

# FFPE 샘플이용 total RNA-Seq 실험분석



2017

Never Ending Service



## BIO-Experiment & Analysis Service

### Microarray

- ❖ Gene Expression
- ❖ miRNA
- ❖ CGH / CNV
- ❖ ChIP on chip
- ❖ Methylation
- ❖ Agilent/Affymetrix
- ❖ Exiqon

### NGS

- ❖ RNA-Seq
- ❖ small RNA-Seq
- ❖ ChIP-Seq
- ❖ MBD-Seq
- ❖ Exome-Seq
- ❖ Target DNA-Seq
- ❖ Illumina/IonProton

### qRT-PCR

- ❖ mRNA
- ❖ microRNA
- ❖ PCR Array
- ❖ Qiagen
- ❖ Genosensor
- ❖ Others

### Antibody Array

- ❖ Protein Profiling
- ❖ Phosphorylation
- ❖ FullmoonBio
- ❖ RayBiotech
- ❖ Others

### Microarray



- ❖ Meaningful Data from Any Genome

### NGS



- ❖ Next Generation Sequencing

Metabolic engineering of *Corynebacterium glutamicum* for L-arginine production

Seok Hyun Park, Hyun Uk Kim, Tae Yong Kim, Jun Seok Park, Suok-Su Kim

Affiliations | Contributions | Corresponding author



## DNA



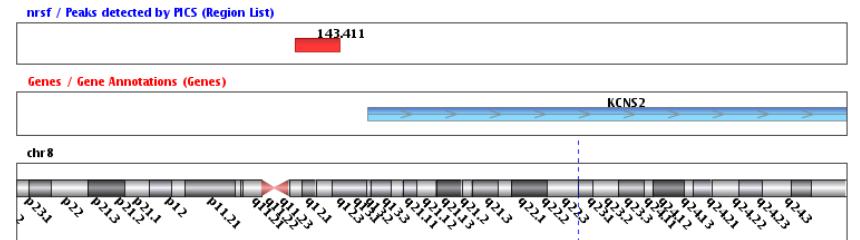
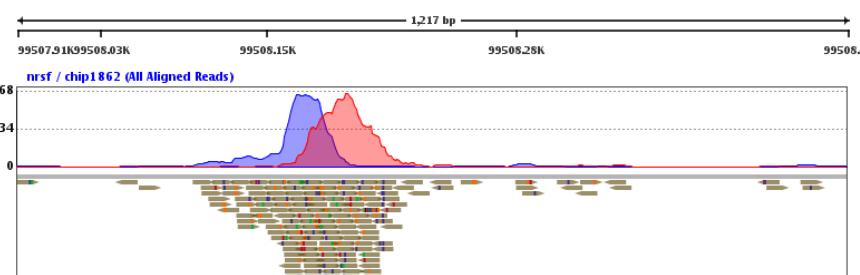
- DNA Methylation Profiling
- Epigenome 분석
- gDNA 샘플준비



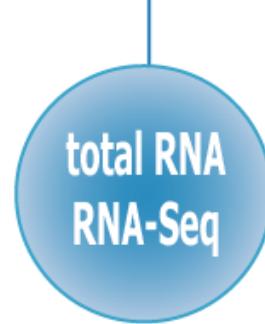
- DNA-Protein Interactions
- Histone modifications
- IP-DNA 샘플준비



- 특정영역 DNA 위치를 집중적으로 Sequencing
- SNP, CNV 분석외
- gDNA 샘플준비



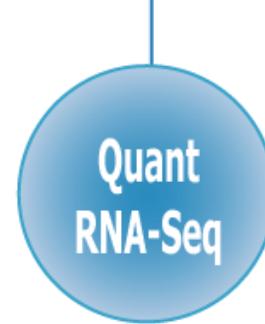
## RNA



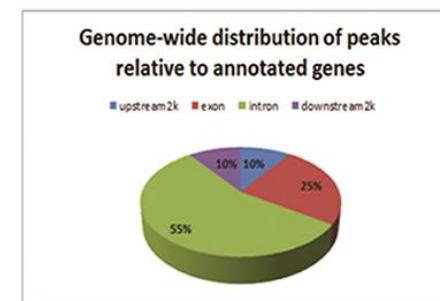
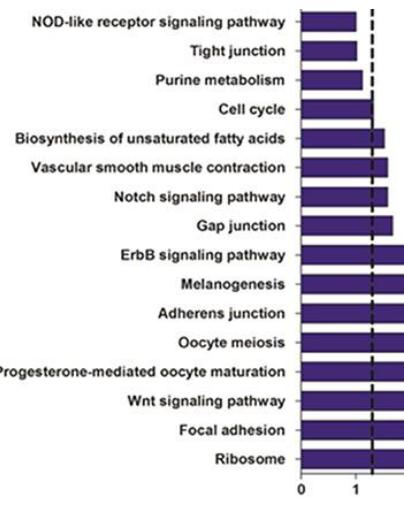
- mRNA-Seq 분석외 LncRNA 분석가능
- Whole transcriptome
- total RNA 샘플준비



- Gene Expression, Isoform, GO/Pathway
- Splicing, Gene Fusion외
- total RNA 샘플준비



- DEG 분석에 집중
- 극미량, FFPE 샘플도 실험 가능
- total RNA 샘플준비

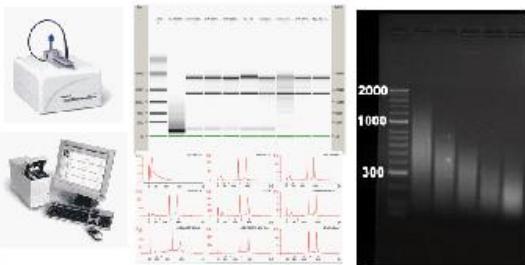


# RNA-Seq Process

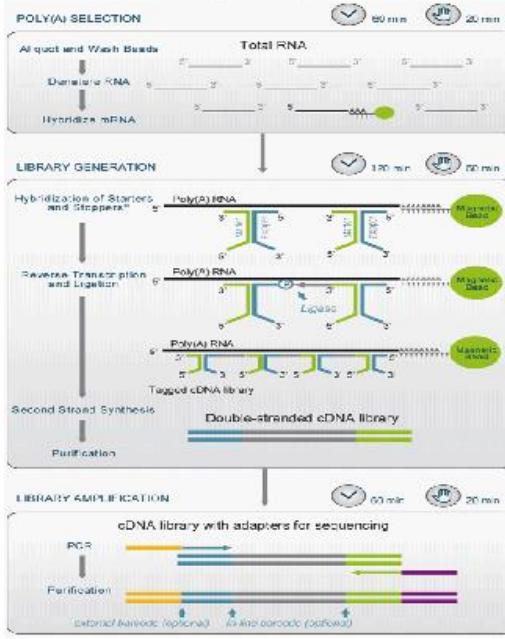


## Sample Preparation

### Sample Prep & QC

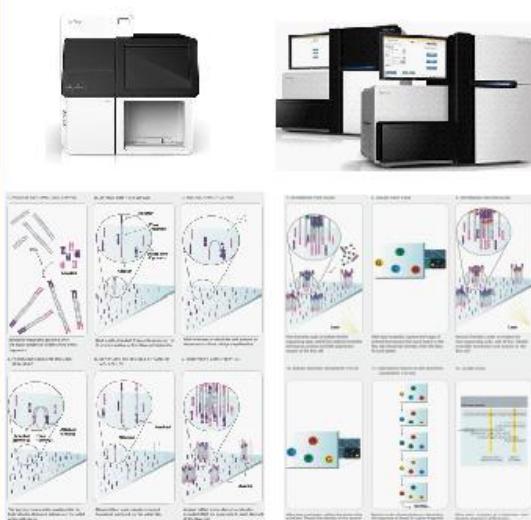


### Library Prep & QC

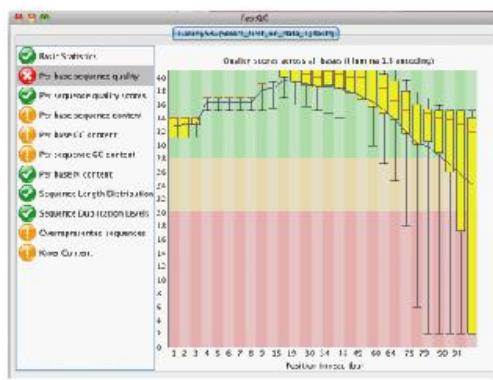


## Sequencing

### Cluster Generation & Sequencing

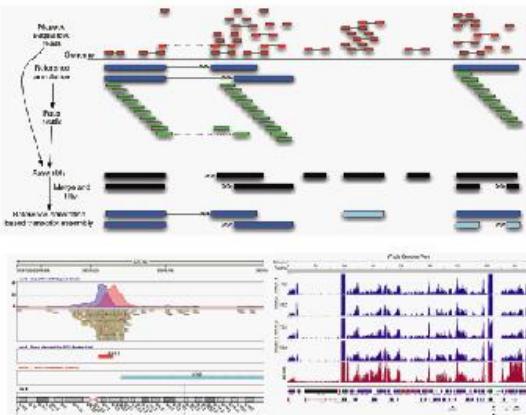


### FastQC

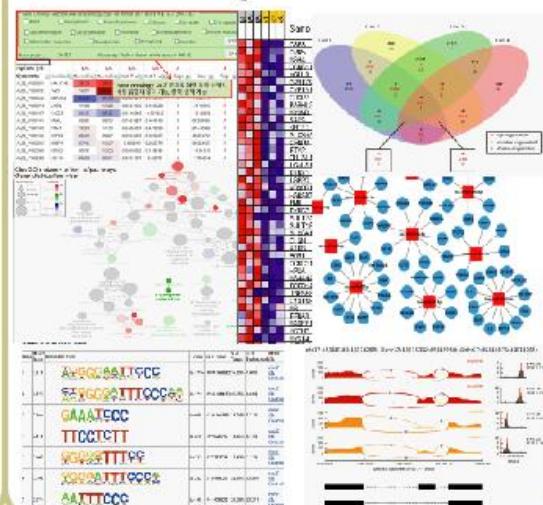


## Data Analysis

### Genome Mapping & Analysis



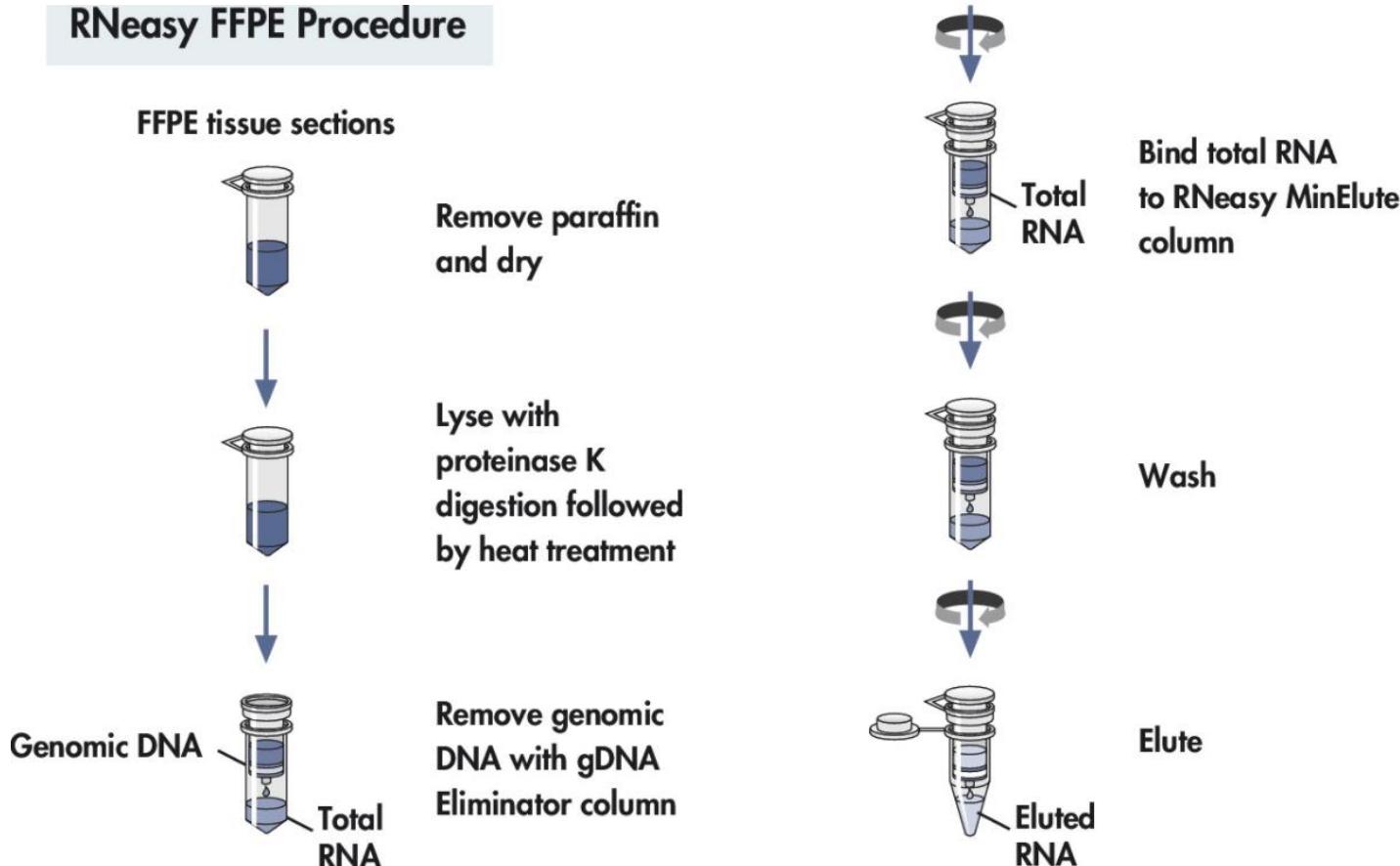
### Data Mining & Visualization



# RNA Sample Prep.(Qiagen's Rneasy FFPE)



## RNeasy FFPE Procedure

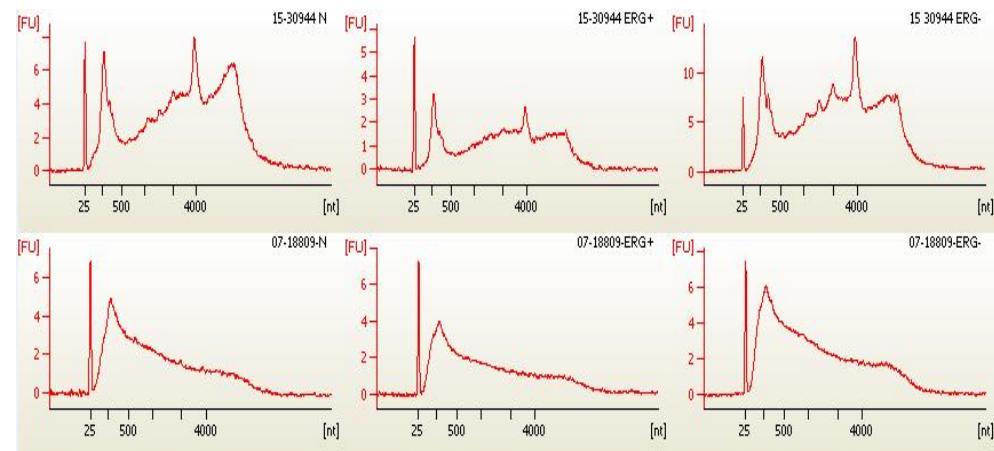
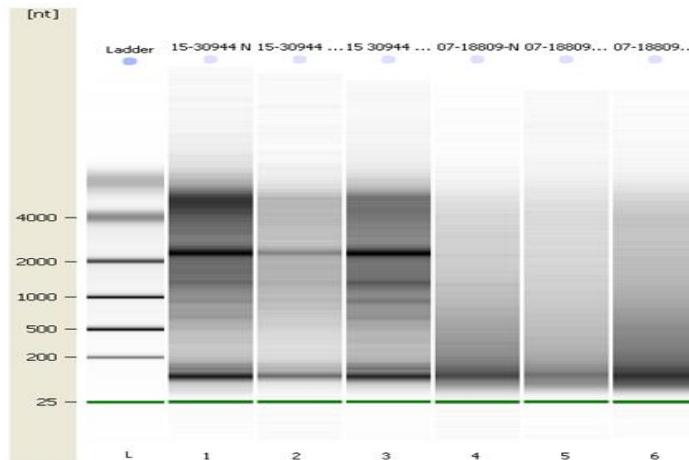


- FFPE samples에서 최적화된 결과 — formalin crosslinking을 제거하는 참신한 방법
- High RNA yields — efficient release of RNA without compromising RNA integrity
- 빠른 처리 과정 — 약 70분 정도만에 RNA를 얻을 수 있는 프로토콜

# RNA Quality Control



Sample	ng/ $\mu$ l	OD <sub>260/280</sub>	OD <sub>260/230</sub>	Total (ng)	Ratio(28s/18s)	RIN	Result
15-30944 N	92.3	1.92	2.2	2307.5	0.0	2.9	Check
15-30944 ERG+	61	1.91	2.33	1525	0.2	3.0	Check
15-30944 ERG-	178.9	1.91	1.9	4472.5	0.2	3.2	Check
07-18809 N	88.9	1.87	2.3	2222.5	0.0	2.4	Check
07-18809 ERG+	63.6	1.82	2.05	1590	0.0	2.4	Check
07-18809 ERG-	109.9	1.85	2.07	2747.5	0.0	2.3	Check



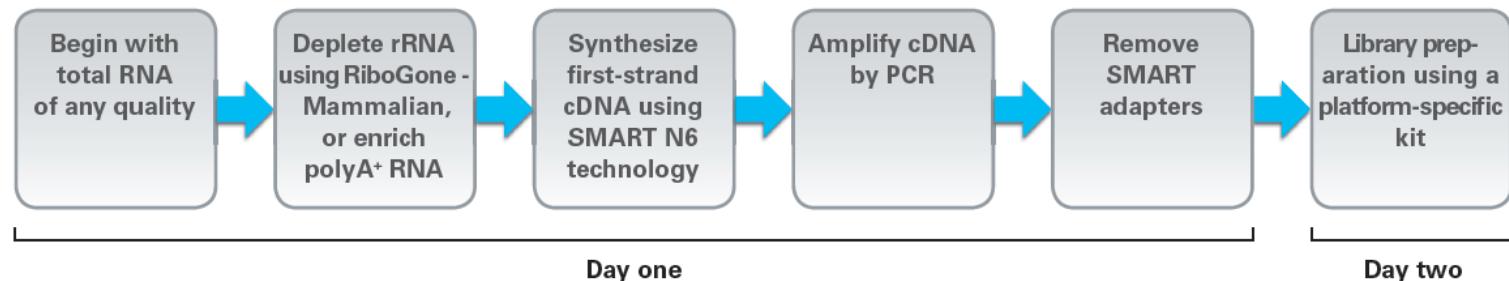
- RIN(RNA Integrity Number) :

Agilent社에서 제공하는 software tool로 Eukaryote total RNA sample에 적용되며, electrophoretic trace에 의해 integrity가 결정됩니다. 1~10 까지의 값을 가지며, RIN값에 대한 다양한 결과는 [http://www.chem.agilent.com/rin/\\_rinSearch.aspx](http://www.chem.agilent.com/rin/_rinSearch.aspx)에서 찾아 보실 수 있습니다.

# RiboGone™ rRNA removal & SMARTer cDNA synthesis

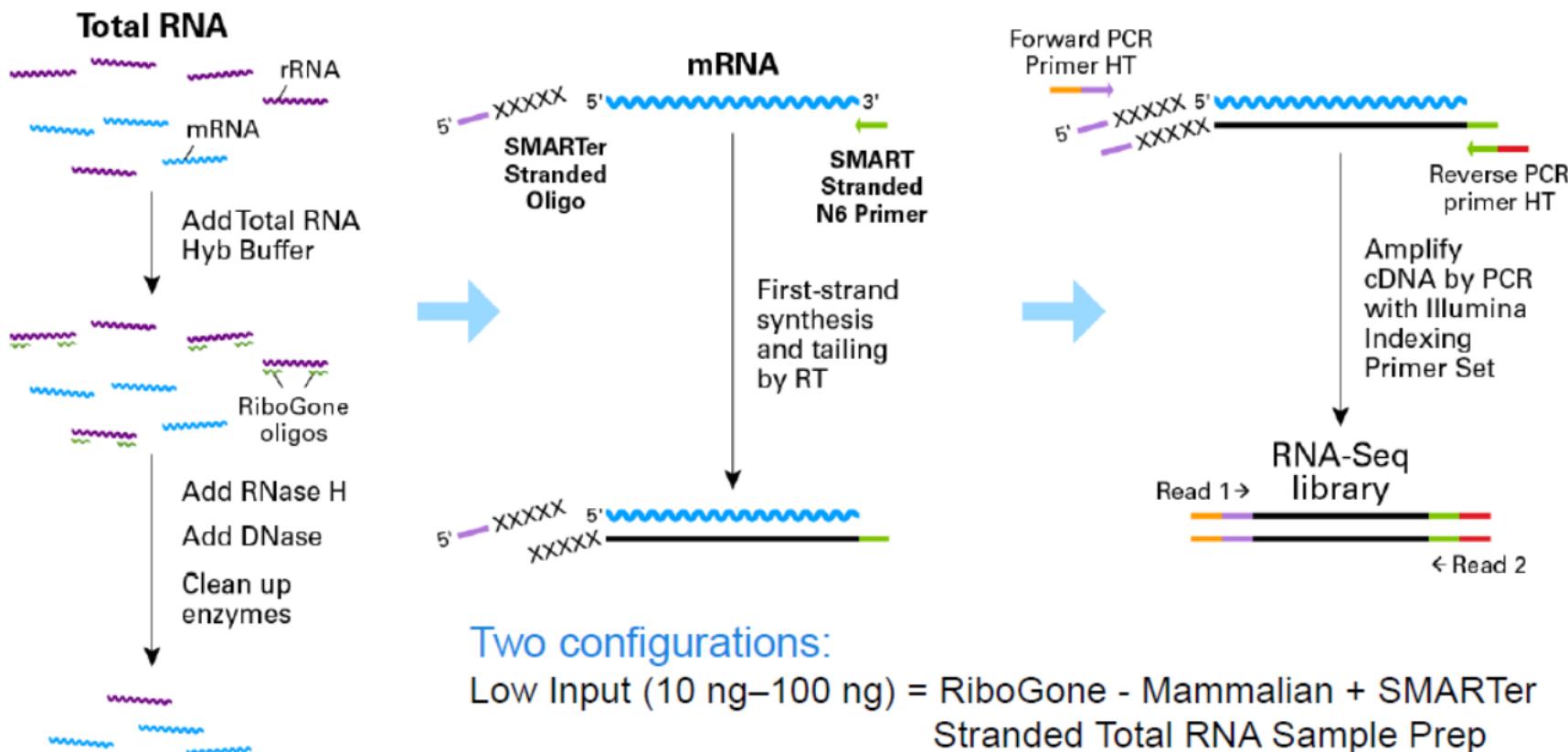


**Figure 1. Workflow for RiboGone rRNA depletion.** This kit is designed for use with low input samples containing 10–100 ng of total RNA, and works with full-length or degraded RNA. Samples processed using the RiboGone kit are ready for cDNA synthesis with any random-primed SMARTer RNA-Seq kit, including the SMARTer Stranded RNA-Seq Kit, SMARTer Universal Low Input RNA Kit for Sequencing, and SMARTer Universal Low Input RNA Library Prep Kit.



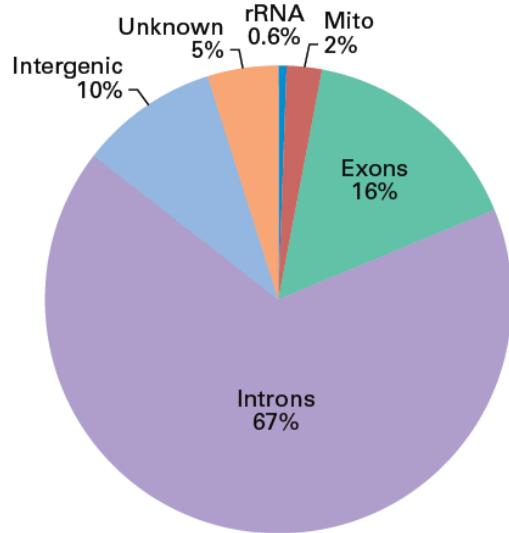
**Figure 3. Workflow for random-primed cDNA synthesis with SMARTer Universal Low Input RNA kits.** SMARTer Universal cDNA synthesis is random-primed, which makes it ideal for use with compromised mammalian RNA samples, e.g. RNA from FFPE tissue. Ribosomal RNA must be removed with RiboGone - Mammalian prior to SMARTer Universal cDNA synthesis.

# RiboGone™ rRNA removal & SMARTer cDNA synthesis



High Input (100 ng–1 mg) = SMARTer Stranded Total RNA Sample Prep Kit - HI

# Summary for SMARTer Kit Using



## High quality RNA-seq data from FFPE samples

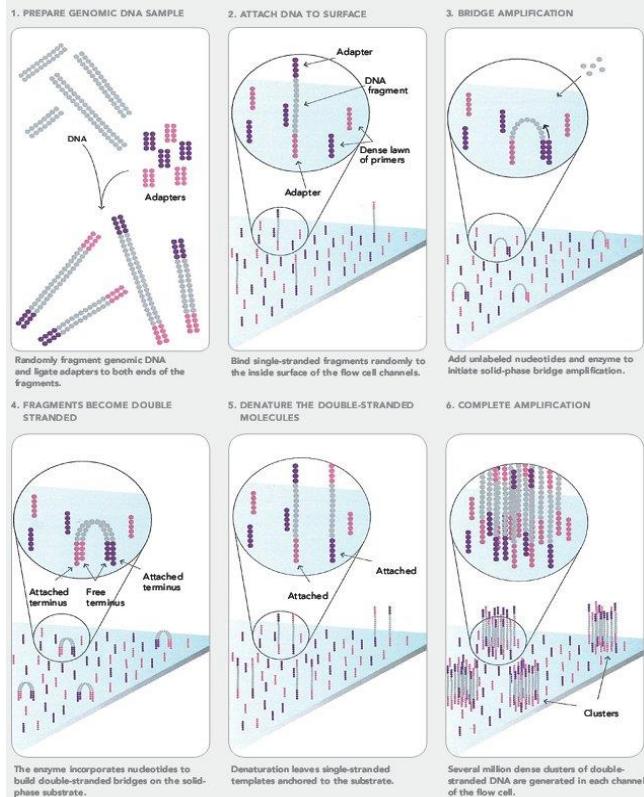
The library was sequenced on an Illumina MiSeq® instrument with ~6M 1 x 50 bp paired end reads. rRNA reads were reduced to 0.6% of total reads, and 16,463 genes were identified. The number of reads that mapped to introns, exons, intergenic regions, rRNA, mitochondrial RNA, and unknown sources are shown as percentages of the total reads (Figure 4).

**Figure 4. RiboGone treatment and random-primed SMARTer cDNA synthesis preserve transcriptome data while eliminating rRNA.** Total RNA was extracted, cleared of rRNA, converted to cDNA and prepared for Illumina sequencing as described above. The cDNA was sequenced on an Illumina MiSeq Platform with 1 x 50 bp reads, and the reads were trimmed by CLC Genomics Workbench and mapped to rRNA, the mitochondrial genome, and the human genome with RefSeq masking using CLC (% reads indicated). 16,463 genes were identified with an RPKM (reads per kilobase of exon per million of reads) of at least 0.1. The number of reads that map to introns or exons is a percentage of the total reads.

## Summary

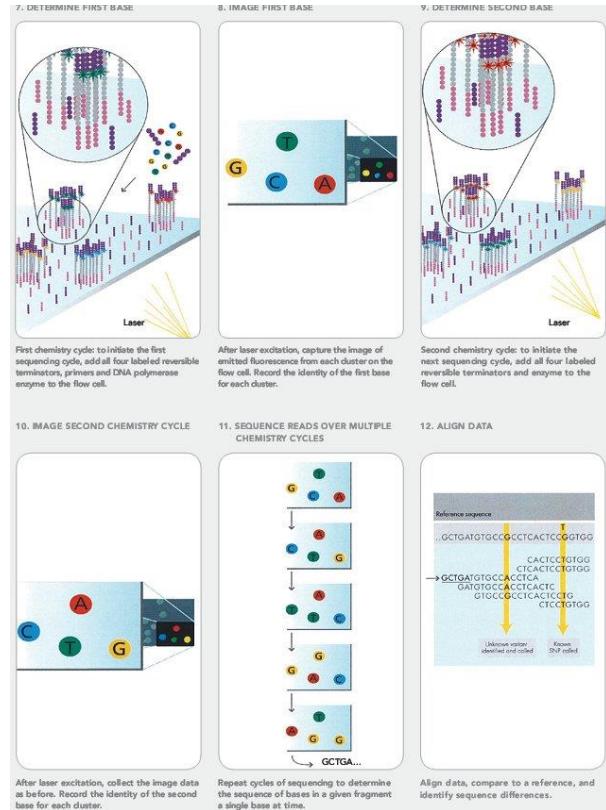
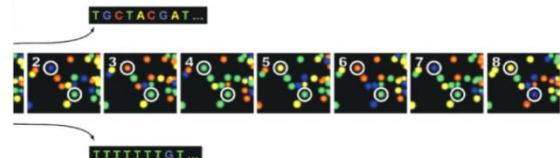
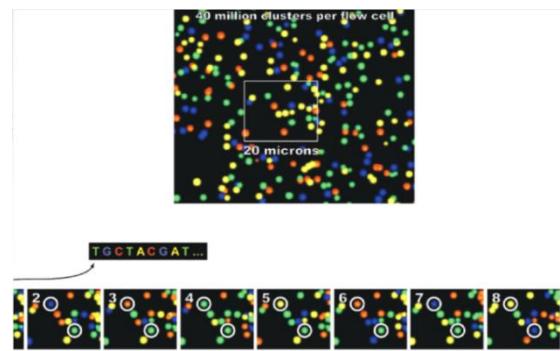
Random priming extends the applicability of transcriptome analysis to include samples which contain non-polyadenylated and/or compromised input RNA. However, in order to maximize RNA-Seq data quality and quantity, random primed RNA-Seq kits must be paired with rRNA removal methods. The RiboGone - Mammalian kit specifically removes 5S, 5.8S, 18S, and 28S rRNA sequences (as well as 12S mitochondrial rRNA sequences) from human, mouse, or rat total RNA. In this study, 16,463 genes were identified with an RPKM  $\geq 0.1$ , while rRNA and mtRNA reads were reduced to <1% and ~2% of the RNA-Seq library reads, respectively (Figure 4). These data indicate that SMARTer random-primed cDNA synthesis paired with RiboGone rRNA depletion yields high-value RNA-Seq data, even from challenging samples such as small quantities of FFPE tissue.

# Sequencing

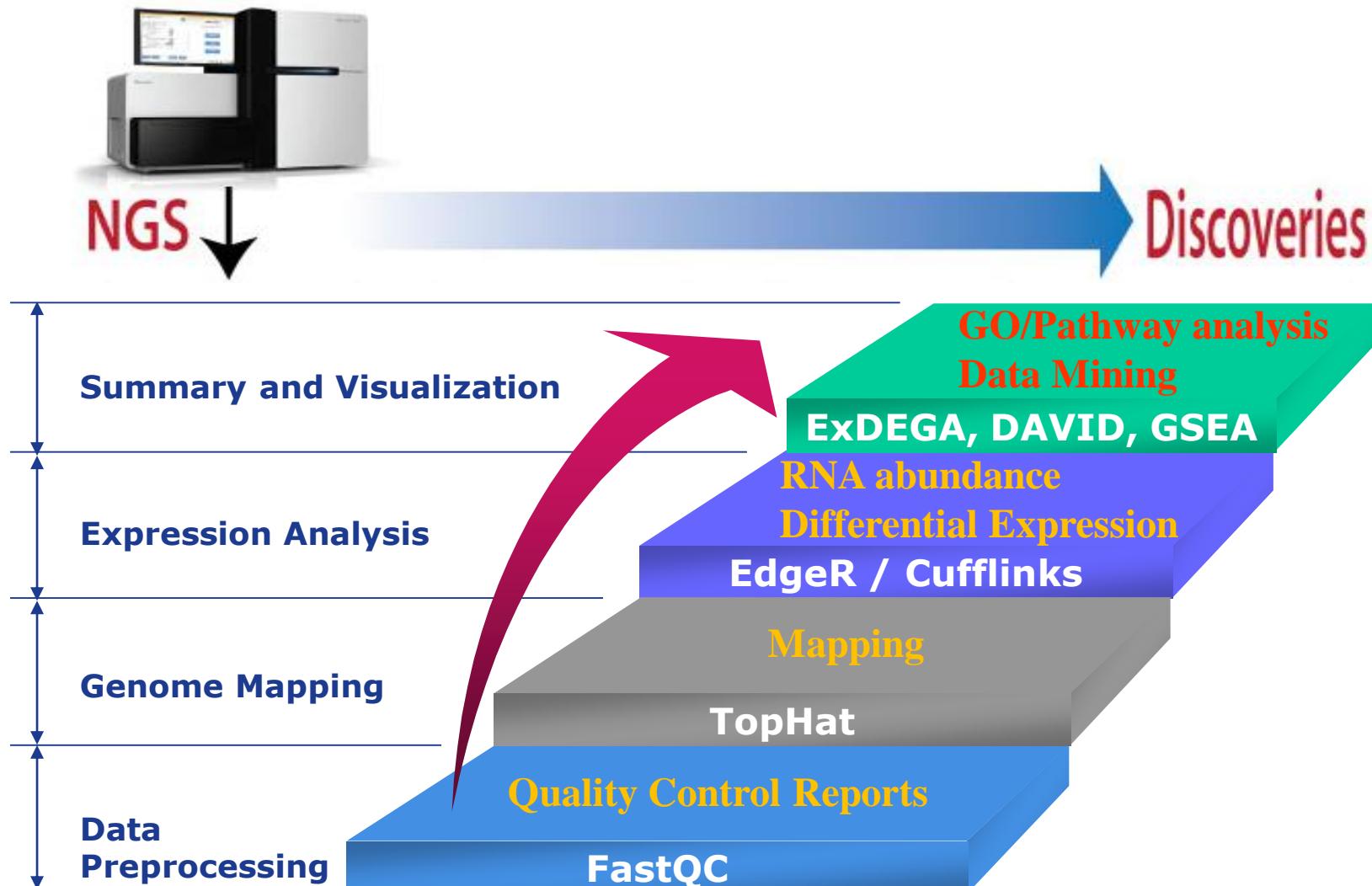


Run Format	Read Length	# of Reads	High-Quality Output (Gb)	
			/lane	/FlowCell
<b>Single End</b>	1 x 50bp	~150 million/lane	7.5 Gb	135-150 Gb
	1 x 100bp		15 Gb	270-300 Gb
<b>Paired End</b>	2 x 50bp	~300 million/lane	15 Gb	270-300 Gb
	2 x 100bp		30 Gb	540-600 Gb

## Illumina HiSeq-2000/2500 Illumina NextSeq 500



# Work Flow of Data Analysis



Other Data Analysis Tools for Data Processing, Mining, Visualization : MISO, Quick GO, ClueGO, CytoScape, DAVID, GSEA, UCSC Genome, IGV, IPA, Others

# Sequencing Data QC

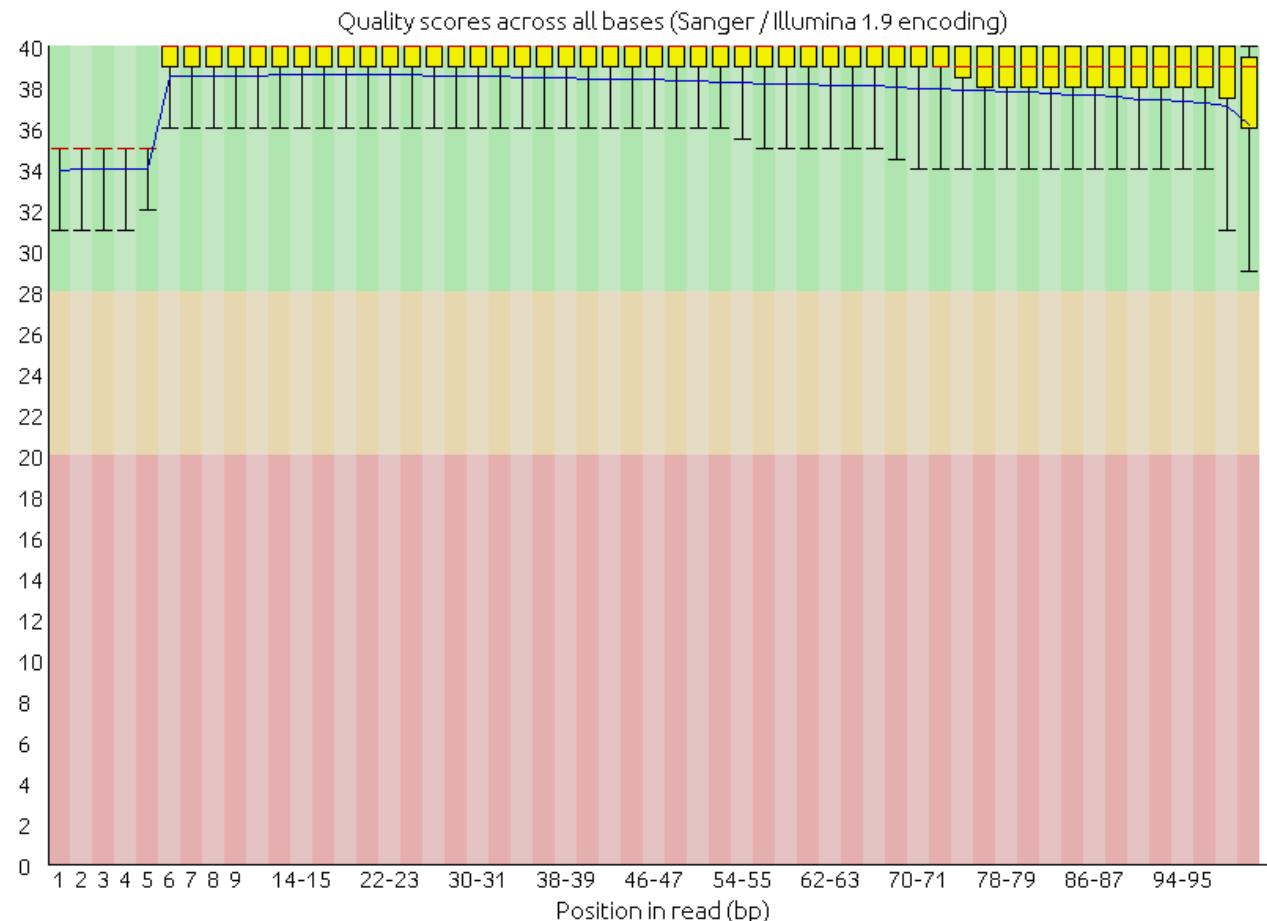


FastQ 파일 안에서 각 position의 base에 대한 quality 값의 영역을 보여 줌

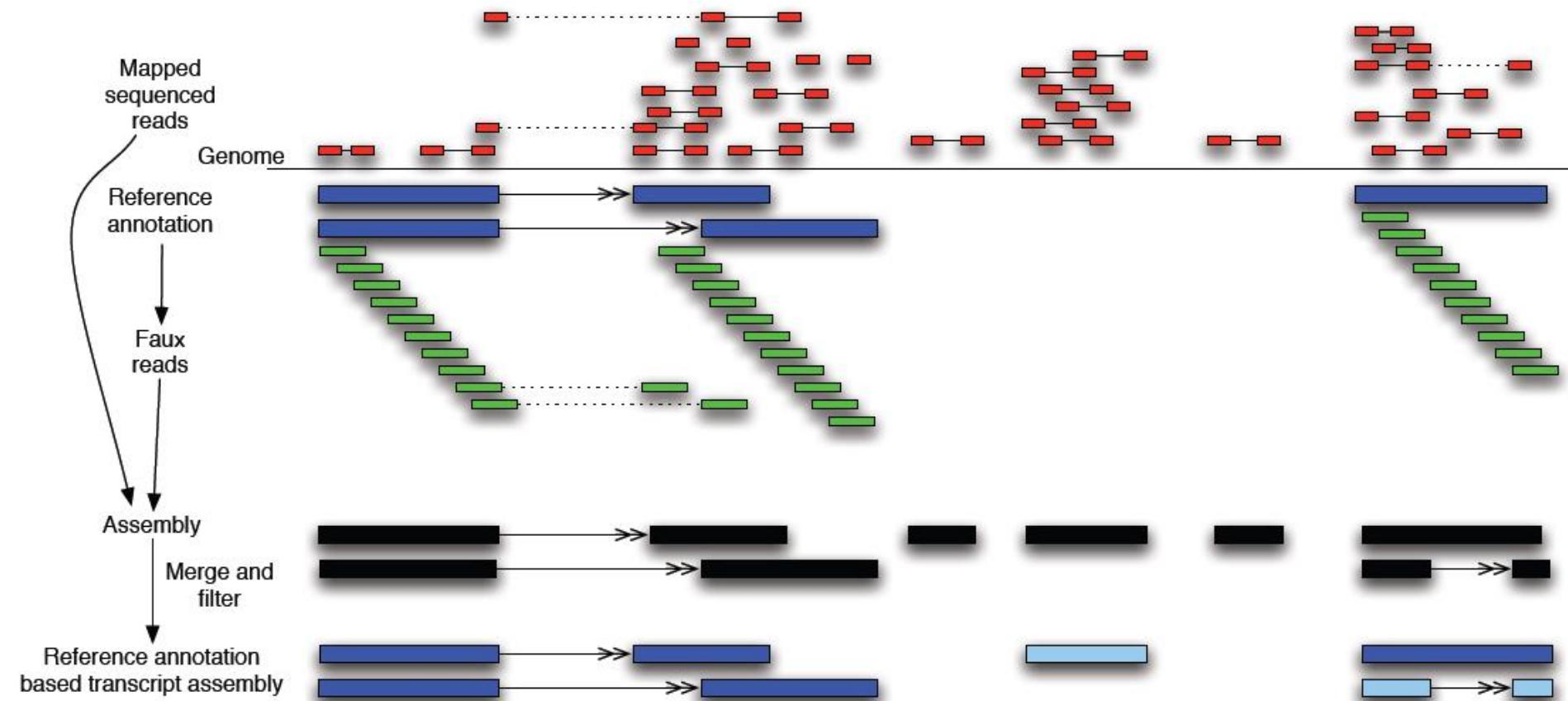
## Summary

- ✓ [Basic Statistics](#)
- ✓ [Per base sequence quality](#)
- ✓ [Per tile sequence quality](#)
- ✓ [Per sequence quality scores](#)
- ✗ [Per base sequence content](#)
- ! [Per sequence GC content](#)
- ✓ [Per base N content](#)
- ✓ [Sequence Length Distribution](#)
- ✓ [Sequence Duplication Levels](#)
- ✓ [Overrepresented sequences](#)
- ✓ [Adapter Content](#)
- ✗ [Kmer Content](#)

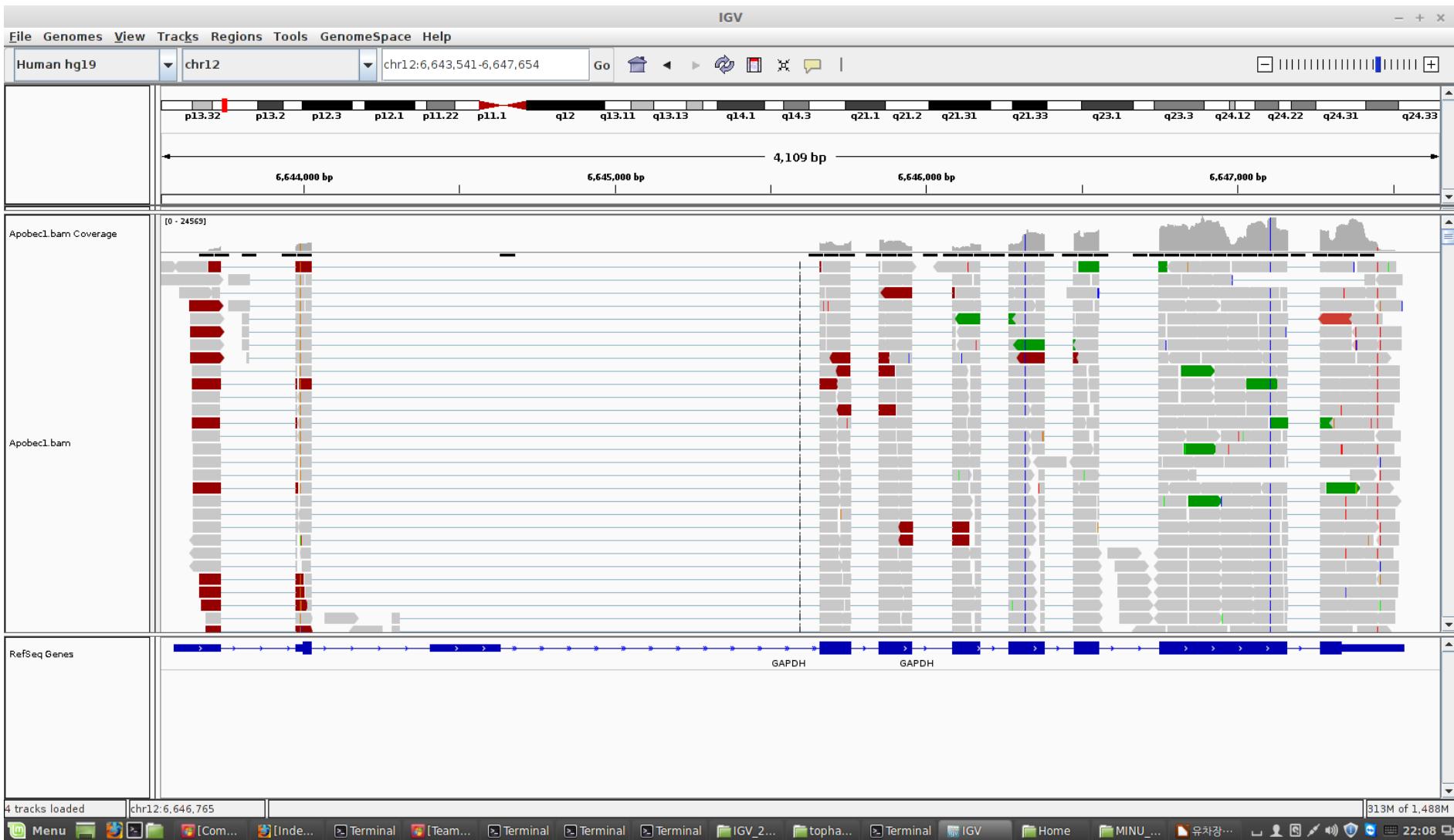
## Per base sequence quality



# Data Analysis – TopHat, Cufflinks



# Data Analysis – IGV



# Data Analysis – ExDEGA

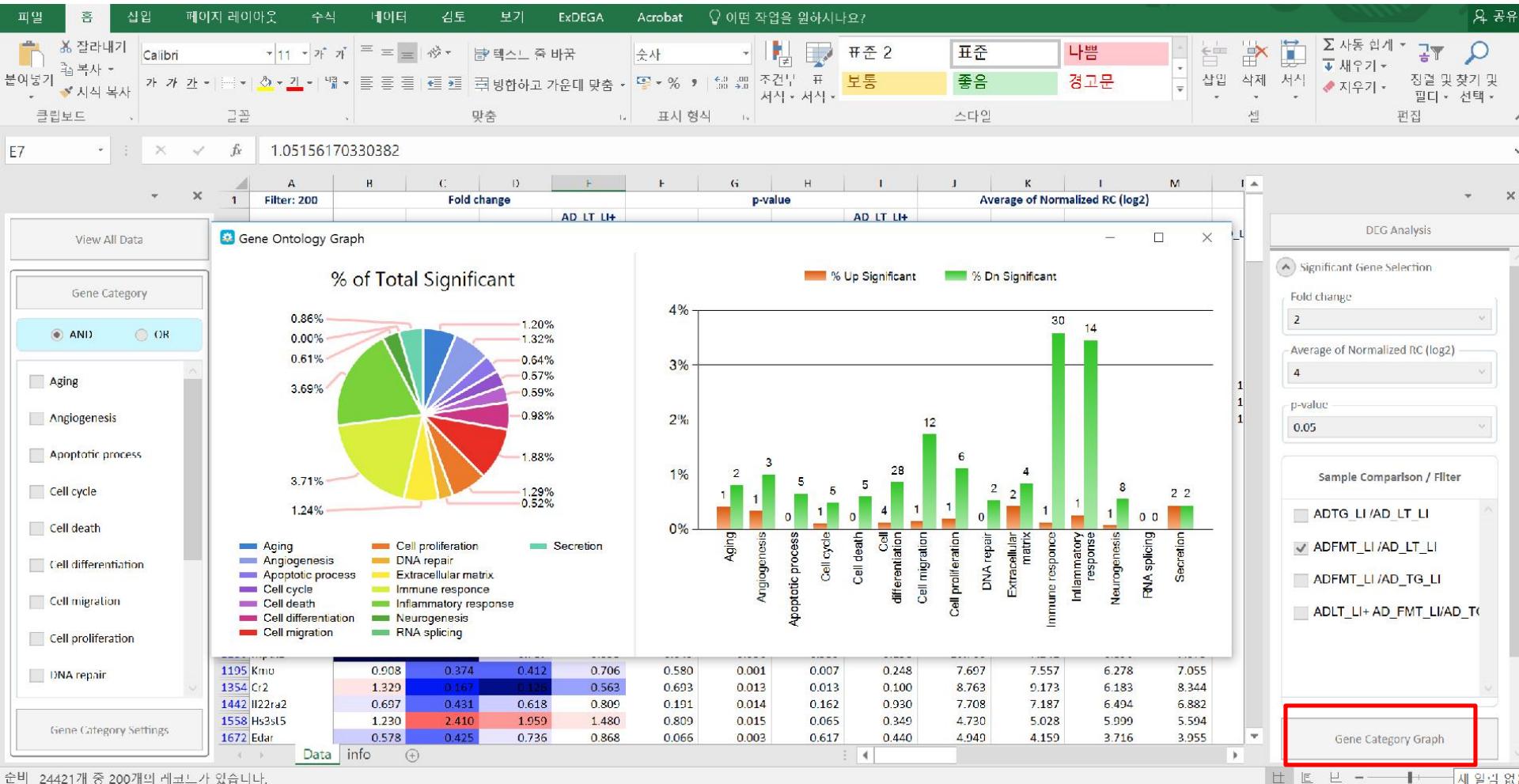


ExDEGA : Excel based Differentially Expressed Gene Analysis tool

	A	B	C	D	F	G	H	I	J	K	L	M	N	O	
1	Filter: 200		Fold change				p-value				Average of Normalized RC (log2)				
2	Gene Symbol	/AD_LT_LI	/AD_FMT_LI	/AD_FMT_LT_LI	/AD_TG_LI	/AD_LT_LI+ /AD_FMT_LI/ /AD_TG_LI	/AD_LT_LI	/AD_FMT_LI	/AD_FMT_LT_LI/ /AD_TG_LI	/AD_LT_LI+	/AD_FMT_LI	/AD_LT_LI	/AD_FMT_LI	/AD_LT_LT_LI+ /AD_FMT_LT_LI/ /AD_TG_LT_LI	
22	Mybl1	0.561	0.401	0.715	0.857	0.053	0.004	0.115	0.670	7.279	6.445	5.961	6.224	1	
41	Slc5a1	0.752	0.419	0.557	0.779	0.330	0.005	0.049	0.711	4.923	4.513	3.659	4.151	1	
253	Pms1	0.660	0.407	0.742	0.871	0.017	0.009	0.218	0.891	6.274	5.694	5.264	5.495	1	
288	Aux3	0.571	0.203	0.356	0.678	0.090	0.000	0.101	0.936	4.389	3.581	2.091	3.021	1	
326	Icos	0.654	0.472	0.722	0.861	0.222	0.037	0.201	0.089	7.292	6.679	6.209	6.463	1	
489	Ccl20	0.612	0.191	0.313	0.656	0.655	0.035	0.045	0.392	5.343	4.635	2.057	4.027	1	
499	A53002D15Rik	1.175	0.408	0.348	0.674	0.974	0.001	0.021	0.166	7.769	8.002	6.477	7.432	1	
501	C13002G12Rik	1.033	0.256	0.248	0.624	0.958	0.005	0.010	0.168	10.417	10.465	8.452	9.784	1	
502	Sp110	1.000	0.378	0.378	0.689	0.854	0.037	0.017	0.172	12.297	12.297	10.893	11.759	1	
503	Sp140	0.914	0.259	0.284	0.642	0.886	0.016	0.023	0.292	11.258	11.128	9.310	10.488	1	
505	A630001G21Rik	1.266	0.471	0.372	0.686	0.478	0.016	0.008	0.057	7.612	7.952	6.527	7.408	1	
729	Tiam1e163	0.739	0.412	0.557	0.779	0.369	0.019	0.254	0.857	5.292	4.855	4.012	4.494	1	
742	Cxcr4	0.823	0.379	0.455	0.727	0.463	0.001	0.003	0.267	10.017	9.754	8.617	9.294	1	
752	Fcamr	1.143	0.470	0.411	0.705	0.599	0.042	0.010	0.094	8.873	9.066	7.783	8.562	1	
754	Fcmr1	1.867	0.176	0.547	0.547	0.452	0.009	0.008	0.050	9.491	10.392	6.984	9.522	1	
800	Rgs13	0.638	0.396	0.620	0.810	0.253	0.044	0.320	1.000	6.491	5.843	5.153	5.539	1	
804	Brip1	1.345	2.003	1.489	1.245	0.064	0.006	0.089	0.854	4.884	5.312	5.887	5.628	1	
1025	Sell	1.312	0.166	0.111	0.563	0.565	0.001	0.001	0.040	9.018	9.409	6.428	8.581	1	
1036	Xcl1	0.643	0.425	0.660	0.830	0.162	0.011	0.475	0.710	5.871	5.234	4.636	4.966	1	
1081	Sh2d1b1	0.841	0.418	0.497	0.748	0.369	0.016	0.081	0.488	5.672	5.422	4.412	5.004	1	
1089	Fcrla	1.216	0.270	0.222	0.611	0.884	0.001	0.007	0.112	10.526	10.808	8.636	10.097	1	
1163	BC094016	1.709	0.363	0.212	0.606	0.412	0.008	0.008	0.043	5.384	6.157	3.922	5.435	1	
1165	Pylin1	1.150	0.350	0.302	0.651	0.445	0.029	0.003	0.050	7.123	7.336	5.609	6.717	1	
1186	Mplxl1	0.001	0.001	0.001	0.787	0.803	0.049	0.036	0.939	0.198	10.700	7.242	6.896	7.079	1
1195	Kmu	0.908	0.374	0.412	0.706	0.580	0.001	0.007	0.248	7.697	7.557	6.278	7.055	1	
1354	C12	1.329	0.167	0.141	0.563	0.693	0.013	0.013	0.100	8.763	9.173	6.183	8.344	1	
1442	Il22ra2	0.697	0.431	0.618	0.809	0.191	0.014	0.162	0.930	7.708	7.187	6.494	6.882	1	
1558	H3s3t5	1.230	2.410	1.959	1.480	0.809	0.015	0.065	0.349	4.730	5.028	5.099	5.504	1	
1672	Edar	0.578	0.425	0.736	0.868	0.066	0.003	0.617	0.440	4.940	4.159	3.716	3.955	1	

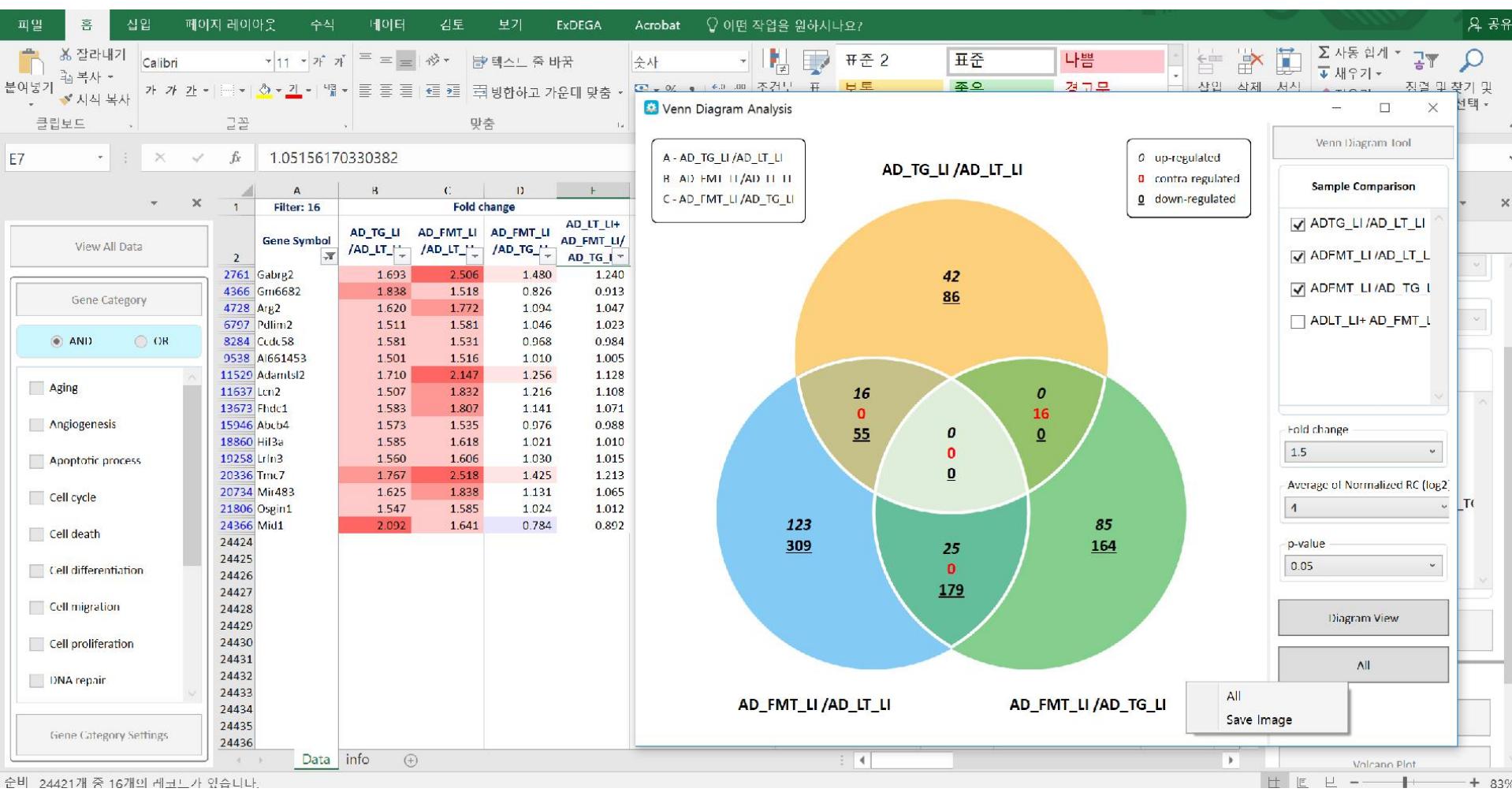
- ❖ Add Another GO 기능을 통해 사용자가 원하는 GO를 자유롭게 구성할 수 있습니다.
- ❖ Significant gene을 매우 빠르고 쉽게 데이터를 취할 수 있고 그라프로 표현할 수 있습니다.

# Data Analysis – ExDEGA



- ❖ Pie chart를 통해 Significant gene 대상으로 BioFunction 분포를 확인하고 영역을 클릭하면 해당 up/down 유전자가 필터링됨.
- ❖ Bar graph를 통해 BioFunction 별로 up/down의 분포를 확인하고 bar를 클릭하면 해당 유전자를 확인할 수 있음.

# Data Analysis – ExDEGA



# Data Analysis – ExDEGA



File Home Page Layout Tools View Insert Cells Styles Charts Page Layout Formulas Data Power BI Reports Add-ins Tell me what you want? Acrobat How can we help you?

A11637 Lcn2

Filter: 16

	B	C	D	E	F	G	H	I	J	K	L	M
Gene Symbol	AD_TG_LI /AD_LT_LI	AD_FMT_LI /AD_LT_LI	AD_FMT_LI /AD_TG_LI	AD_LT_LI /AD_TG_LI	AD_TG_LI /AD_LT_LI	AD_FMT_LI /AD_LT_LI	AD_FMT_LI /AD_TG_LI	AD_LT_LI /AD_TG_LI	AD_LT_LI /AD_TG_LI	AD_LT_LI /AD_FMT_LI	AD_LT_LI /AD_FMT_LI	AD_LT_LI /AD_FMT_LI
2761												
4366												
4728												
6797												
8284												
9538												
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24434												
24435												
24436												

Gene Graph Tool

View All Data

Gene Category

AND OR

Aging Angiogenesis Apoptotic process Cell cycle Cell death Cell differentiation Cell migration Cell proliferation DNA repair

Gene Category Settings

Average of Normalized RC (log2)

Line chart showing Average of Normalized RC (log2) for various genes across four conditions: AD\_LT\_LI, AD\_TG\_LI, AD\_FMT\_LI, and AD\_LT\_FMT\_LI.

Legend:

- Lcn2
- Fhdc1
- Abcb4
- Hif3a
- Lrfn3
- Tmc7
- Mir483
- Osgin1

Analysis Graph

Venn Diagram

Volcano Plot

Selected Gene Graph (Gene Symbol)

Graph View

Gene Search

DEG Analysis

Gene Category Graph

Line chart showing Fold Change (log2) for selected genes across four conditions: AD\_TG\_LI / AD\_LT\_LI, AD\_FMT\_LI / AD\_LT\_LI, AD\_LT\_LI / AD\_TG\_LI, and AD\_FMT\_LI / AD\_TG\_LI.

Legend:

- Lcn2
- Fhdc1
- Abcb4
- Hif3a
- Lrfn3
- Tmc7
- Mir483
- Osgin1

대상을 선택한 다음 <Enter> 키를 누르거나 [붙여넣기]를 선택합니다.

Page: 8

# Additional Data Analysis



## GO & Pathway

### QuickGO

**QuickGO**  
A fast browser for Gene Ontology terms and annotations.

**QuickGO Databases**

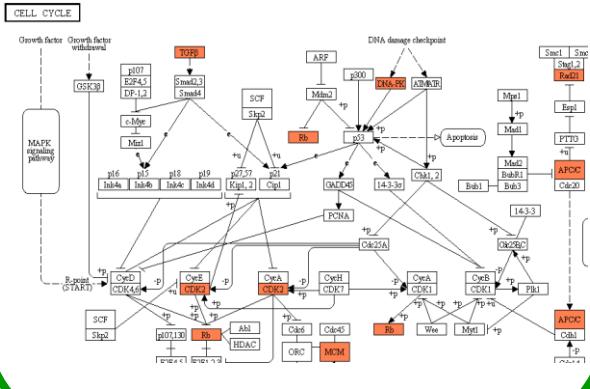
**Search and filter**

**Investigate**

**View the history**

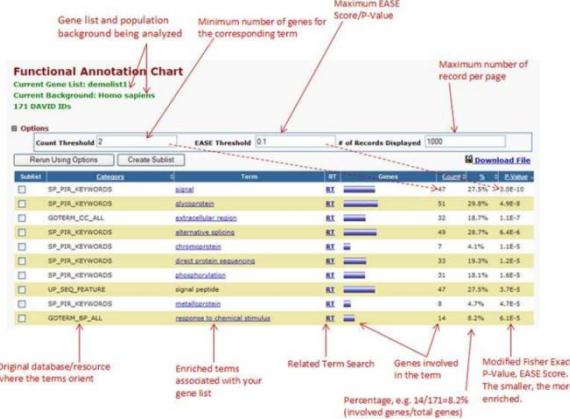
Please send comments, suggestions or bug reports to [gca@ebi.ac.uk](mailto:gca@ebi.ac.uk). Click [here](#) for details of how to cite UniProt-GOA and QuickGO.

## KEGG Mapper



## Gene Set Enrichment

### DAVID



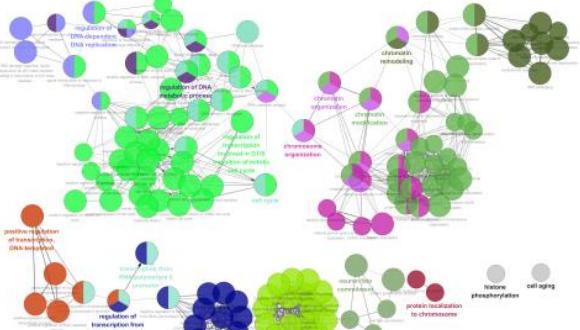
### GSEA

**GENESET**

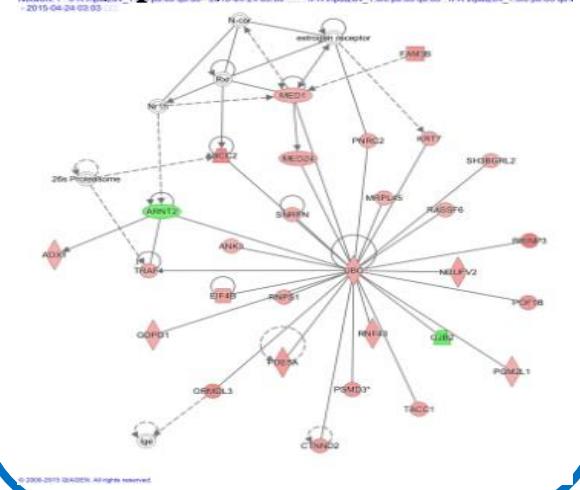
ES	NES	NP	FDR	PVAL	
gene_sets.gmt#REACTOME_INSULIN_RECEPTOR_RECYLCLING	0.7051	1.6909	0.0108	0.4703	0.93
gene_sets.gmt#KEGG_ALLOGRAFT_REJECTION	0.6831	1.7429	0.0029	0.3305	0.713
gene_sets.gmt#KEGG_TYPE_I_DIABETES_MELLITUS	0.6831	1.8278	0.0	0.1588	0.258
gene_sets.gmt#REACTOME_PHOSPHORYLATION_OF_CD3_AND_TCR_ZETA_CHAINS	0.6804	1.5191	0.0398	1	1
gene_sets.gmt#KEGG_GRAFT_VERSUS_HOST_DISEASE	0.6777	1.7734	0.0016	0.2722	0.54
gene_sets.gmt#REACTOME_P1_SIGNALING	0.6696	1.5046	0.0478	1	1
gene_sets.gmt#KEGG_ASTHMA	0.6609	1.6640	0.0076	0.4892	0.975
gene_sets.gmt#REACTOME_TRANSFERRIN_ENDOCYTOSIS_AND_RECYLCLING	0.6577	1.5666	0.0219	1	1
gene_sets.gmt#BIOCARTA_CMP_PATHWAY	0.6528	1.5084	0.0538	1	1
gene_sets.gmt#KEGG_ANTIGEN_PROCESSING_AND_PRESENTATION	0.6393	1.4677	0.0521	1	1
gene_sets.gmt#KEGG_AUTOMUNE_THYROID_DISEASE	0.635	1.8849	0	0.1041	0.091
gene_sets.gmt#KEGG_GLYCOSPHINGOLIPID_BIOSYNTHESIS_LACTO_AND_NEOLACTO_SERIES	0.6196	1.6902	0.0556	0.4034	0.93
gene_sets.gmt#REACTOME_GENERATION_OF_SECOND_MESSENGER_MOLECULES	0.6157	1.4880	0.0279	1	1
gene_sets.gmt#BIOCARTA_JL10_PATHWAY	0.6102	1.4898	0.0464	1	1
gene_sets.gmt#KEGG_leishmania_infection	0.6035	1.3206	0.1449	1	1
gene_sets.gmt#KEGG_OTHER_GLYCAN_DEGRADATION	0.5932	1.6972	0.0014	0.5178	0.914
gene_sets.gmt#REACTOME_RNA_POLI_TRANSCRIPTION_INITIATION	0.5819	1.2691	0.1631	1	1
gene_sets.gmt#KEGG_INTESTINAL_IMMUNE_NETWORK_FOR_IgA_PRODUCTION	0.5771	1.3739	0.0972	1	1
gene_sets.gmt#REACTOME_TIE_SIGNALING	0.5703	1.553	0.02	1	1
gene_sets.gmt#BIOCARTA_HS27_PATHWAY	0.5694	1.2409	0.1968	1	1
gene_sets.gmt#KEGG_RAF1_SIGNALING	0.5639	1.2429	0.2194	1	1
gene_sets.gmt#BIOCARTA_RAF1_SIGNALING	0.5603	1.444	0.0248	1	1

## Network Analysis

### Cytoscape (ClueGO)



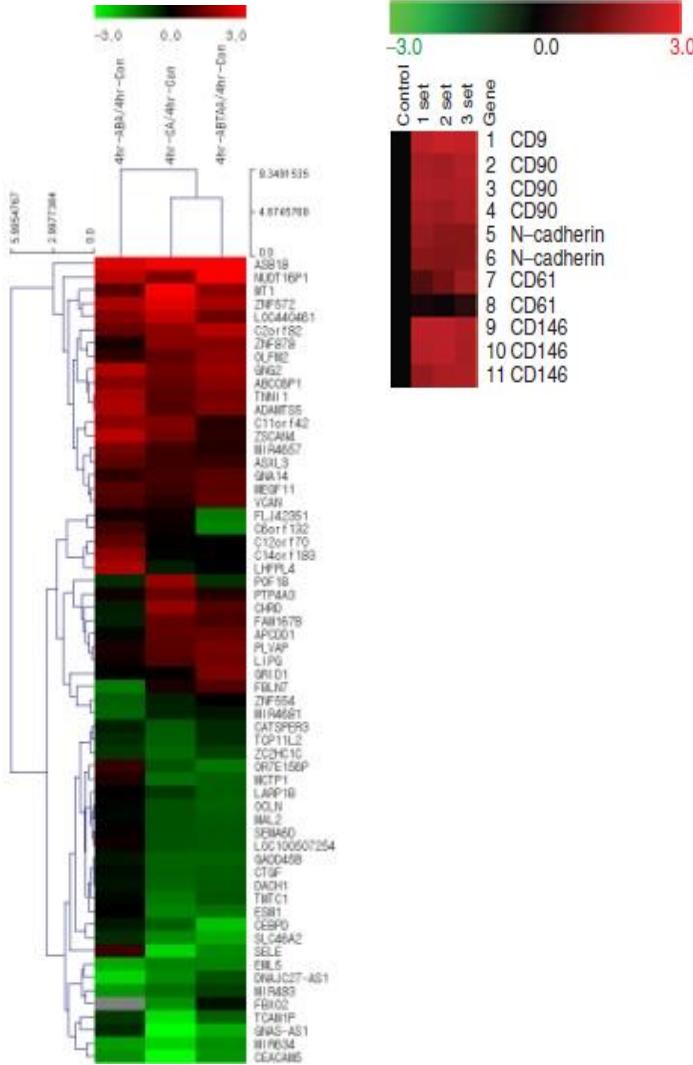
### IPA (Option)



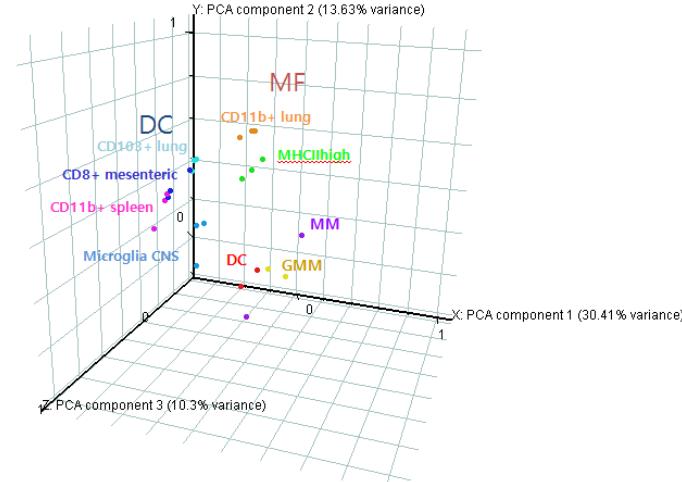
# Data Analysis – Clustering



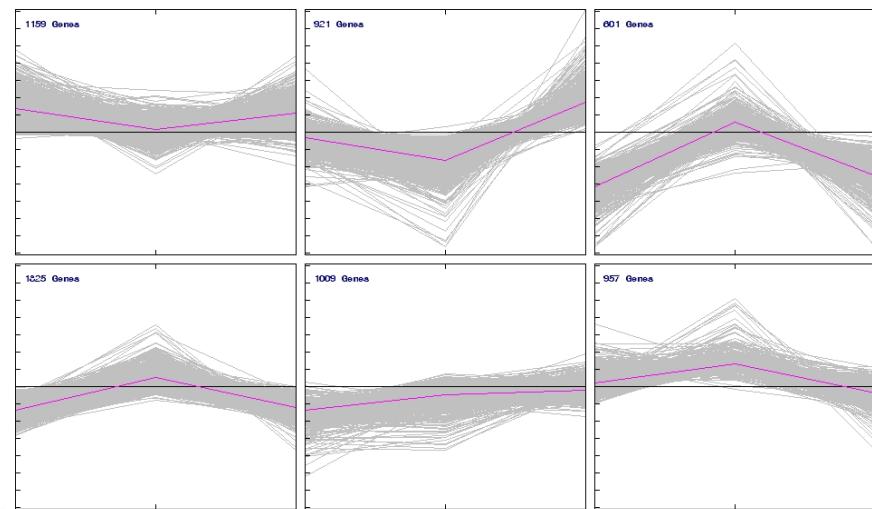
Hierarchical Clustering (HCL)



Principal Component Analysis (PCA)



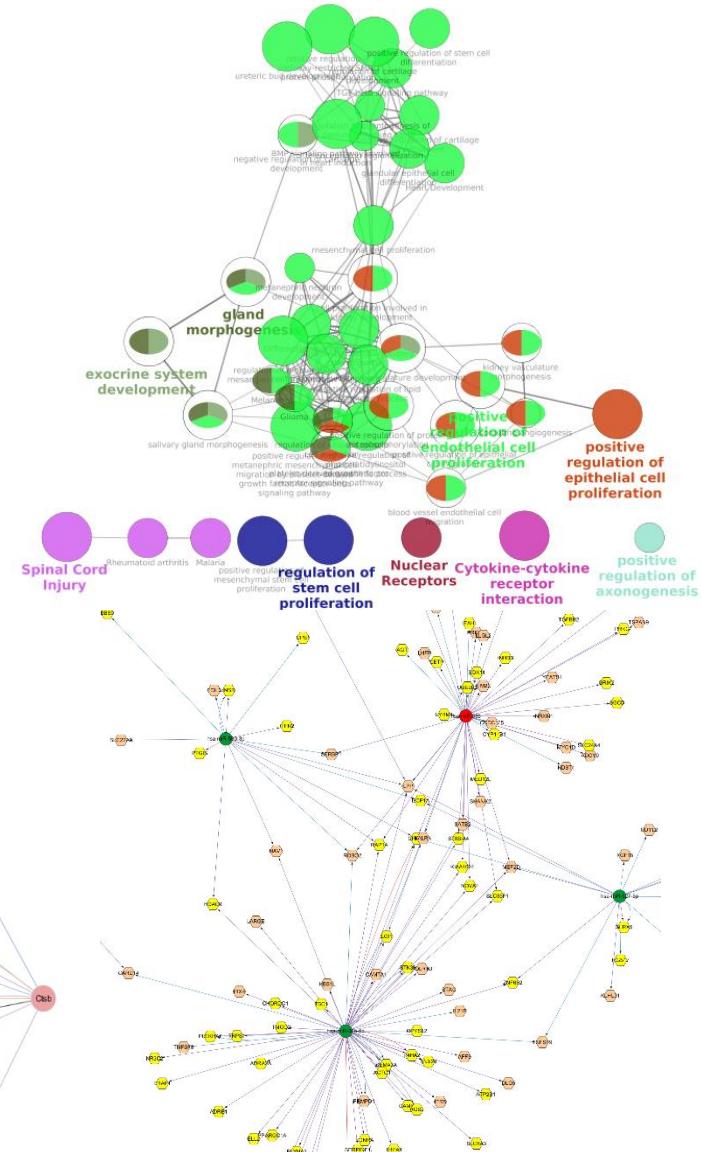
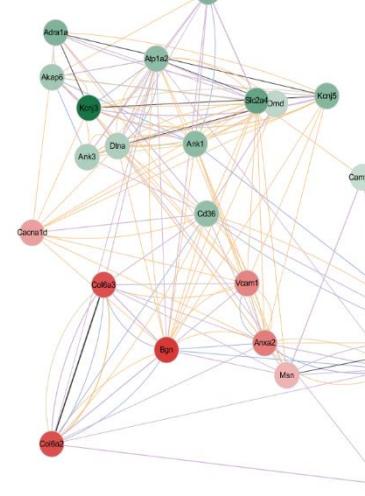
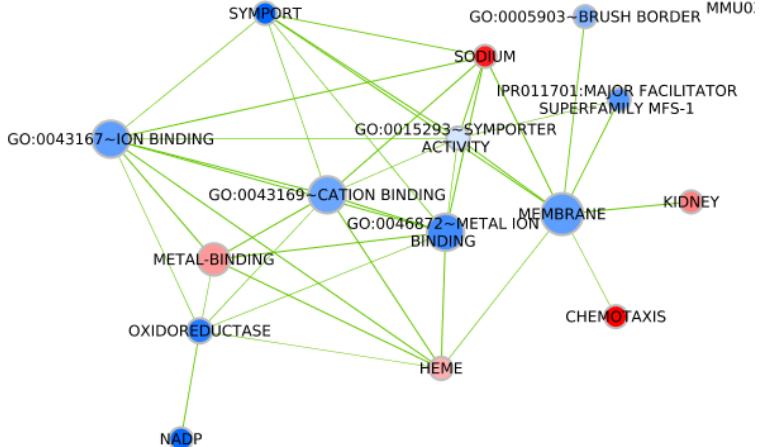
K-means clustering (KMC)



# Data Analysis – Networks



- ❖ Gene Network Generation : String
- ❖ GO & Pathway Analysis with ClueGO
- ❖ Gene Set Enrichment Analysis with DAVID
- ❖ Gene Set Enrichment Analysis with GeneMania
- ❖ Transcription Factor Analysis with iRegulon
- ❖ miRNA Target Analysis : CyTargetLinker



# Data Analysis – Exon skipping



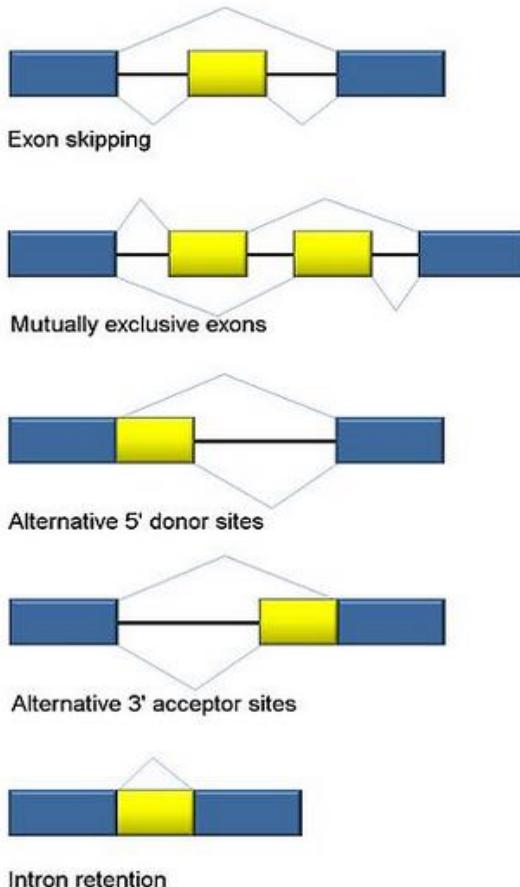
Nat Methods, 2010 Dec;7(12):1009-15. doi: 10.1038/nmeth.1528. Epub 2010 Nov 7.

## Analysis and design of RNA sequencing experiments for identifying isoform regulation.

Katz Y<sup>1</sup>, Wang ET, Airoldi EM, Burge CB.

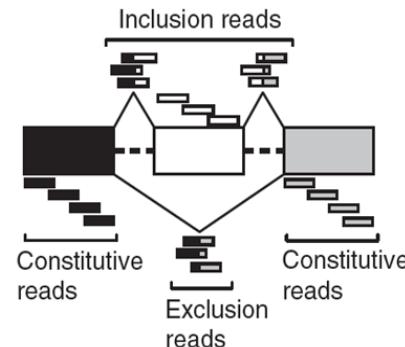
### Author information

## Splicing Patterns

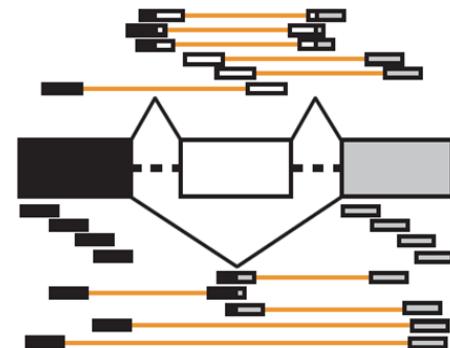


(a)

- ... Intron
- Skipped exon
- Constitutive exons

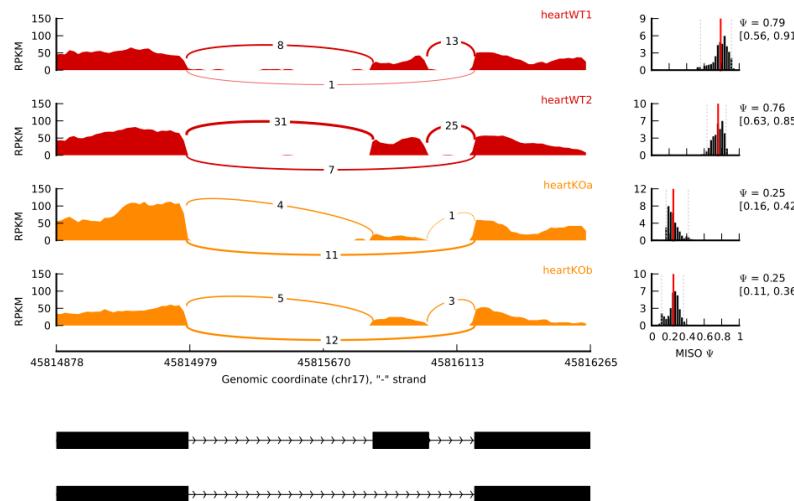


(b)



Paired-end estimate,  $\Psi$

chr17:45816186:45816265:-@chr17:45815912:45815950:-@chr17:45814875:45814965:-



# Data Mining & Visualization



A)

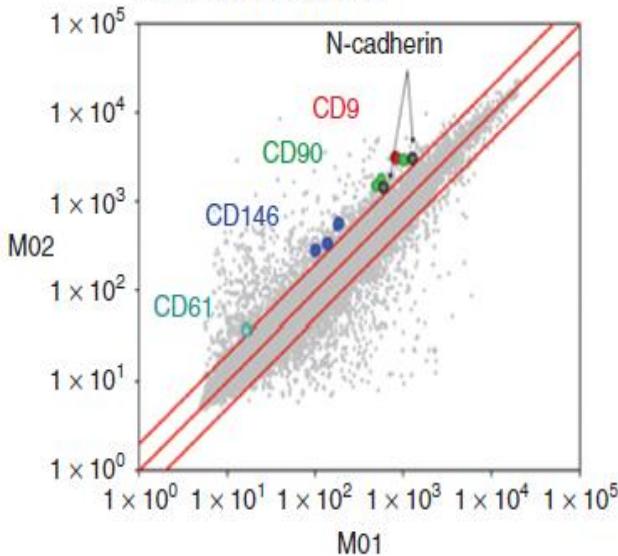
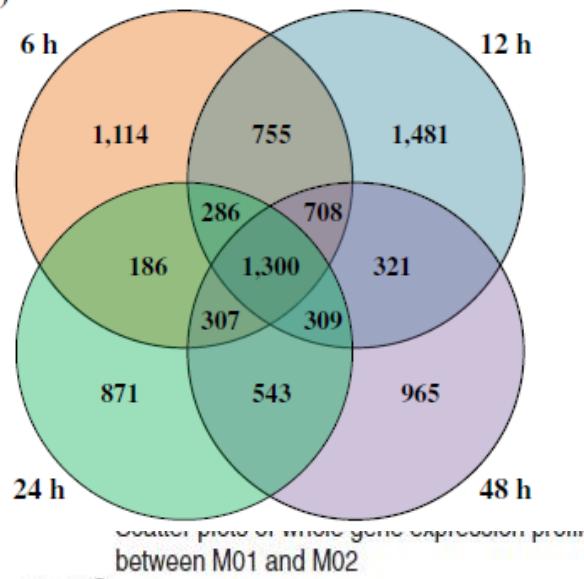
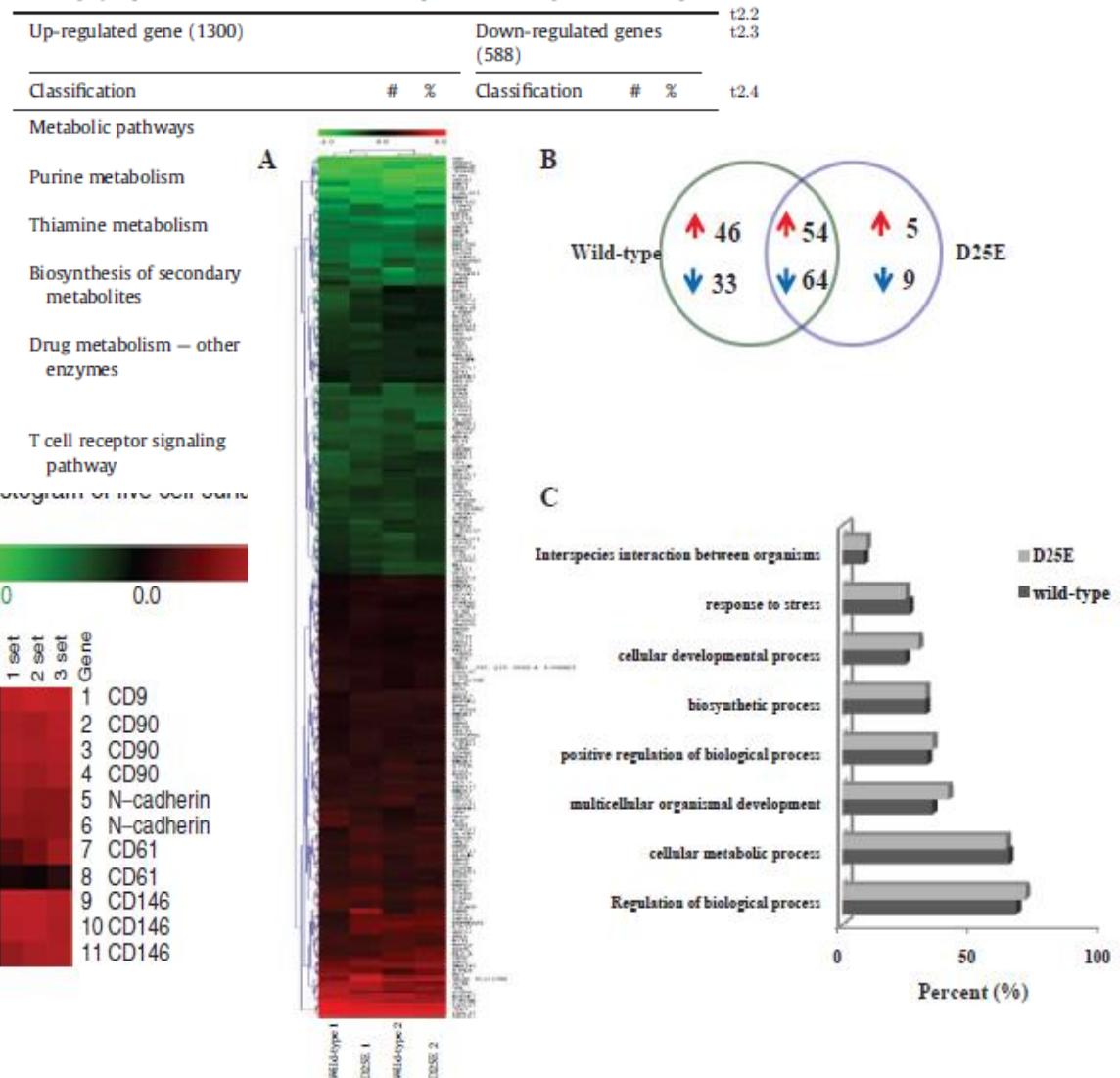


Table 2

Most highly represented KEGG classifications in up- and down-regulated transcripts.



# Paper Support



Gene Expression Omnibus

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**Gene Expression Omnibus:** a public functional genomics data repository supporting MIAME submissions. Array- and sequence-based data are accepted. Tools are provided to help users download experiments and curated gene expression profiles. [More information »](#)

## GEO navigation



A	B
1 SERIES	Murine ES Cells: Control vs. Triple-Fusion Transfected
2 title	Transcriptional profiling of mouse embryonic stem cells comp
3 summary	Two-condition experiment, ES vs. TF-ES cells. Biological repl
4 overall design	
5 contributor	Jane,Doe
6 contributor	John,A,Smith
7	
8 SAMPLES	# The corresponding example matrix table is included in the next worksheet.
9	
10 Sample name	title
11 ES-rep1	Control Embryonic Stem Cell Replicate 1
12 ES-rep2	Control Embryonic Stem Cell Replicate 2
13 ES-rep3	Control Embryonic Stem Cell Replicate 3
14 ES-rep4	Control Embryonic Stem Cell Replicate 4
15 TF-ES-rep1	Triple-Fusion Transfected Embryonic Stem Cells Replicate 1
16 TF-ES-rep2	Triple-Fusion Transfected Embryonic Stem Cells Replicate 2
17 TF-ES-rep3	Triple-Fusion Transfected Embryonic Stem Cells Replicate 3
18	

Jang et al. *Virology Journal* 2011, 8:453  
<http://www.virologyj.com/content/8/1/453>



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## N-cadherin Determines Individual Variations in the Therapeutic Efficacy of Human Umbilical Cord Blood-derived Mesenchymal Stem Cells in a Rat Model of Myocardial Infarction

Eun Ju Lee<sup>1</sup>, Eue-Keun Choi<sup>1,2</sup>, Soo Kyoung Kang<sup>1</sup>, Gi-Hwan Kim<sup>1</sup>, Ju Young Park<sup>1</sup>, Hyun-Jae Kang<sup>1,2</sup>, Sae-Won Lee<sup>1</sup>, Keum-Hyun Kim<sup>1</sup>, Jin Sook Kwon<sup>3</sup>, Ki Hong Lee<sup>4</sup>, Youngkeun Ahn<sup>4</sup>, Ho-Jae Lee<sup>1</sup>, Hyun-Jai Cho<sup>1,2</sup>, Soo Jin Choi<sup>5</sup>, Won Il Oh<sup>5</sup>, Young-Bae Park<sup>1,2</sup> and Hyo-Soo Kim<sup>1,2,6</sup>

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Mi Jang<sup>†</sup>, Jee Eun Rhee<sup>†</sup>, Dai-Ho Jang and Sung Soon Kim\*



Hepatology Research



Hepatology Research 2011; 41: 170–183

doi: 10.1111/j.1872-034X.2010.00711.x

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## Expression profiles of miRNAs in human embryonic stem cells during hepatocyte differentiation

Nury Kim,<sup>1</sup> Hyemin Kim,<sup>1</sup> Inkyung Jung,<sup>2</sup> Yeji Kim,<sup>1</sup> Dongsup Kim<sup>2</sup> and Yong-Mahn Han<sup>1</sup>

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