

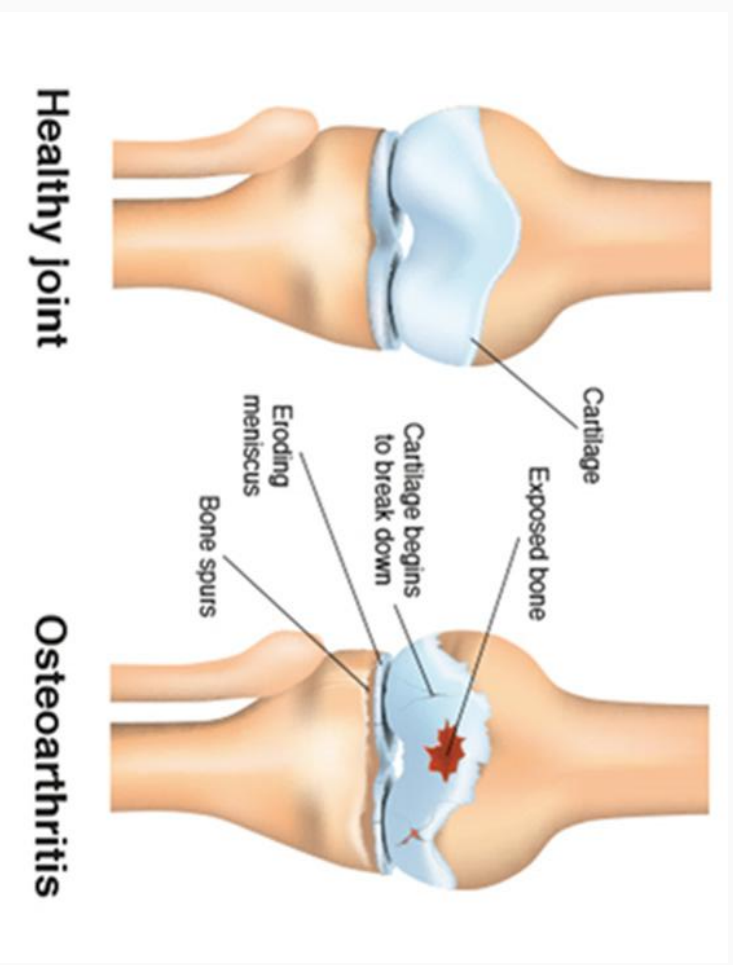
BIOINFORMATICS APPLICATIONS IN OSTEOARTHRITIS

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Introduction

Osteoarthritis:

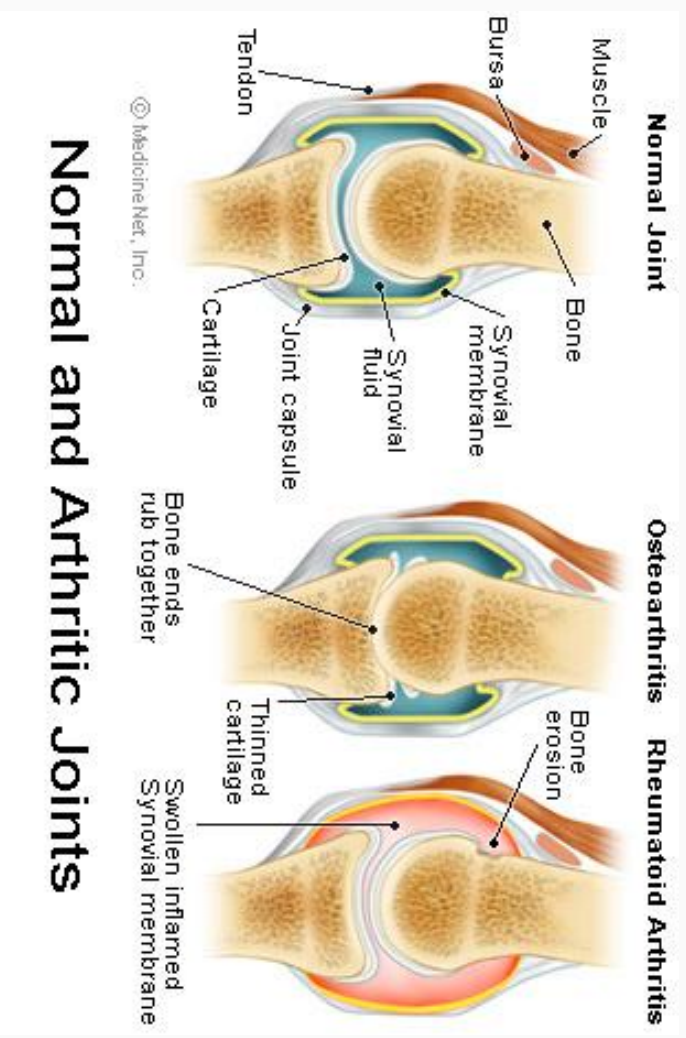
- Cartilage between joints breaks down leading to pain, stiffness, and swelling
- Most common chronic condition of the joints
- Affects 27 million Americans



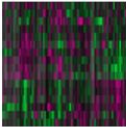
Introduction

Osteoarthritis:

- Important to distinguish from other types of arthritis
- Typically a result of a traumatic joint injury
- Progression may lead to joint replacement surgery



Data Description

DataSet Record GDS5402: Expression Profiles Data Analysis Tools Sample Subsets			
Title:	Rheumatoid arthritis and osteoarthritis: synovial tissues (Leipzig dataset)		
Summary:	Analysis of synovial tissues from patients with rheumatoid arthritis or osteoarthritis. Results used to generate rule-based classifiers to distinguish patients with rheumatoid arthritis from those with osteoarthritis.		
Organism:	<i>Homo sapiens</i>		
Platform:	GPL96: [HG-U133A] Affymetrix Human Genome U133A Array		
Citation:	Woetzel D, Huber R, Kupfer P, Pohlers D et al. Identification of rheumatoid arthritis and osteoarthritis patients by transcriptome-based rule set generation. <i>Arthritis Res Ther</i> 2014 Apr 1;16(2):R84. PMID: 24690414		
Reference Series:	GSE55584	Sample count:	16
Value type:	count	Series published:	2014/03/05
		<div>Cluster Analysis</div> <div></div>	
		<div>Download</div> <div>DataSet full SOFT file</div> <div>DataSet SOFT file</div> <div>Series family SOFT file</div> <div>Series family MINML file</div> <div>Annotation SOFT file</div>	

- 16 patients: 10 RA, 6 OA
- Synovial membrane samples
- RNA microarray analysis

Analysis Methods

Project:

- Log2 transformation
- eBayes function to identify differentially expressed genes
- Clustering (kmeans, cmeans)
- Heatmap clustering
- Gene Interaction

Paper:

- Classifier training & testing- rules assign a to rank a gene
- Rules applied to samples prior to clustering

Results & Discussion

ID	adj.P.Val	Gene Symbol	Gene.title
206134_at	0.00020571	ADAMDEC1	ADAM like decysin 1
221003_s_at	0.00020571	CAB39L	calcium binding protein 39 like
209604_s_at	0.00020665	GATA3	GATA binding protein 3
205890_s_at	0.00092858	UBD///GABB	ubiquitin D///gamma-aminobutyric acid type B receptor subunit 1
205159_at	0.00103936	CSF2RB	colony stimulating factor 2 receptor beta common subunit
204279_at	0.00119727	PSMB9	proteasome subunit beta 9
204223_at	0.00176448	PRELP	proline and arginine rich end leucine rich repeat protein
203915_at	0.00176448	CXCL9	C-X-C motif chemokine ligand 9
210031_at	0.00176448	CD247	CD247 molecule
217986_s_at	0.00176448	BAZ1A	bromodomain adjacent to zinc finger domain 1A

Results & Discussion

K-means clustering:

Clustering vector:

GSM1339618	GSM1339619	GSM1339620	GSM1339621	GSM1339622	GSM1339623	GSM1339624	GSM1339625
2	1	1	2	2	2	1	2
GSM1339626	GSM1339627	GSM1339628	GSM1339629	GSM1339630	GSM1339631	GSM1339632	GSM1339633
2	1	2	1	1	1	1	1

C-means fuzzy clustering: data point can belong to one or more cluster

Closest hard clustering:

GSM1339618	GSM1339619	GSM1339620	GSM1339621	GSM1339622	GSM1339623	GSM1339624	GSM1339625
1	2	2	1	1	1	2	1
GSM1339626	GSM1339627	GSM1339628	GSM1339629	GSM1339630	GSM1339631	GSM1339632	GSM1339633
1	1	1	2	2	2	2	2

Results & Discussion

```
> table(cluster$clust)
```

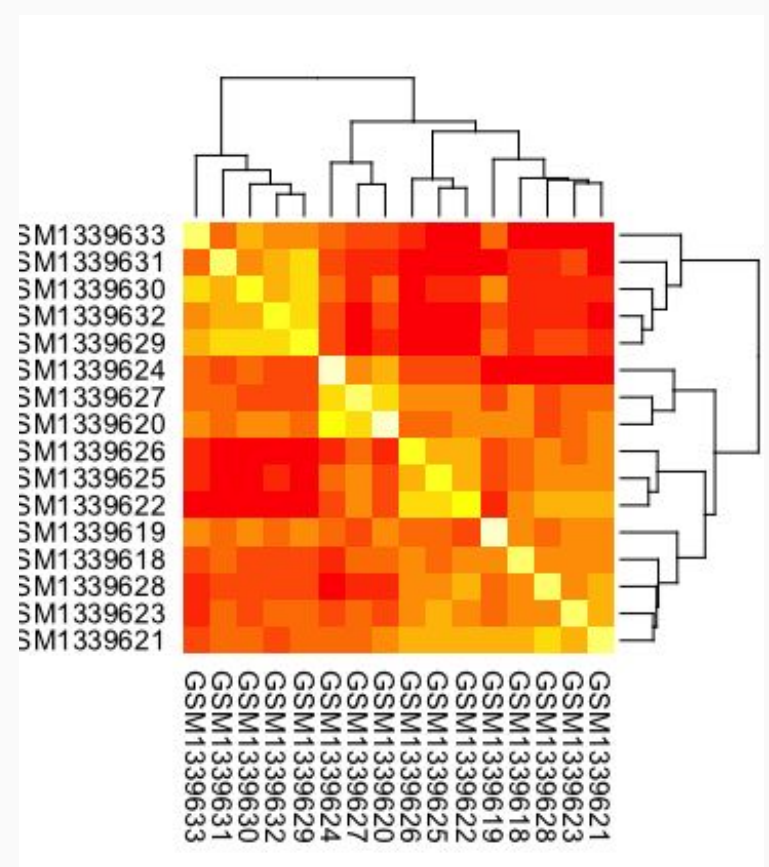
```
1 2
9 7
70% ACCURATE
```

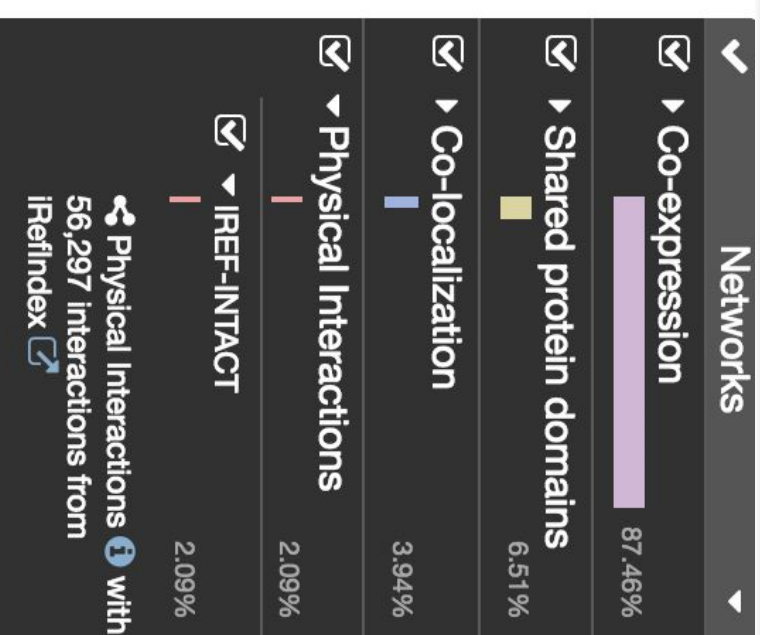
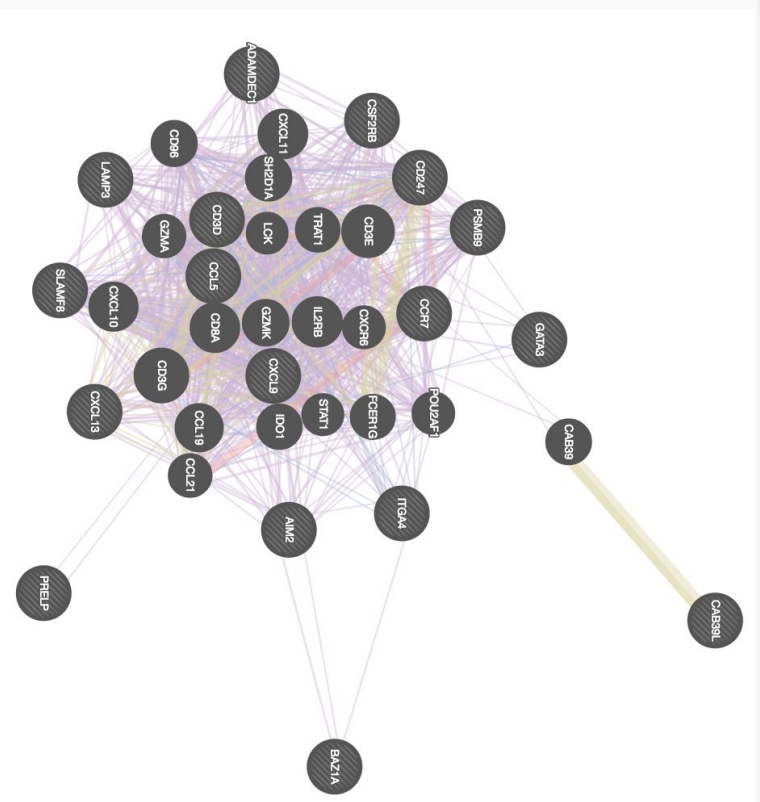
```
> table(ccluster$clust)
```

```
1 2
8 8
68% ACCURATE
```

```
>
```

Group	Accession	
RA	GSM1339618	
RA	GSM1339619	
RA	GSM1339620	
RA	GSM1339621	
RA	GSM1339622	
RA	GSM1339623	
RA	GSM1339624	
RA	GSM1339625	
RA	GSM1339626	
RA	GSM1339627	
OA	GSM1339628	
OA	GSM1339629	
OA	GSM1339630	
OA	GSM1339631	
OA	GSM1339632	
OA	GSM1339633	





Conclusion

- Identifying patients with OA purely on the basis of differential gene expression and clustering methods is not very accurate
- Outcomes indicate application of rule-based clustering is a more appropriate method (91 % accuracy)
- More accurate rule-based clustering methods may allow for identification of pathogenetically or therapeutically relevant genetic targets

Bibliography

- <http://www.arthritis.org/about-arthritis/types/osteoarthritis/>
- https://www.niams.nih.gov/health_info/osteoarthritis/osteoarthritis_ff.asp
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4060460/#B46>
- <http://www.webmd.com/osteoarthritis/osteoarthritis-causes>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2694558/>
- <http://genemania.org/>