	0.9444	0.6250	0.8462	0.8835	0.7458	0.8333	5
CV5	0.7742	0.8235	0.7917	0.9000	0.7600	0.8500	6
Mean	0.8855	0.7353	0.8306	0.8761	0.7736	0.8391	6

CV1: fpca_1, fpca_4, fpca_38

CV2: fpca_1, fpca_2, fpca_4, fpca_18, fpca_31, fpca_38, fpca_49, fpca_87,
fpca_96, fpca_171, fpca_182

CV3: fpca_1, fpca_2, fpca_4, fpca_22, fpca_45

CV4: fpca_1, fpca_2, fpca_4, fpca_38, fpca_182

CV5: fpca_1, fpca_2, fpca_4, fpca_17, fpca_18, fpca_38

QQ-Plot of KIRC RNA-seq Association Test

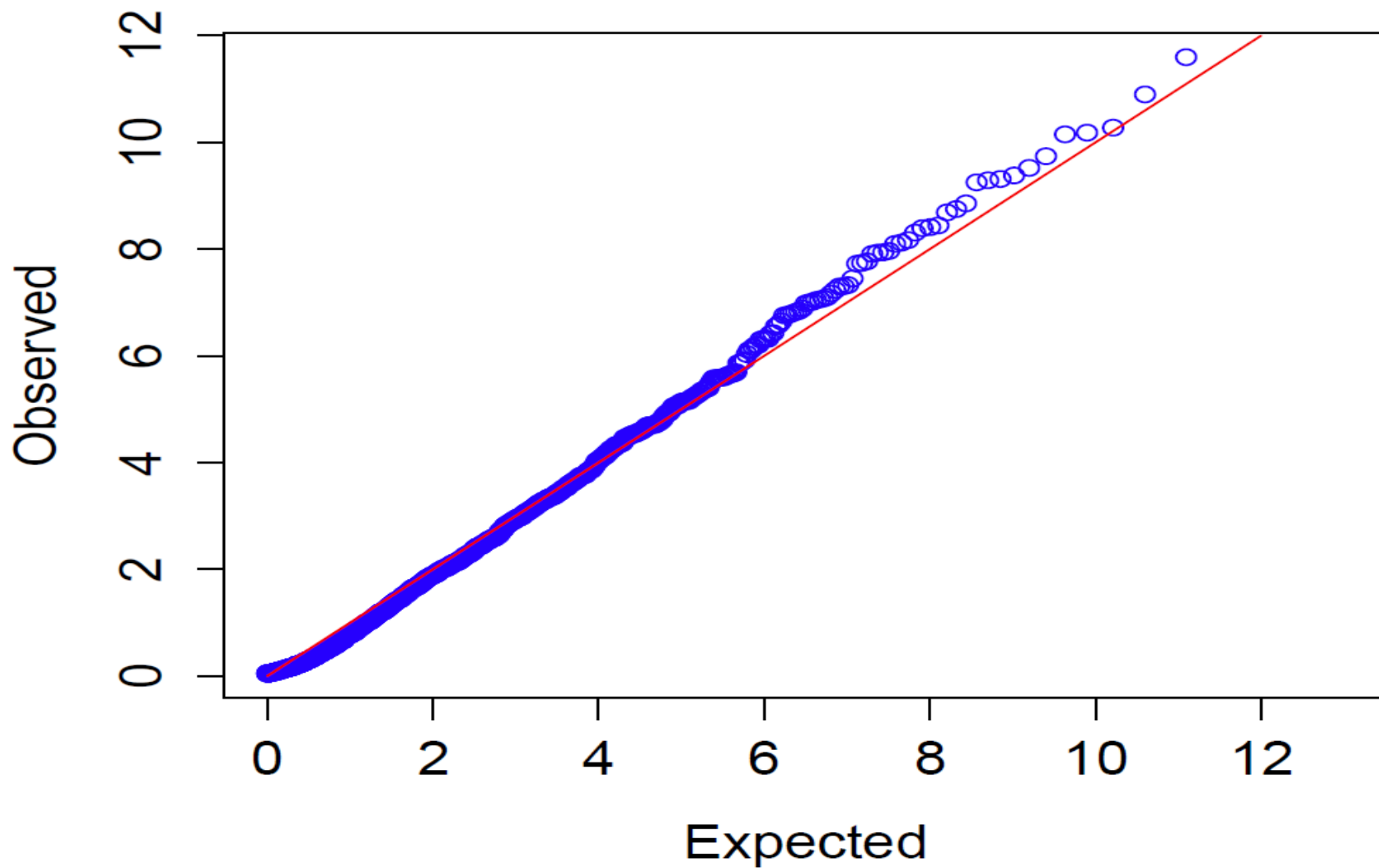
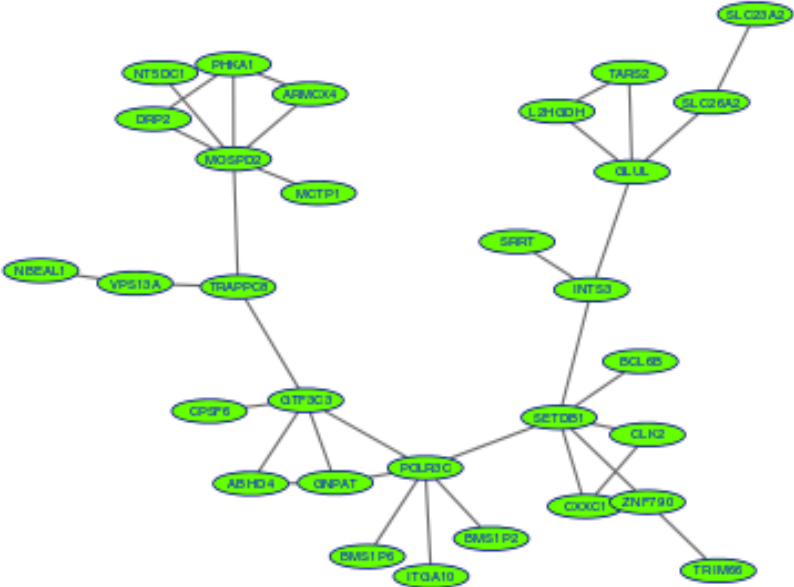


Table 2. P-values of three statistics for testing association of expression with images in KIRC study.

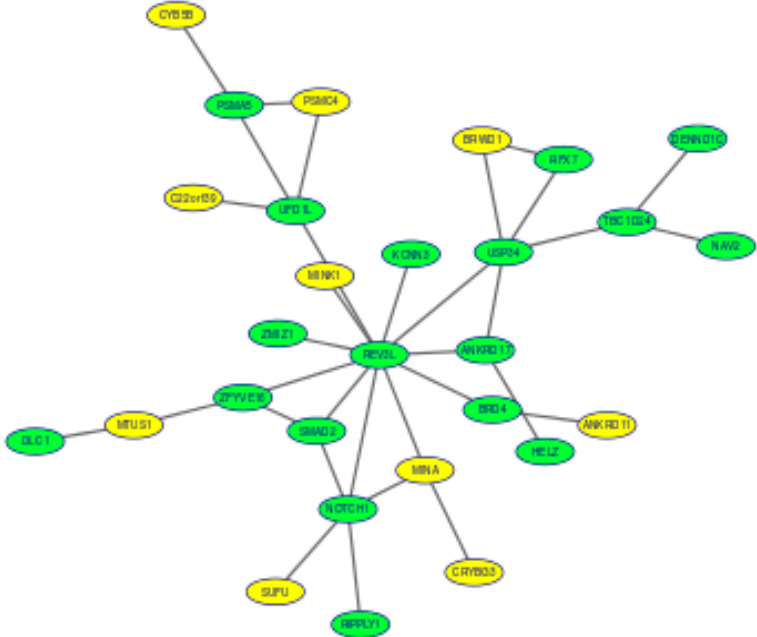
Gene	P-value			Gene	P-value		
	MFLM (FPC)	MFLM (Descriptor)	MLM		MFLM(FPC)	MFLM(Descriptor)	MLM
<i>HELZ</i>	6.62E-16	6.08E-01	8.79E-01	<i>ZNF81</i>	9.95E-08	2.06E-07	7.25E-01
<i>9-Mar</i>	2.12E-15	1.02E-06	7.58E-01	<i>GAB2</i>	1.04E-07	1.34E-02	6.38E-01
<i>SLC2A12</i>	2.52E-12	9.94E-03	2.76E-08	<i>LOC647859</i>	1.43E-07	8.56E-02	1.23E-03
<i>BRWD1</i>	1.26E-11	5.61E-03	9.54E-01	<i>C2orf68</i>	1.49E-07	4.83E-03	7.84E-01
<i>RFX7</i>	5.29E-11	1.00E+00	9.58E-01	<i>SDR39U1</i>	1.57E-07	8.83E-04	5.88E-01
<i>C22orf39</i>	6.55E-11	1.29E-03	5.77E-01	<i>ZRANB3</i>	1.66E-07	1.03E-03	9.59E-01
<i>NSD1</i>	7.06E-11	1.67E-02	9.74E-01	<i>PSMC4</i>	1.71E-07	1.39E-02	8.87E-01
<i>RTF1</i>	1.82E-10	9.49E-01	8.58E-01	<i>FLJ12825</i>	1.74E-07	1.39E-04	7.08E-01
<i>MBD5</i>	3.00E-10	1.08E-04	9.33E-01	<i>ARHGEF11</i>	2.26E-07	8.24E-03	8.55E-01
<i>ZSCAN16-AS1</i>	4.16E-10	6.08E-02	NA	<i>LOC100289019</i>	2.61E-07	8.50E-04	NA
<i>SESNI</i>	4.84E-10	3.42E-01	6.71E-01	<i>SUFU</i>	2.79E-07	1.99E-01	5.84E-01
<i>ITGA9</i>	5.12E-10	2.11E-02	9.52E-01	<i>ZNF555</i>	3.75E-07	2.16E-02	3.75E-01
<i>PPMIK</i>	5.60E-10	1.48E-01	1.11E-04	<i>KHNYN</i>	3.85E-07	1.54E-01	4.62E-01
<i>USP42</i>	1.39E-09	9.79E-01	9.06E-01	<i>ANKRD11</i>	4.80E-07	1.00E+00	8.92E-01
<i>FAM47E-STBD1</i>	1.77E-09	1.11E-02	NA	<i>BOLA2</i>	4.82E-07	9.88E-02	8.33E-01
<i>ZNF710</i>	2.05E-09	1.22E-01	9.82E-01	<i>BOLA2B</i>	4.82E-07	9.88E-02	NA
<i>TECPR2</i>	3.59E-09	9.53E-04	5.63E-01	<i>SAPCD1</i>	4.97E-07	4.24E-01	NA

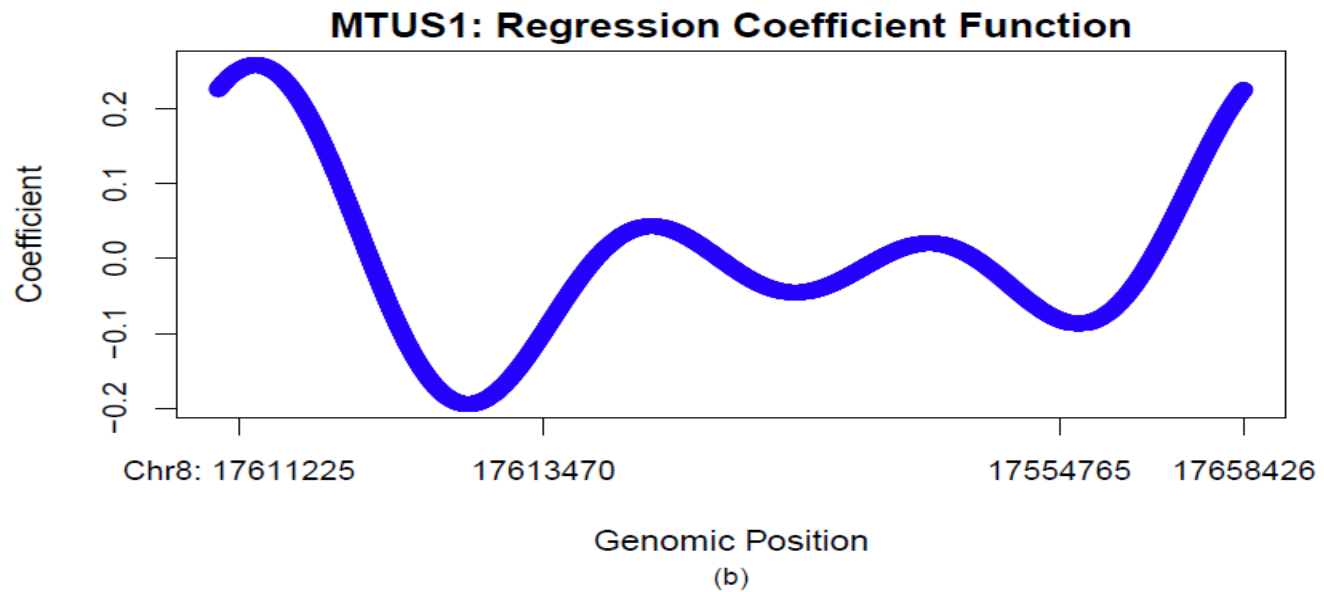
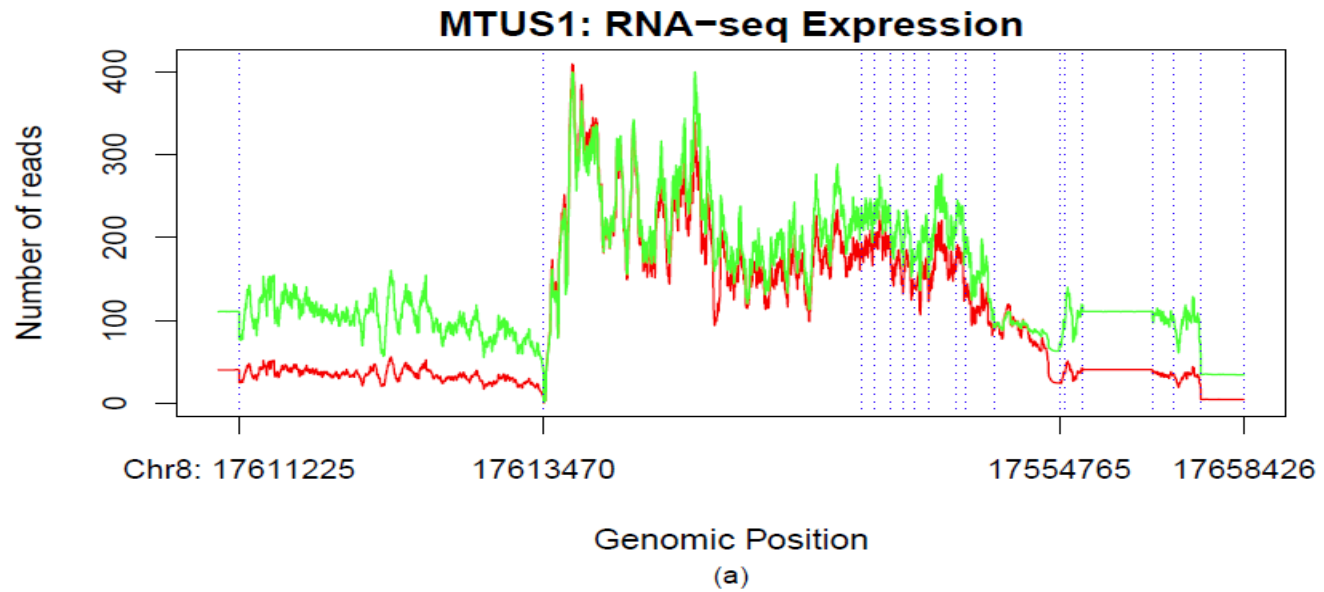
Protein-Protein Interaction Networks

Ovarian cancer

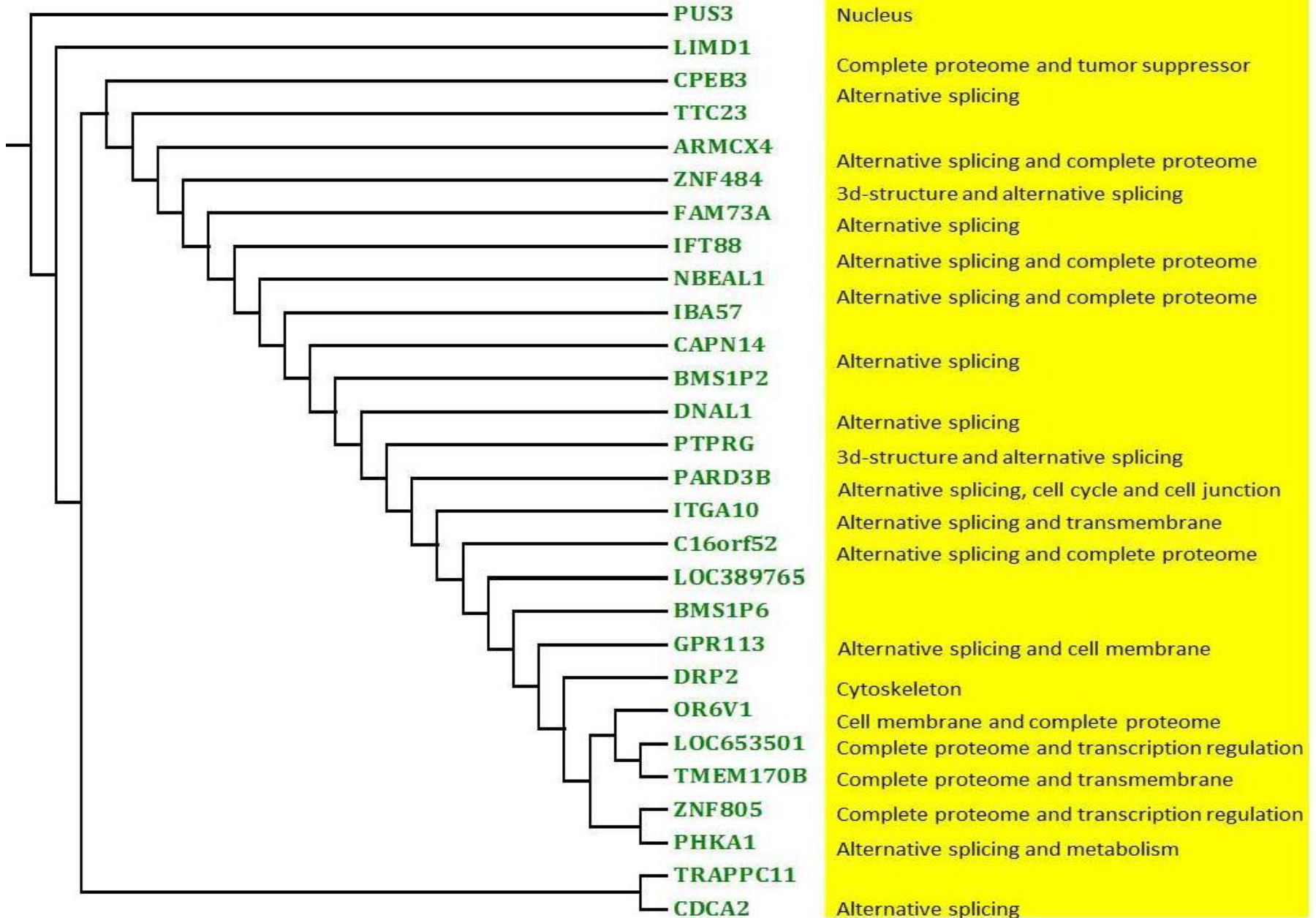


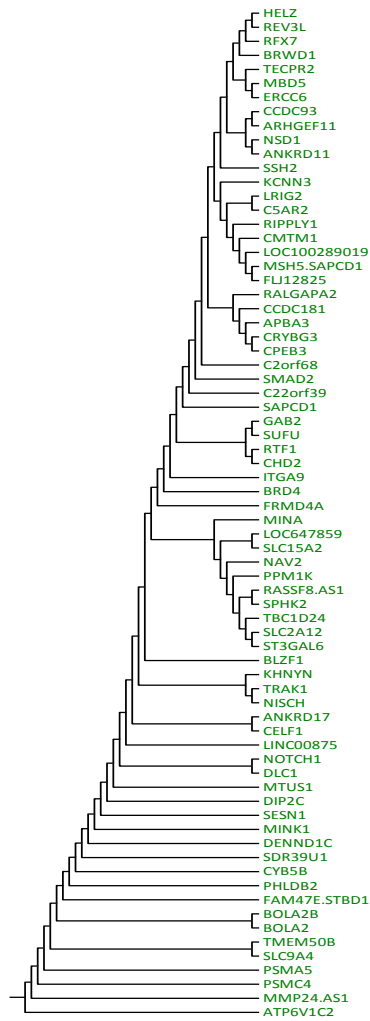
Kidney cancer





Ovarian Cancer





- Alternative splicing
- Activator and alternative splicing
- Alternative splicing and complete proteome
- Atp-binding and cataract
- 3d-structure and coiled coil
- Activator and alternative splicing
- 3d-structure, actin-binding and alternative splicing
- Transmembrane and transport
- Alternative splicing and complete proteome
- Alternative splicing and chemotaxis
- Alternative splicing and complete proteome
- 3d-structure and complete proteome
- Alternative splicing and complete proteome
- 3d-structure and alternative splicing
- 3d-structure and pathways in cancer
- 3d-structure and alternative splicing
- Pathways in cancer
- 3d-structure and acetylation
- Alternative splicing and atp-binding
- 3d-structure and alternative splicing
- Alternative splicing and complete proteome
- Transmembrane and transport
- 3d-structure, alternative splicing and atp-binding
- 3d-structure, alternative splicing, complete
- Alternative splicing and atp-binding
- Acetylation and alternative splicing
- Transmembrane and transport
- 3d-structure and coiled coil
- Alternative splicing and coiled coil
- Alternative splicing and ank repeat
- RNA Splicing, 3d-structure and alternative splicing
- Cell morphogenesis
- Regulation of cell shape
- Microtubule-associated tumor suppressor 1
- Complete proteome and polymorphism,
- Complete proteome and phosphoprotein
- Alternative splicing and complete proteome
- Transmembrane and transport
- Alternative splicing and coiled coil
- Acetylation and alternative splicing
- Acetylation and alternative splicing
- Transmembrane and transport
- Acetylation and complete proteome
- 3d-structure and acetylation
- Alternative splicing and complete proteome

KIRC

Acknowledgment

UT School of Public Health

- Junhai Jiang
- Nan Lin
- Shicheng Guo

UT MD Anderson Cancer Center

- Jane Chen

Let Us Meet Again

We welcome you all to our future conferences of
OMICS International

Please Visit:

<http://transcriptomics.conferenceseries.com/>

<http://conferenceseries.com/>

<http://www.conferenceseries.com/genetics-and-molecular-biology-conferences.php>