Introduction to Bioinformatics

Introduction to NGS/Genomics Technologies (GSEA)

2021.

A preview of the past few weeks

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There are profiles of …

- RNA Transcripts (mRNA, miRNA, lncRNA, ...)
- Proteins (total expression, phosphorylation, ubiquitination …)
- Metabolites (intra cellular, secreted, …)
- Epigenetics (DNA methylation, histone methylation, histone acetylation)
- Transcription factor binding (ChIP)
- DNA copy number variation
- Microbiomes (16S rRNA, Metagenomes, …)

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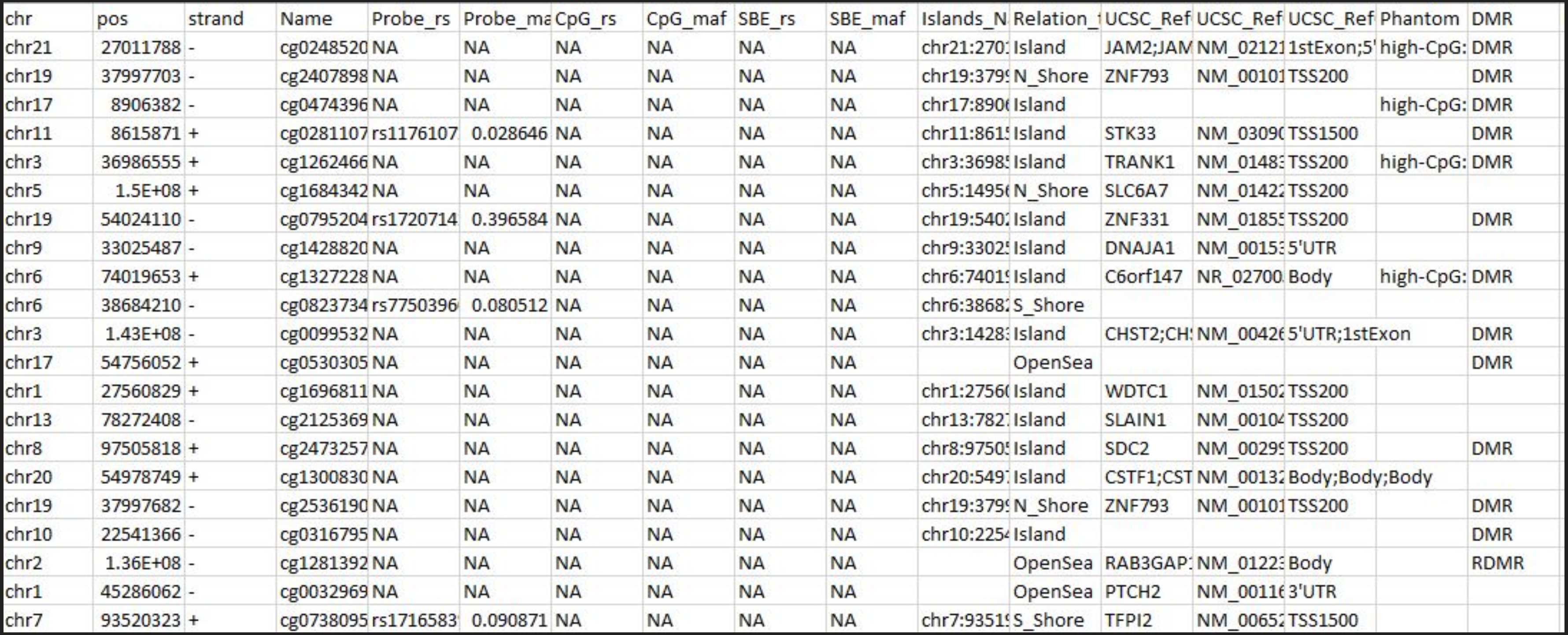
Profiles are lists of quantified molecular features

Profiles can be generated by different technologies

- RNA Transcripts (microarray, nanoString, RNAseq)
- Proteins (MassSpec, protein array)
- Metabolites (NMR, MassSpec,...)
- Epigenetics (ChIP-seq, bisulfate sequencing, ATAC-seq)
- Transcription factor binding (ChIP)
- DNA copy number variation (aCGH, NGS)
- Immune cell infiltration (FACS, imaging, proteomics)
- Microbiomes (arrays, 16S rRNA-seq)

We got this Excel now what?



chr	pos	strand	Name	Probe_rs	Probe_ma	CpG_rs	CpG_maf	SBE_rs	SBE_maf	Islands_N	Relation_	UCSC_Ref	UCSC_Ref	UCSC_Ref	Phantom	DMR
chr21	27011788	-	cg0248520	NA	NA	NA	NA	NA	NA	chr21:270	Island	JAM2;JAM	NM_02121	1stExon;5'	high-CpG:	DMR
chr19	37997703	-	cg2407898	NA	NA	NA	NA	NA	NA	chr19:379	N_Shore	ZNF793	NM_00101	TSS200		DMR
chr17	8906382	-	cg0474396	NA	NA	NA	NA	NA	NA	chr17:890	Island				high-CpG:	DMR
chr11	8615871	+	cg0281107	rs1176107	0.028646	NA	NA	NA	NA	chr11:861	Island	STK33	NM_0309	TSS1500		DMR
chr3	36986555	+	cg1262466	NA	NA	NA	NA	NA	NA	chr3:3698	Island	TRANK1	NM_0148	TSS200	high-CpG:	DMR
chr5	1.5E+08	+	cg1684342	NA	NA	NA	NA	NA	NA	chr5:1495	N_Shore	SLC6A7	NM_0142	TSS200		
chr19	54024110	-	cg0795204	rs1720714	0.396584	NA	NA	NA	NA	chr19:540	Island	ZNF331	NM_0185	TSS200		DMR
chr9	33025487	-	cg1428820	NA	NA	NA	NA	NA	NA	chr9:3302	Island	DNAJA1	NM_0015	5'UTR		
chr6	74019653	+	cg1327228	NA	NA	NA	NA	NA	NA	chr6:7401	Island	C6orf147	NR_02700	Body	high-CpG:	DMR
chr6	38684210	-	cg0823734	rs7750396	0.080512	NA	NA	NA	NA	chr6:3868	S_Shore					
chr3	1.43E+08	-	cg0099532	NA	NA	NA	NA	NA	NA	chr3:1428	Island	CHST2;CH	NM_0042	5'UTR;1stExon		DMR
chr17	54756052	+	cg0530305	NA	NA	NA	NA	NA	NA		OpenSea					DMR
chr1	27560829	+	cg1696811	NA	NA	NA	NA	NA	NA	chr1:2756	Island	WDTC1	NM_0150	TSS200		
chr13	78272408	-	cg2125369	NA	NA	NA	NA	NA	NA	chr13:782	Island	SLAIN1	NM_0010	TSS200		
chr8	97505818	+	cg2473257	NA	NA	NA	NA	NA	NA	chr8:9750	Island	SDC2	NM_0029	TSS200		DMR
chr20	54978749	+	cg1300830	NA	NA	NA	NA	NA	NA	chr20:549	Island	CSTF1;CST	NM_0013	Body;Body;Body		
chr19	37997682	-	cg2536190	NA	NA	NA	NA	NA	NA	chr19:379	N_Shore	ZNF793	NM_00101	TSS200		DMR
chr10	22541366	-	cg0316795	NA	NA	NA	NA	NA	NA	chr10:225	Island					DMR
chr2	1.36E+08	-	cg1281392	NA	NA	NA	NA	NA	NA		OpenSea	RAB3GAP	NM_0122	Body		RDMR
chr1	45286062	-	cg0032969	NA	NA	NA	NA	NA	NA		OpenSea	PTCH2	NM_0011	3'UTR		
chr7	93520323	+	cg0738095	rs1716583	0.090871	NA	NA	NA	NA	chr7:9351	S_Shore	TFPI2	NM_0065	TSS1500		

Gene Set Enrichment Analysis

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Gene Set Enrichment Analysis (GSEA) for Interpreting Gene Expression Profiles. Jing Shi et al.

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- In array experiments where no single gene shows statistically significant differential expression between phenotypes, GSEA has identified significant differentially expressed sets of genes
- GSEA is likely to be more powerful than conventional single-gene methods for studying the large number of common diseases in which many genes each make subtle contributions

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Why GSEA?

- The conventional statistical analysis method for array experiments is to
  - examine one gene at a time,
  - determine a p-value that the gene is differentially expressed/methylated in different phenotypes
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