

生命科学研究所としての 公共遺伝子発現DBのメタ解析

大学共同利用機関法人 情報・システム研究機構

データサイエンス共同利用基盤施設

ライフサイエンス統合データベースセンター

(DBCLS)

坊農 秀雅

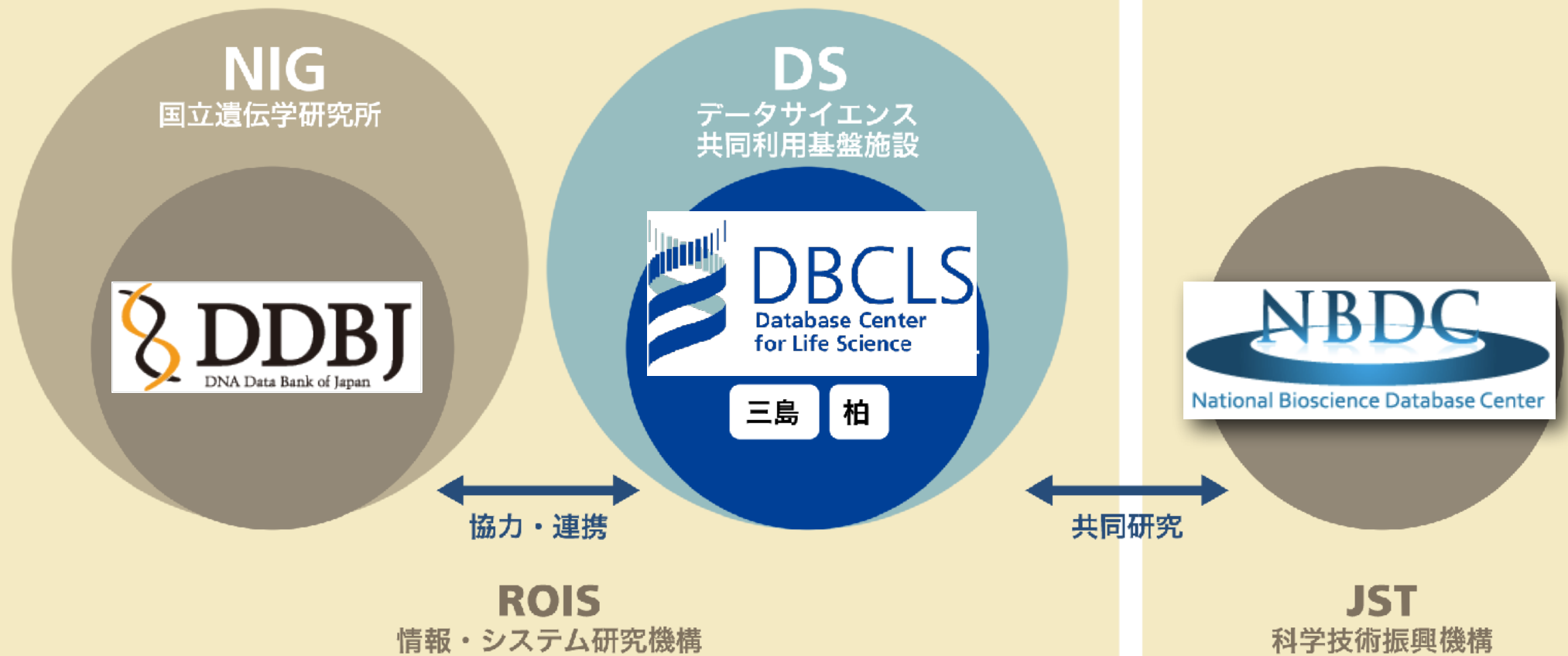
<https://DBCLS.rois.ac.jp/~bono/>

Hidemasa Bono, PhD. (坊農秀雅)



- ライフサイエンス統合データベースセンター
(Database Center for Life Science
(DBCLS)) 特任研究員 (特任准教授)
- JST バイオサイエンスデータベースセンター
(NBDC) と共同研究
- 国立遺伝学研究所(静岡県三島市)に居候
 - DNA DataBank of Japan (DDBJ) の隣で協力関係





- DDBJ: DNAデータアーカイブ
- DBCLS: データベース統合基盤技術開発
- NBDC: 戦略立案、funding

<https://dbcls.rois.ac.jp/about.html>



Hidemasa Bono, PhD. (坊農秀雅)



- 専門: バイオインフォマティクス、遺伝子発現解析
- KEGG の研究室で大学院生(京大化研) 
- FANTOM の名付け親(理研) 
- SayaMatcher(狭山茶)で転写因子結合領域解析 (埼玉医大)
→ GGRNA, GGGenome, **CRISPRdirect** へ発展中
- 公共DBを使い倒した生命科学データ解析 (DBCLS)
 - 統合TV、統合データベース講習会AJACS (2007-)
 - 次世代シーケンサー**DRY解析教本** (2015)
 - Dr.Bonoの**生命科学データ解析** (2017)
 - 生命科学データベース・ウェブツール (2018)
 - 生命科学データ解析を支える**情報技術** (2019)



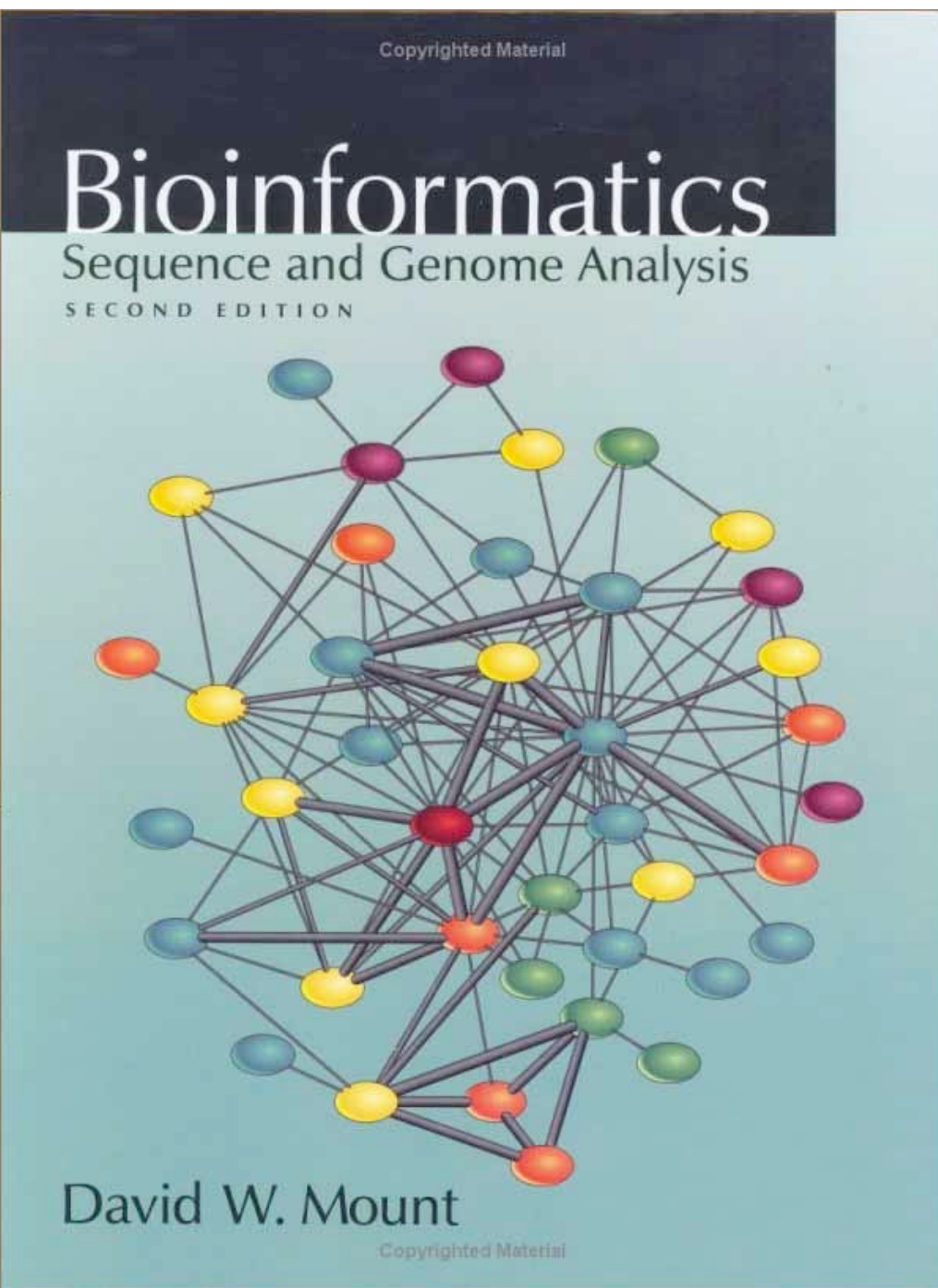
1 バイオインフォマティクス とは

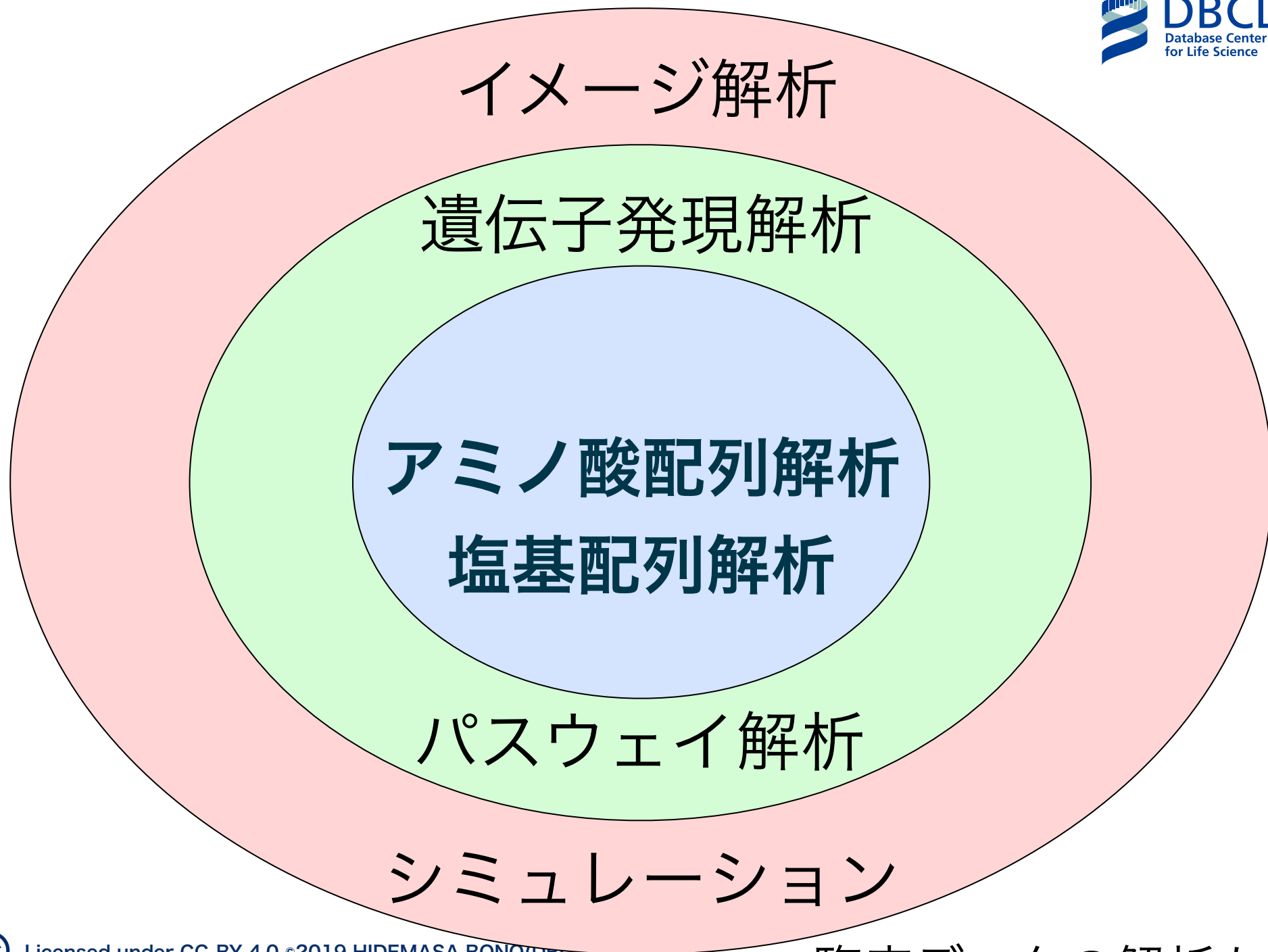
コンピュータを実験デバイスとして使って、
生物学的に有意な結論を引き出そうとする学問

坊農秀雅 「バイオインフォマティクス入門」 羊土社
2002



かつては翻訳版の教科書がありました





- ・ アルゴリズム屋
 - ・ 方法を考える人
 - ・ 「NP完全」がキーワード

・ 実装屋

- ・ プログラムやツールを書く人

・ 解析屋

- ・ プログラムを使って実際に生データを相手に手を動かす人

数学的
抽象的

生物的
具体的

Biologistの範疇

これからは、生物学者自身が データ解析する時代なんです

Nature ダイジェスト
2015年1月号

バイオインフォマティクスは
専門技術ではなくなっている
＝生命科学研究の主要な手法

誰もあなたのデータ解析はやってくれない
→自分でやるしかない



これから始める人は幸運です

書籍が充実してきた

- 各種プロトコール本
- 生命科学データ解析の教科書

インターネット上に膨大な情報

- 統合TV（講習会の動画を含む）
- 研究者のブログなど

TOGO  TV

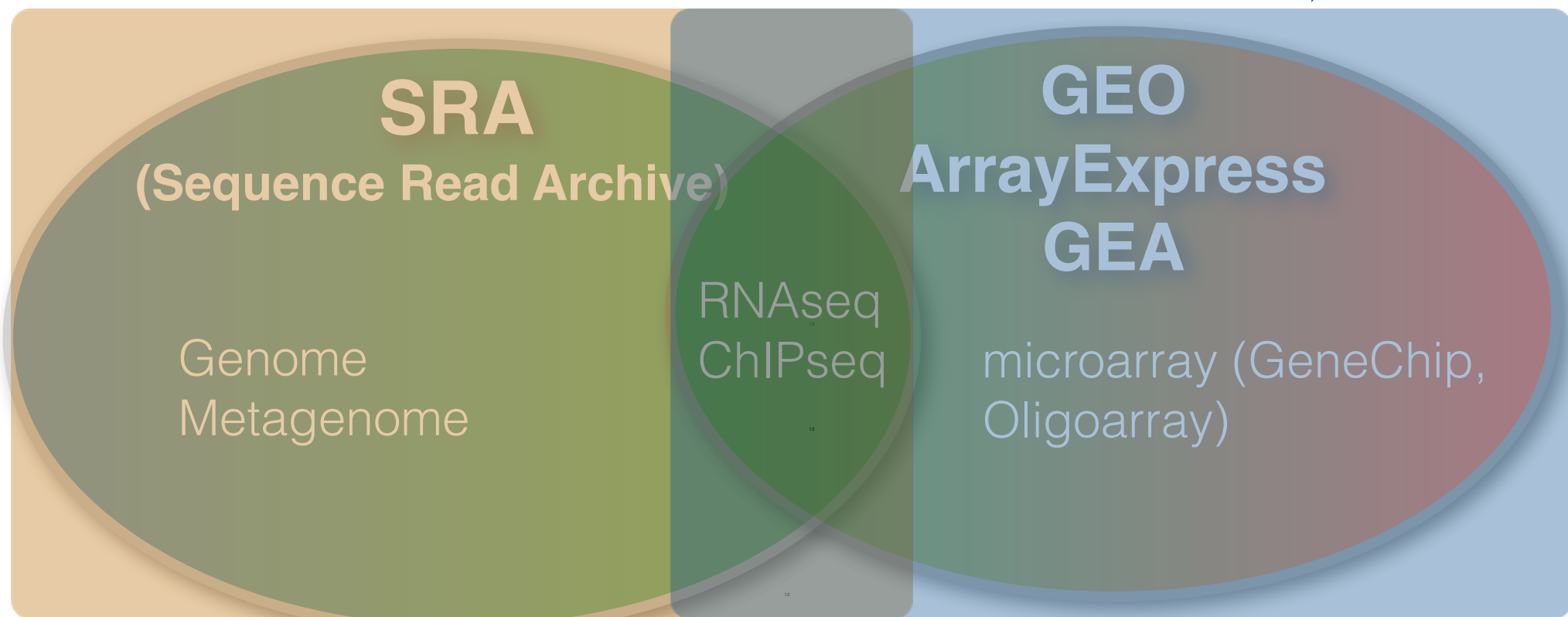
<https://togotv.dbcls.jp/>



そして、公共データベース(**DB**)が充実！

2 遺伝子発現DBのメタ解析

公共塩基配列DBと公共遺伝子発現DB



DBCLS SRA
(DDBJ search)



AOE



DDBJ search (DBCLS SRA)



DDBJ Search > sra

✓ SRA

BioProject

BioSample

Keyword : hypoxia

Accession :

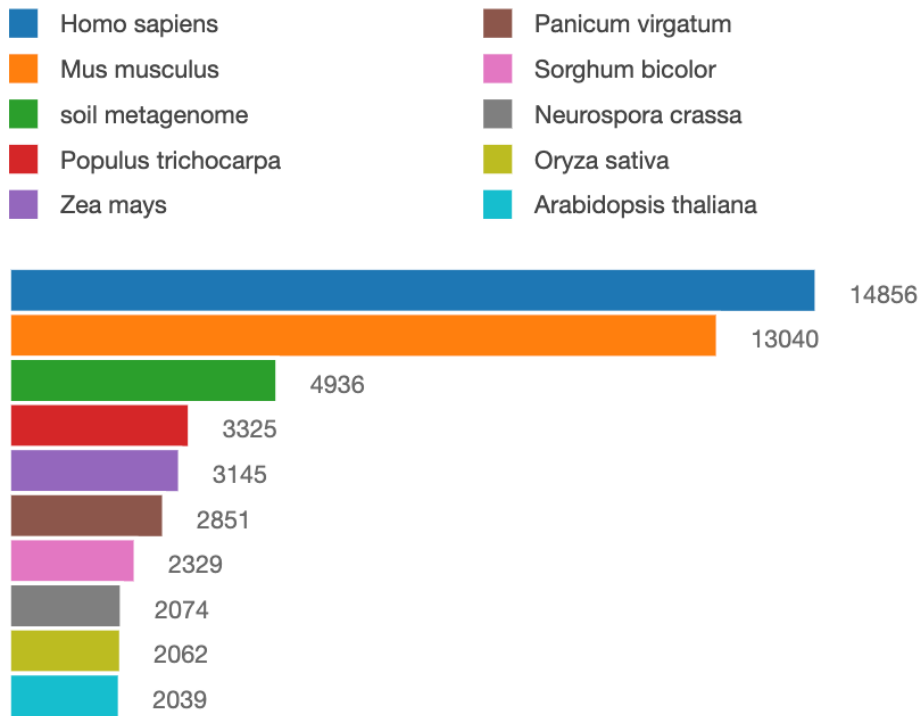
Advanced search

Show 20 records Sort by ACCESSION Search Clear

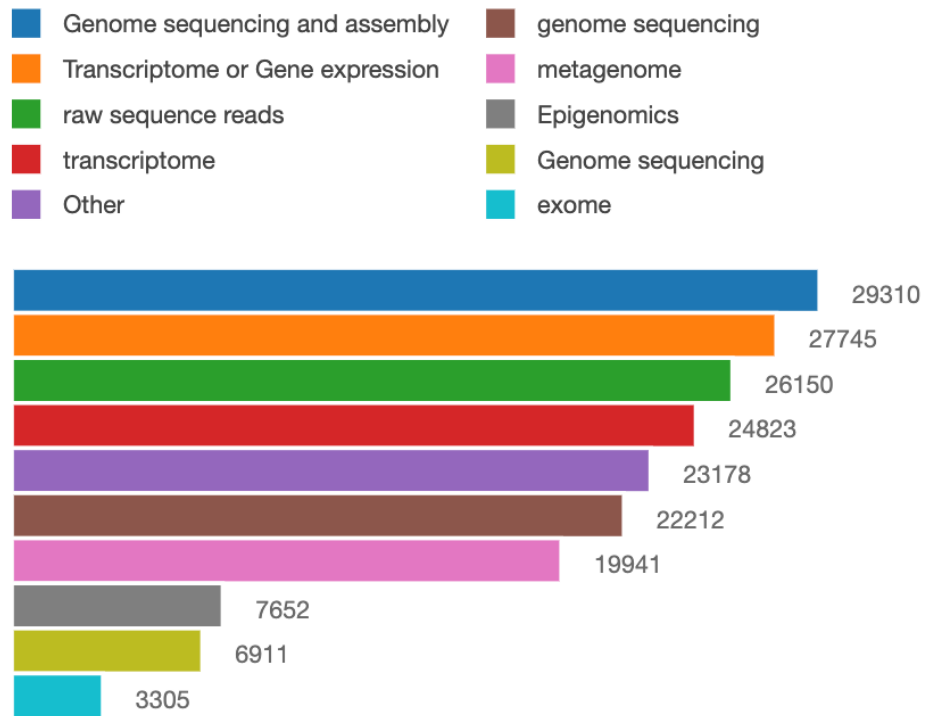
http://sra.dbcls.jp/

Data Last Update 2019-07-19

Organism Name



BioProject Datatype



DDBJ search (DBCLS SRA)



Show records Sort by

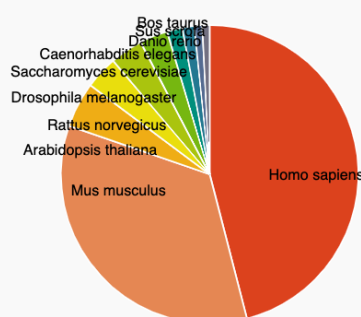
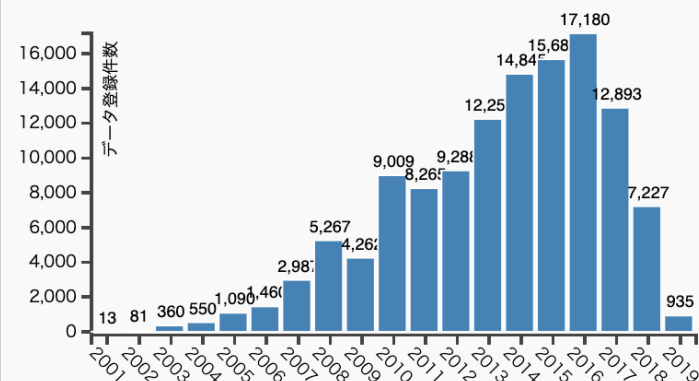
Search Results for term: hypoxia - 458 sra entries

ACCESSION	TITLE	ABSTRACT	STUDY_TYPE
SRP137723	The placental transcriptome in late gestational hypoxia resulting in murine intrauterine gro...	Intrauterine growth restriction (IU...	Transcriptome Analysis
SRP066244	Activation of the pluripotency factor OCT4 in smooth muscle cells is atheroprotective. doi: ...	The multiple claims about reactiv...	Transcriptome Analysis
SRP029190	Genome-wide maps of H3K27ac, PPARB/d and Pol II localization in HUVECs	H3K27Ac is one of the expressed...	Other
SRP045156	TET1 regulates hypoxia-induced epithelial-mesenchymal transition through DNA demethyl...	In order to explore the status of ...	Transcriptome Analysis
SRP061261	H3K4me3 and H3K27me3 ChIP-seq profiling in MCF7 cell lines under hypoxia and reoxyg...	Purpose: Study hypoxia and reox...	Other
SRP139248	RNA-seq transcriptional profiling in primary human hepatocyte(in vitro/in vivo) and Proliferti...	The source of human hepatocyte...	Transcriptome Analysis
SRP007414	Transcriptome analysis of the cowpea bruchid: Oxygen deprivation alters gene expression ...	Oxygen is of fundamental import...	Transcriptome Analysis
SRP028757	Transcriptional changes in cultured mus musculus hippocampal neurons following accute ...	The goal of this study is to deter...	Other
SRP192710	Methylome and transcriptome analysis of foetal hypoxia effect on developmental program...	Antenatal hypoxia has critial imp...	Transcriptome Analysis
SRP102913	Hypoxia is a Key Driver of Alternative Splicing in Human Breast Cancer Cells	Adaptation to hypoxia, a hallmar...	Transcriptome Analysis
SRP062493	Danio rerio Raw sequence reads	Zebrafish Hypoxia RNAseq	Metagenomics
SRP061650	Tumor hypoxia causes DNA hypermethylation by reducing TET activity (DIP-Seq)	Hypermethylation of tumor suppr...	Other
DRP004733	Transcriptomic analysis reveals abundant differential gene expression and alternative splici...	Using RNA-seq, we surveyed the...	Other
SRP043151	Mus musculus Transcriptome or Gene expression	Two main features common to all...	Other
DRP004442	RNA-seq analysis of RPTEC under hypoxic condition with Dznep.	Hypoxia plays important roles in ...	Other
SRP148528	Litopenaeus vannamei metagenome Metagenome	it was hepatopancreas of Litopen...	Whole Genome Sequencing
SRP162406	Histone methylation landscape in response to short hypoxic exposure	H3K4me3 and H3K36me3 ChIP s...	Other
SRP061648	Tumor hypoxia causes DNA hypermethylation by reducing TET activity (Bisulfite-Seq)	Hypermethylation of tumor suppr...	Other
SRP093657	Exosome-mediated transfer of cardio-protective miRNAs between cardiomyocytes prevent...	Recent evidence suggests that h...	Transcriptome Analysis
SRP136880	Human osteoblast- (hFOB 1.19 (ATCC CRL-1137) Transcriptome	objectives--Oxygen is a main par...	Other

AOE: index of ArrayExpress + GEO + GEA

生物種別登録データランキング

選択した項目でリストを表示



1	Homo sapiens	42,168	
2	Mus musculus	31,457	
3	Arabis thaliana	4,513	
4	Rattus norvegicus	3,276	
5	Drosophila melanogaster	3,260	
6	Saccharomyces cerevisiae	2,812	
7	Caenorhabditis elegans	1,536	
8	Danio rerio	1,187	
9	Sus scrofa	786	
10	Bos taurus	725	

show more

Togo picture gallery by DBCLS is licensed under a [Creative Commons Attribution 2.1 Japan license \(cc\)](#)

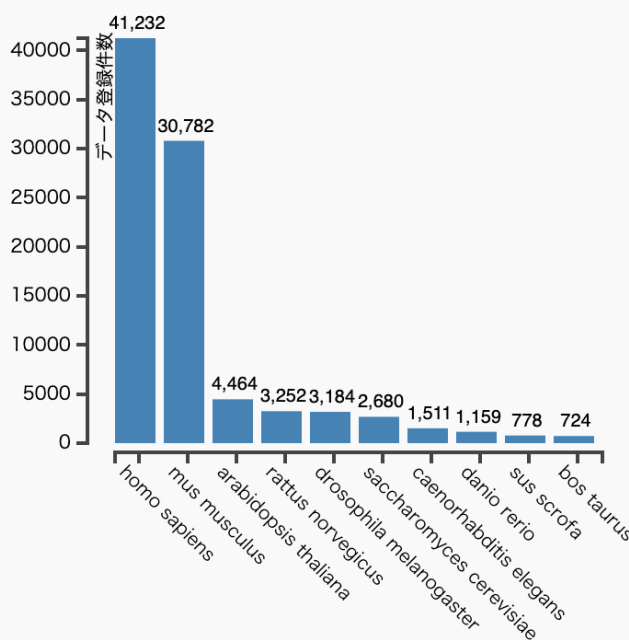
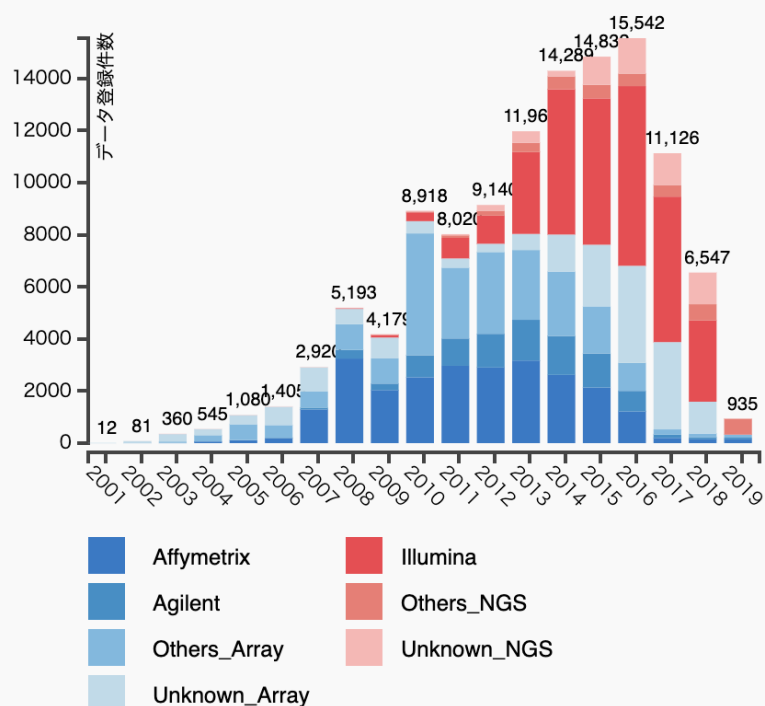


AOE

手法別登録データランキング

手法別登録データランキング

選択した項目でリストを表示



1	Illumina	32,252
2	Affymetrix	24,974
3	Others_Array	22,994
4	Unknown_Array	17,811
5	Agilent	9,292
6	Unknown_NGS	5,915
7	Others_NGS	3,855

the 10th ANNUAL
BioHackathon

BioHackathon

2018



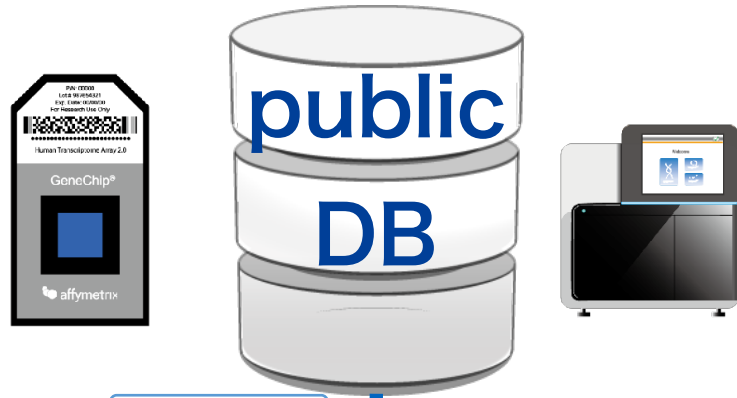
もっと使ってもらうには
どうしたらいいか？



低酸素(hypoxia)



AOE利用実例: 低酸素刺激による トランスクリプトーム変動のメタ解析



Manual
data
curation

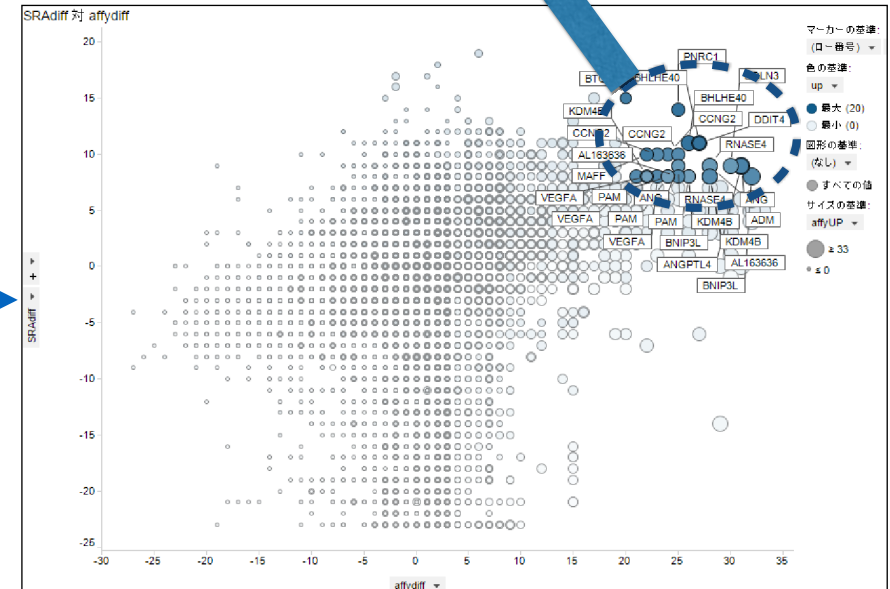
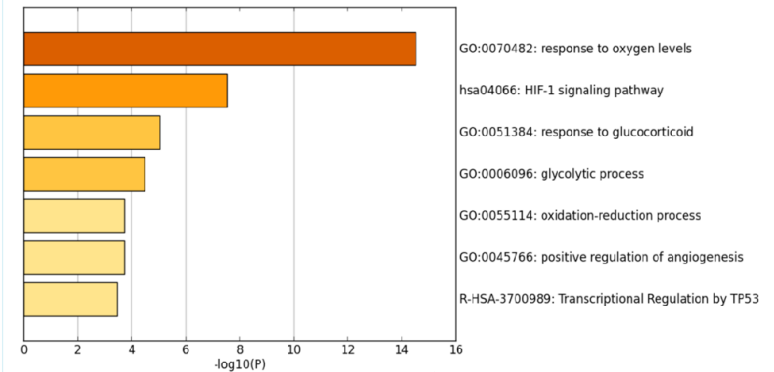
Expression
quantification

up/down/
unchanged
Classification

Data visualization
& evaluation

Enrichment Summary

Figure 1. Heatmap of enriched terms across input gene lists, colored by p-values.



Data collection & curation (RNA-seq)

- Manually collecting RNA-seq data using public DB
- 23** pairs in 7 series from human



Hypoxia vs normoxia dataset in human (NGS) ★

bono@dbcls.riks.ac.jp

ファイル 編集 表示 挿入 表示形式 データ ツール アドオン ヘルプ 変更内容をすべてドライブに保存しました

コメント

共有

100% 123 Arial 10 B I U A

fx

	B	C	D	E	F	G	H	I	J	K	L	M	N
1	human	hypoxia(GSM)	normoxia(GSM)	SRP	hypoxia(SRX)	hypoxia(SRR)	normoxia(SRX)	normoxia(SRR)	single_or_paired	NGS	sample	hypoxia condition	
2	GSE70330	GSM1724090	GSM1724087	SRP059925	SRX1074658	SRR2079880	SRX1074655	SRR2079883	paired	Hiseq2000	HUVEC	0.1-0.2% O2	
3		GSM1724091	GSM1724088		SRX1074659	SRR2079881	SRX1074656	SRR2079884	paired	Hiseq2000	HUVEC	0.1-0.2% O2	
4		GSM1724092	GSM1724089		SRX1074660	SRR2079882	SRX1074657	SRR2079885	paired	Hiseq2000	HUVEC	0.1-0.2% O2	
5	GSE59987	GSM1463076	GSM1463078	SRP045156	SRX667431	SRR1533836	SRX667433	SRR1533838	single	Hiseq2000	FADU	1% O2	
6	GSE55391	GSM1335296	GSM1335295	SRP038987	SRX476317	SRR1177128	SRX476316	SRR1177127	single	Hiseq2500	SK-N-BE(2)	1% O2	
7	GSE44801	GSM1091924	GSM1091922	SRP019229	SRX248415	SRR771372	SRX248413	SRR771370	NA	AB SOLiD 4 Syst	HeLa	1% O2	
8	E-MTAB-4264	MCF7_Hypoxia	MCF7_Normoxia_R2		ERX1622160	ERR1551404	ERX1622164	ERR1551408	paired	Hiseq2000	MCF7	0.5% O2	16h
9		MCF7_Hypoxia	MCF7_Normoxia_R2		ERX1622161	ERR1551405	ERX1622165	ERR1551409	paired	Hiseq2000	MCF7	0.5% O2	16h
10	GSE76743	GSM2037124	GSM2037122	SRP068307	SRX1527121	SRR3096874	SRX1527119	SRR3096872	paired	Hiseq2000	HUVEC	1% O2	24h
11		GSM2037125	GSM2037123		SRX1527122	SRR3096875	SRX1527120	SRR3096873	paired	Hiseq2000	HUVEC	1% O2	24h
12		GSM2037126	GSM2037128		SRX1527123	SRR3096876	SRX1527125	SRR3096878	paired	Hiseq2000	HUVEC	1% O2	48h
13		GSM2037127	GSM2037129		SRX1527124	SRR3096877	SRX1527126	SRR3096879	paired	Hiseq2000	HUVEC	1% O2	48h
14	GSE81513	GSM2155007	GSM2155004	SRP075272	SRX1769924	SRR3535659,SR	SRX1769921	SRR3535647,SR	paired	Hiseq2500	HCT116	1% O2	1h
15		GSM2155008	GSM2155005		SRX1769925	SRR3535663,SR	SRX1769922	SRR3535651,SR	paired	Hiseq2500	HCT116	1% O2	1h
16		GSM2155009	GSM2155006		SRX1769926	SRR3535667,SR	SRX1769923	SRR3535655,SR	paired	Hiseq2500	HCT116	1% O2	1h
17		GSM2155010	GSM2155004		SRX1769927	SRR3535671,SRR3535672,SRR3535673,SRR3535			paired	Hiseq2500	HCT116	1% O2	2h
18		GSM2155011	GSM2155005		SRX1769928	SRR3535675,SRR3535676,SRR3535677,SRR3535			paired	Hiseq2500	HCT116	1% O2	2h
19		GSM2155012	GSM2155006		SRX1769930	SRR3535679,SRR3535680,SRR3535681,SRR3535			paired	Hiseq2500	HCT116	1% O2	2h
20		GSM2155013	GSM2155004		SRX1769931	SRR3535683,SRR3535684,SRR3535685,SRR3535			paired	Hiseq2500	HCT116	1% O2	24h
21		GSM2155014	GSM2155005		SRX1769932	SRR3535687,SRR3535688,SRR3535689,SRR3535			paired	Hiseq2500	HCT116	1% O2	24h
22		GSM2155015	GSM2155006		SRX1769932	SRR3535691,SRR3535692,SRR3535693,SRR3535			paired	Hiseq2500	HCT116	1% O2	24h
23	E-MTAB-2580	MC1	MC3	ERP005876	ERX472413	ERR507061	ERX472421	ERR507060	single	Hiseq2000	HEK293	1% O2	24h
24		MC5	MC7		ERX472422	ERR507062	ERX472412	ERR507057	single	Hiseq2000	HEK293	1% O2	24h
25		MC9	MC11		ERX472416	ERR507058	ERX472415	ERR507063	single	Hiseq2000	HEK293	1% O2	24h
26	GSE68297	GSM1667181	GSM1667173							Ion Torrent Proto	HCT116	1% O2	24h
27		GSM1667182	GSM1667174							Ion Torrent Proto	HCT116	1% O2	24h

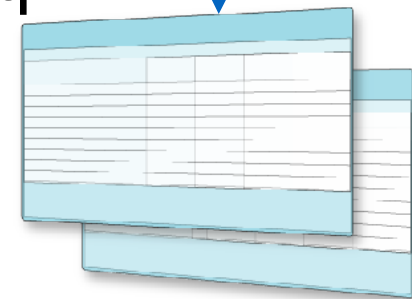
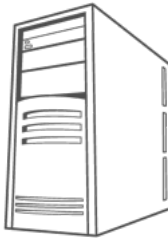
1. Data processing (RNA-seq)

1. Data download from DDBJ FTP site
2. fastq-dump (.sra -> .fastq)
3. trim_galore (trimming -> fastqc)
4. RSEM (RNA-Seq by Expectation Maximization)
 - https://github.com/bli25ucb/RSEM_tutorial
5. Differential Expression Analysis using EBSeq
 - Hypoxia vs Normoxia



Reference
genome

Genome
annotation



2. Data processing (GeneChip)

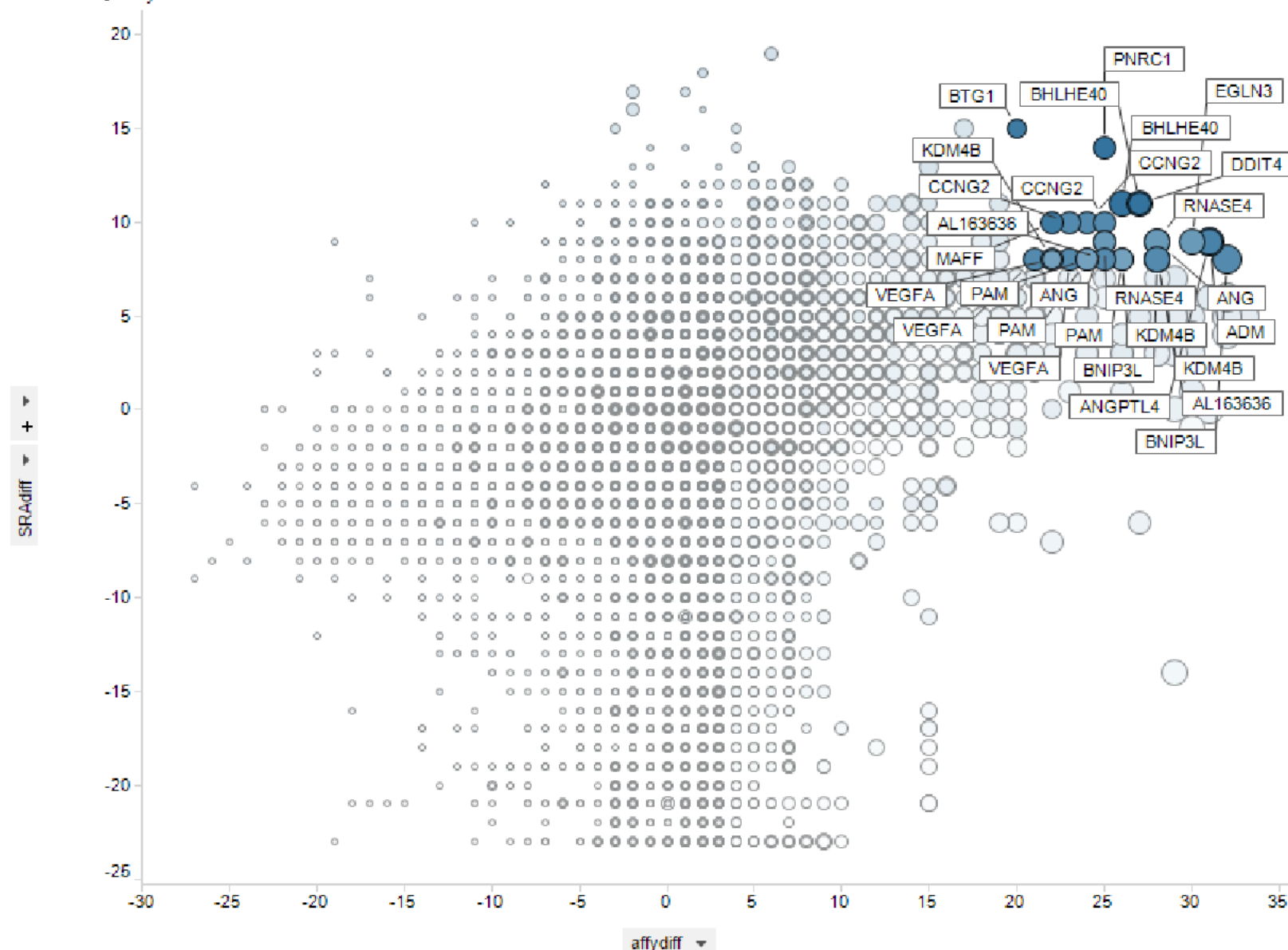
- Normalization: justRMA() (in R/Bioconductor affy)
- Threshold: >1.5 fold for up/down regulated
- Ortholog gene mapping by Biomart (Ensembl)

Pairs	
Human	37
Mouse	53

human_id	human_UP	human_DOWN	human...	human ...	mous...	Affy mouse4...	mouse_UP	mouse_DOWN	mouse_UNC...	CIS_hypoxia
202912_at	32	1	4	ADM	Adm	1416077_at	35	2	16	64
209183_s_at	23	2	12	C10orf10	84304...	1433837_at	37	0	16	58
209182_s_at	19	0	18	C10orf10	84304...	1433837_at	37	0	16	56
202364_at	32	0	5	MXI1	Mxi1	1425732_a_at	21	0	32	53
227337_at	33	1	3	ANKRD37	Ankrd37	1436538_at	24	5	24	51
202364_at	32	0	5	MXI1	Mxi1	1450376_at	16	0	37	48
211527_x_at	24	1	12	VEGFA	Vegfa	1451959_a_at	29	4	20	48
212171_x_at	23	1	13	VEGFA	Vegfa	1451959_a_at	29	4	20	47
201631_s_at	15	4	18	IER3	Ier3	1419647_a_at	37	2	14	46
210513_s_at	23	2	12	VEGFA	Vegfa	1451959_a_at	29	4	20	46
202464_s_at	32	1	4	PFKFB3	Pfkfb3	1456676_a_at	14	0	39	45
222847_s_at	31	0	6	EGLN3	Egln3	1418649_at	18	4	31	45
210512_s_at	22	3	12	VEGFA	Vegfa	1451959_a_at	29	4	20	44
219232_s_at	30	0	7	EGLN3	Egln3	1418649_at	18	4	31	44
201313_at	33	0	4	ENO2	Eno2	1418829_a_at	11	1	41	43
221009_s_at	31	0	6	ANGPTL4	Angptl4	1417130_s_at	15	3	35	43
221031_s_at	11	4	22	APOLD1	Apold1	1441228_at	38	2	13	43
222847_s_at	31	0	6	EGLN3	Egln3	1418648_at	14	2	37	43
218274_s_at	30	1	6	ANKZF1	Ankzf1	1419817_s_at	13	0	40	42
219232_s_at	30	0	7	EGLN3	Egln3	1418648_at	14	2	37	42
200632_s_at	31	0	6	NDRG1	Ndr1	1450977_s_at	15	5	33	41
202284_s_at	10	1	26	CDKN1A	Cdkn1a	1424638_at	34	2	17	41
202620_s_at	29	0	8	PLD2	Plod2	1416686_at	13	1	39	41
202733_at	30	0	7	AC063976.6	P4ha2	1417149_at	15	4	34	41
202733_at	30	0	7	P4HA2	P4ha2	1417149_at	15	4	34	41
204284_at	23	1	13	PPP1R3C	Ppp1r3c	1433691_at	21	2	30	41

3. Data visualization & validation (GeneChip vs RNA-seq in human)

SRAdiff 対 affydiff



マーカーの基準:

(ロー番号)

色の基準:

up

最大 (20)

最小 (0)

図形の基準:

(なし)

すべての値

サイズの基準:

affyUP

≥ 33

≤ 0

Spotfire®
TIBCO Software

PerkinElmer®
For the Better

4. Data availability

<https://doi.org/10.1101/267310>



bioRxiv
THE PREPRINT SERVER FOR BIOLOGY

[HOME](#) | [ABOUT](#) | [SUBMIT](#) | [ALERTS / RSS](#) | [CHANNELS](#)



[Advanced Search](#)

New Results

Meta-analysis of hypoxic transcriptomes from public databases

Hidemasa Bono

doi: <https://doi.org/10.1101/267310>

This article is a preprint and has not been peer-reviewed [what does this mean?].

Abstract

[Info/History](#)

[Metrics](#)

[Preview PDF](#)

Abstract

Hypoxia is an insufficient level of oxygen supply in the cell, and hypoxia-inducible factor is a central regulator of oxygen homeostasis. In order to elucidate functional insights in hypoxic response in data-driven way, we attempted meta-analysis of hypoxic transcriptome for public expression data which have been archived as microarray and RNA-seq data in public databases, NCBI Gene Expression Omnibus (GEO) and EBI ArrayExpress. While various hypoxic conditions (oxygen concentration and duration of hypoxia) and cell lines are taken in the stored data, we manually curated possible pairs of transcriptome before and after hypoxic stress from microarray and RNA-seq data. As a result, we got 37 pairs in human and 53 pairs in mouse from microarray and 23 pairs in human from RNA-seq. We counted the number of experiments for all genes and classified into three categories, which are up-regulated, down-regulated, and unchanged. We then compared human and mouse in microarray, and microarray and RNA-seq in human. Genes up-regulated in all records contained well-studied

Previous

Next

Posted February 23, 2018.

Download PDF

Share

Email

Citation Tools

Tweet

いいね! 0

Subject Area

Bioinformatics

Subject Areas

All Articles

[Animal Behavior and Cognition](#)

[Biochemistry](#)

[Bioengineering](#)

[Bioinformatics](#)

[Biophysics](#)

[Cancer Biology](#)

[Cell Biology](#)

Data uploaded to figshare

[Browse](#)[Upload](#)[Sign up](#)[Log in](#)

Meta-analysis of hypoxic transcriptomes from public databases

Version 2 ▾ Published on 23 Jan 2018 - 15:21 by **Hidemasa Bono**

Manually annotated possible pairs of transcriptomes before and after hypoxic stress from public expression data. The data process details are described in BioRxiv (<https://doi.org/10.1101/267310>).

CITE THIS COLLECTION

DataCite ▾

Bono, Hidemasa (2018): Meta-analysis of hypoxic transcriptomes from public databases. figshare.

<https://doi.org/10.6084/m9.figshare.c.3983880>

Select your citation style and then place your mouse over the citation text to select it.

or [cite all items](#)

REFERENCES

- <https://doi.org/10.1101/267310>

262
views

1
citations



AUTHORS

Hidemasa Bono

CATEGORIES

- Gene Expression (incl. Microarray and other genome-wide approaches)**

KEYWORD(S)

human

mouse

genechip

RNA-seq

Hypoxia

meta-analysis

<https://doi.org/10.6084/m9.figshare.c.3983880>

5. Data utility

• GeneChip(human)

• さらにCancer / non-cancerに分けて

S6 Table. Hypoxic down-regulation of DNA damage recognition and repair genes in cancer and non-cancer cells analyzed using the NCBI Gene Expression Omnibus database.

<https://doi.org/10.1371/journal.pone.0192136.s006>

No	ID	UP	In cancer cells			In Non-cancer cells			Gene Symbol	Description
			DOWN	UN	UP	DOWN	UN			
1	223758_s_at		0	23	6	1	6	3	GTF2H2	general transcription factor IIH, polypeptide 2, 44kDa [Source:HGNC Symbol;Acc:4656]
2	223758_s_at		0	23	6	1	6	3	GTF2H2C	general transcription factor IIH, polypeptide 2C [Source:HGNC Symbol;Acc:31394]
3	227766_at		0	21	8	0	6	4	LIG4	ligase IV, DNA, ATP-dependent [Source:HGNC Symbol;Acc:6601]
4	209903_s_at		0	20	9	0	5	5	ATR	ataxia telangiectasia and Rad3 related [Source:HGNC Symbol;Acc:882]
5	209902_at		0	19	10	1	5	4	ATR	ataxia telangiectasia and Rad3 related [Source:HGNC Symbol;Acc:882]
6	223511_at		0	19	10	1	5	4	SPRTN	SprT-like N-terminal domain [Source:HGNC Symbol;Acc:25356]
7	204531_s_at		1	19	9	0	4	6	BRCA1	breast cancer 1, early onset [Source:HGNC Symbol;Acc:1100]
8	222889_at		0	19	10	0	3	7	DCLRE1B	DNA cross-link repair 1B [Source:HGNC Symbol;Acc:17641]
9	204768_s_at		2	19	8	1	2	7	FEN1	flap structure-specific endonuclease 1 [Source:HGNC Symbol;Acc:3650]
10	201202_at		1	19	9	0	2	8	PCNA	proliferating cell nuclear antigen [Source:HGNC Symbol;Acc:8729]
11	209804_at		0	19	10	0	1	9	DCLRE1A	DNA cross-link repair 1A [Source:HGNC Symbol;Acc:17660]
12	230177_at		0	18	11	0	7	3	GTF2H2C	general transcription factor IIH, polypeptide 2C [Source:HGNC Symbol;Acc:31394]
13	206235_at		3	18	8	1	5	4	LIG4	ligase IV, DNA, ATP-dependent [Source:HGNC Symbol;Acc:6601]
14	209421_at		0	18	11	1	5	4	MSH2	mutS homolog 2, colon cancer, nonpolyposis type 1 (E. coli) [Source:HGNC Symbol;Acc:7325]
15	209849_s_at		0	18	11	0	4	6	RAD51C	RAD51 homolog C (S. cerevisiae) [Source:HGNC Symbol;Acc:9820]
16	204767_s_at		1	18	10	1	1	8	FEN1	flap structure-specific endonuclease 1 [Source:HGNC Symbol;Acc:3650]
17	201523_x_at		0	18	11	0	1	9	UBE2N	ubiquitin-conjugating enzyme E2N [Source:HGNC Symbol;Acc:12492]
18	222233_s_at		0	17	12	0	6	4	DCLRE1C	DNA cross-link repair 1C [Source:HGNC Symbol;Acc:17642]
19	213007_at		1	17	11	0	4	6	FANCI	Fanconi anemia, complementation group I [Source:HGNC Symbol;Acc:25568]
20	206066_s_at		0	17	12	1	4	5	RAD51C	RAD51 homolog C (S. cerevisiae) [Source:HGNC Symbol;Acc:9820]
21	202330_s_at		4	17	8	1	2	7	UNG	uracil-DNA glycosylase [Source:HGNC Symbol;Acc:12572]
22	205394_at		3	17	9	0	1	9	CHEK1	checkpoint kinase 1 [Source:HGNC Symbol;Acc:1925]
23	205162_at		0	17	12	0	0	10	ERCC8	excision repair cross-complementing rodent repair deficiency, complementation group 8 [Source:HGNC Symbol;Acc:25568]
24	235215_at		1	16	12	0	5	5	ERCC4	excision repair cross-complementing rodent repair deficiency, complementation group 4 [Source:HGNC Symbol;Acc:25568]
25	202907_s_at		0	16	13	1	5	4	NBN	nibrin [Source:HGNC Symbol;Acc:7652]
26	212751_at		0	16	13	0	5	5	UBE2N	ubiquitin-conjugating enzyme E2N [Source:HGNC Symbol;Acc:12492]
27	208694_at		1	16	12	0	3	7	PRKDC	protein kinase, DNA-activated, catalytic polypeptide [Source:HGNC Symbol;Acc:9413]
28	204603_at		2	16	11	0	2	8	EXO1	exonuclease 1 [Source:HGNC Symbol;Acc:3511]
29	235609_at		4	16	9	0	1	9	BRIP1	BRCA1 interacting protein C-terminal helicase 1 [Source:HGNC Symbol;Acc:20473]
30	218689_at		0	16	13	0	1	9	FANCF	Fanconi anemia, complementation group F [Source:HGNC Symbol;Acc:3587]
31	223785_at		2	16	11	1	1	8	FANCI	Fanconi anemia, complementation group I [Source:HGNC Symbol;Acc:25568]
32	206554_x_at		0	16	13	0	1	9	SETMAR	SET domain and mariner transposase fusion gene [Source:HGNC Symbol;Acc:10762]
33	205393_s_at		4	16	9	1	0	9	CHEK1	checkpoint kinase 1 [Source:HGNC Symbol;Acc:1925]
34	221540_x_at		0	15	14	0	6	3	GTF2H2	general transcription factor IIH, polypeptide 2, 44kDa [Source:HGNC Symbol;Acc:4656]
35	221540_x_at		0	15	14	0	6	4	GTF2H2C	general transcription factor IIH, polypeptide 2C [Source:HGNC Symbol;Acc:31394]
36	208643_s_at		0	15	14	1	5	4	XRCC5	X-ray repair complementing defective repair in Chinese hamster cells 5 (double-strand-break rejoin

RESEARCH ARTICLE

Differentiated embryo chondrocyte plays a crucial role in DNA damage response via transcriptional regulation under hypoxic conditions

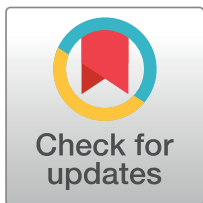
Hideaki Nakamura^{1,2,3,4}, Hidemasa Bono⁵, Keiko Hiyama², Takeshi Kawamoto⁶, Yukio Kato⁶, Takeshi Nakanishi⁷, Masahiko Nishiyama⁸, Eiso Hiyama², Nobuyuki Hirohashi¹, Eisaburo Sueoka³, Lorenz Poellinger⁴, Keiji Tanimoto^{1*}

1 Department of Radiation Medicine, Research Institute for Radiation Biology and Medicine, Hiroshima University, Hiroshima, Japan, **2** Natural Science Center for Basic Research and Development, Hiroshima University, Hiroshima, Japan, **3** Department of Laboratory Medicine, Saga University Hospital, Saga, Japan, **4** Cell and Molecular Biology, Medical Nobel Institute, Karolinska Institutet, Stockholm, Sweden, **5** Database Center for Life Science, Joint Support-Center for Data Science Research, Research Organization of Information and Systems, Mishima, Japan, **6** Department of Dental and Medical Biochemistry, Hiroshima University, Hiroshima, Japan, **7** Nippon Kayaku Co., Ltd., Tokyo, Japan, **8** Department of Molecular Pharmacology and Oncology, Gunma University Graduate School of Medicine, Gunma, Japan

* ktanimo@hiroshima-u.ac.jp

Abstract

Tumor hypoxia contributes to a biologically aggressive phenotype and therapeutic resistance. Recent studies have revealed that hypoxia reduces expression of several DNA damage recognition and repair (DRR) genes *via* both hypoxia-inducible factor (HIF)-independent and -dependent pathways, and this induced genomic instability in cancer cells. We



OPEN ACCESS

Citation: Nakamura H, Bono H, Hiyama K, Kawamoto T, Kato Y, Nakanishi T, et al. (2018) Differentiated embryo chondrocyte plays a crucial role in DNA damage response via transcriptional regulation under hypoxic conditions. PLoS ONE 13 (2): e0192136. <https://doi.org/10.1371/journal.pone.0192136>



高校生・受験生の方

広大へ留学希望の方

一般・地域の方

企業・研究者の方

卒業生の方

在学生・保護者の方

大学案内

入試情報

教育・学生生活
・就職

研究

社会・産学連携

留学・国際交流

学部・大学院等

研究所・施設等

[Home](#) > 【研究成果】放射線の感受性を細胞内でコントロールする分子を発見 - 放射線治療効果を高め、障害から守る方法の開発へ -

広報・報道

採用情報

校友会・同窓会

広島大学基金

公益財団法人広島大学教育
研究支援財団

図書館・博物館等

東京オフィス

大学病院

附属学校

ストリートビュー

キャンパスカメラ

学内ポータル

【研究成果】放射線の感受性を細胞内でコントロールする分子を発見 - 放射線治療効果を高め、障害から守る方法の開発へ -

本研究成果のポイント

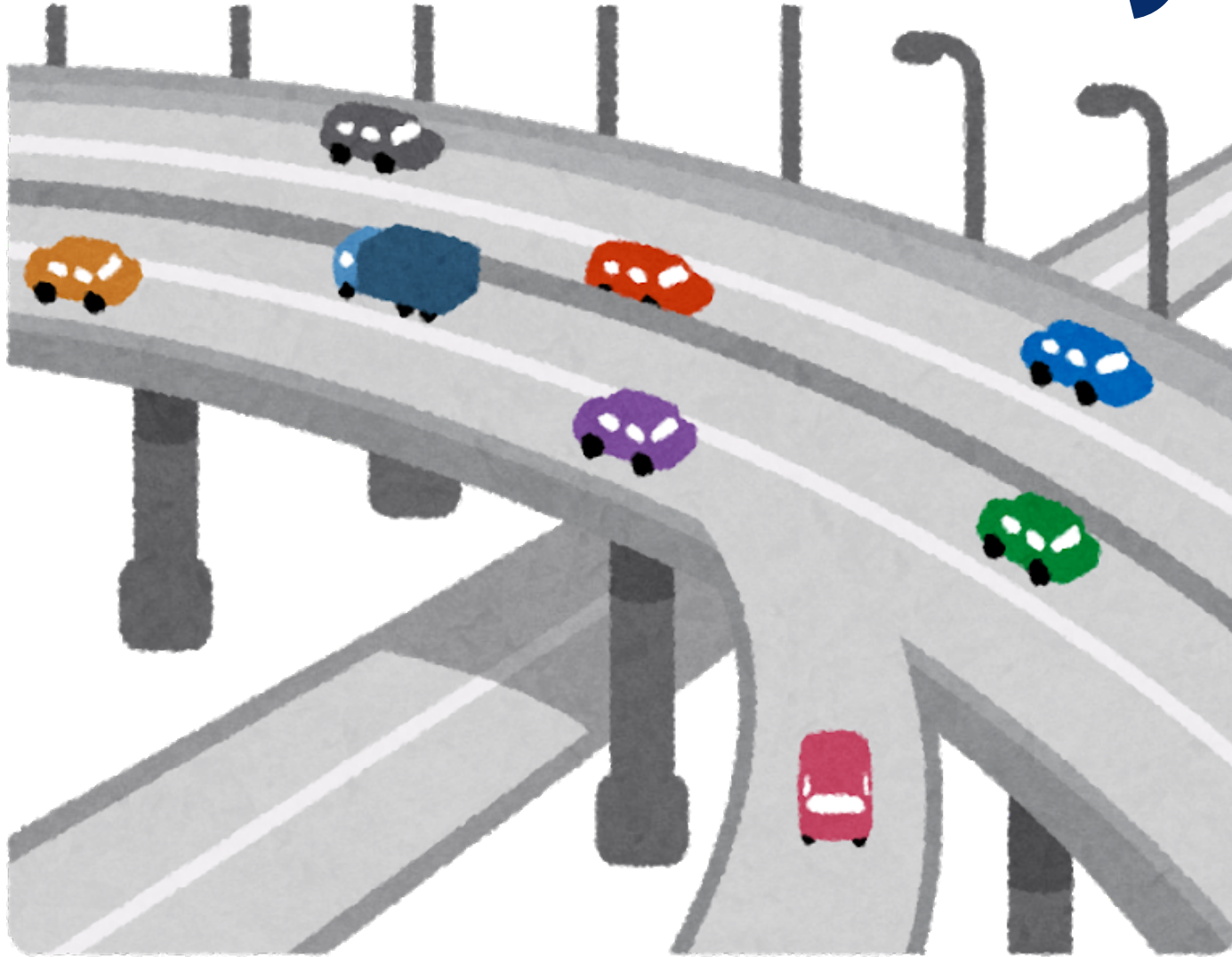
- 低酸素などのストレス環境下にある細胞の中ではDNAの傷を見つけて治したり、治せない時はその細胞を排除したりする働きに関わる一連の遺伝子群の発現量が減ることを発見しました。
- DECという様々なストレスにより活性化するタンパク分子が、それら一連の遺伝子群の量の調節を行なっていることを明らかにしました。
- DECの働きを調節すると、DNAに傷をつける放射線などの効果を調節することが可能なことから、放射線治療や放射線防護法への応用が期待されます。

概要

広島大学原爆放射線医科学研究所の谷本圭司研究所内講師、廣橋伸之教授、大学共同利用機関法人 情報・システム研究機構 データサイエンス共同利用基盤施設 ライフサイエンス統合データベースセンターの坊農秀雅特任准教授らの研究グループは、ヒト細胞を用いた網羅的な遺伝子解析（※1）から、低酸素環境下（※2）にある細胞では、DNAの傷を見つけて治したり、治せない時はその細胞を排除したりする働きに関わる一連の遺伝子群（DNA損傷応答関連遺伝子群）の遺伝子発現量（※3）が抑制されていることを発見しました。

また、公共遺伝子発現データベースの集合知解析（※4）により、その反応が、多くの種類の細胞で共通する一般的な反応であることを見出しました。さらに、DNA損傷応答関連遺伝子群の発現量抑制について、DEC（※5）というストレス応答、概日リズム（※6）、細胞分化などに関わる転写調節因子（※7）が重要な役割を果たしていることを証明しました。そして、DECの量を人工的に調節すると、DNAに傷をつける放射線やある種の抗がん剤に対する細胞応答が変化することを確認しました。

Sustainability



維持していくことが重要



bonohu

@bonohu



半月かかった某計算結果が出てきた。ここからが勝負

9:26 - 2019年6月14日

8件のいいね



8



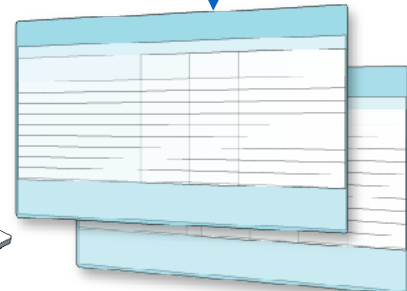
Renewed data processing 2019

1. Data download from DDBJ or NCBI FTP site
 - Convert files by **fastq-dump** (.sra -> .fastq)
 - Compress files by **pigz**
2. Run **ikra** in <https://github.com/yyoshiaki/ikra/>
 - Trimming by **Trim Galore!**
 - Transcript quantification by **Salmon**
3. Count Differentially Expressed Genes (DEGs)
 - Hypoxia vs Normoxia by tiny script at <http://github.com/bonohu/chypoxia/>
 - **HN-score** = [Up_regulated] - [Down_regulated]
4. Visualization by TIBCO Spotfire
 - Ortholog relationship by Ensembl Biomart



Reference transcriptome

Gene annotation



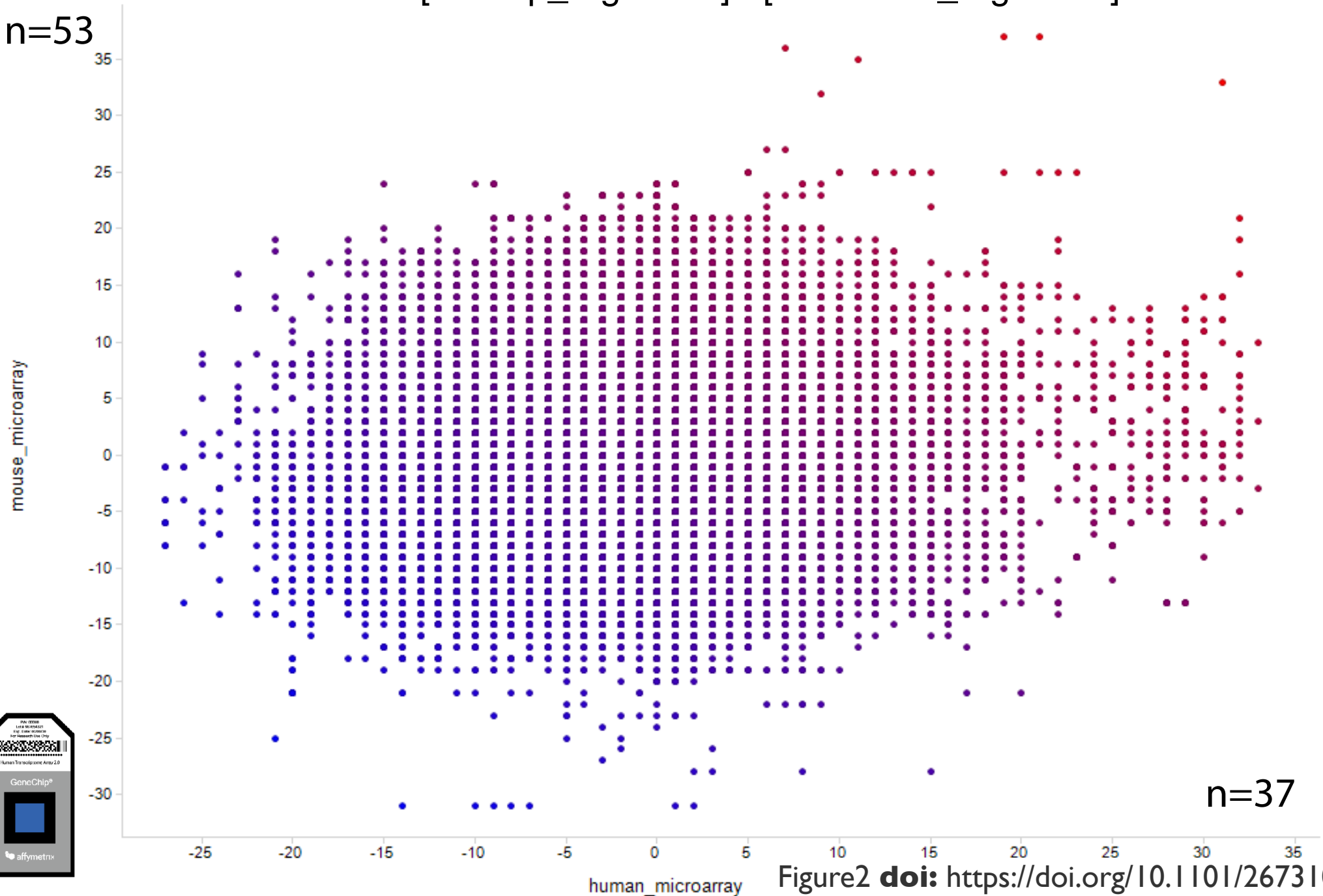
- Manually collect hypoxic transcriptomes by RNA-seq using public DB (SRA)
 - +105 pairs in human => **128** pairs
 - **52** pairs in mouse

More is better!?

HN-scores 2018: human vs mouse

HN-score = [# of Up_regulated] - [# of Down_regulated]

n=53

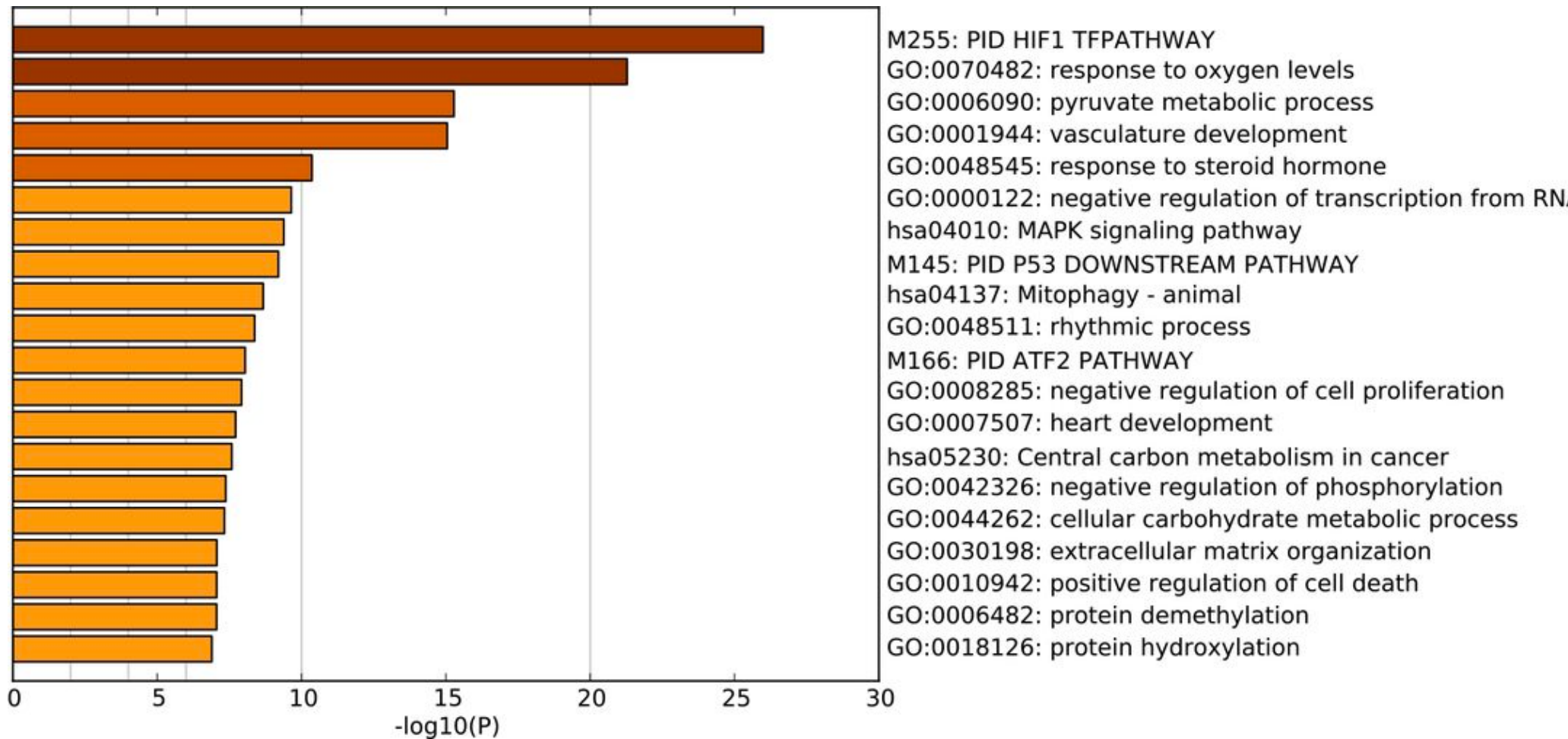


n=37

Figure2 doi: <https://doi.org/10.1101/267310>

MetascapeでEnrichment Analysis 2018

<http://metascape.org/>



Metascape analysis of top genes up-regulated after hypoxic stress. For the extraction of a gene list for metascape input, the score called totaldiff was calculated for all genes. The totaldiff score was calculated by [count of human microarray UP]-[count of human microarray DOWN] + [count of human RNA-seq UP] - [count of human RNA-seq DOWN]. A list of gene was generated by extracting genes whose totaldiff score was over 15, where roughly 1% of all genes could be listed.

まとめ

- 誰でも利用可能なオープンデータ (公共DB) は量、種類とも増えてきている = メタ解析可能
- それをどのように医学研究にいかにかに活かしていくか、が今後の鍵 : More is better!!



やってみいひん
とわからんで！