Biomarker Identification of Oral Squamous Cell Carcinoma through Transcriptomic Expression Analysis

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Oral Squamous Cell Carcinoma (OSCC)

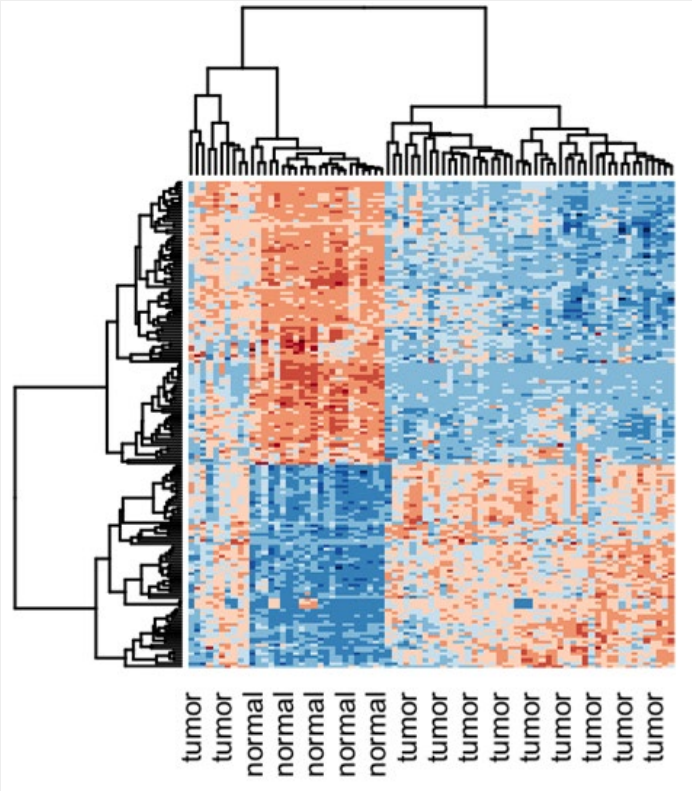
- Accounts for over 90% of all oral malignancies
- Poses a significant risk due to tendency to progress past the initial stages without the production of pain or easily recognizable symptoms
- Usually discovered only after it has metastasized to the lymph nodes of the neck
- Early detection raises survival rate to 80%

Biomarkers

- Biomarkers are measurable indicators that could be useful for early diagnosis of OSCC
  - Ex. differentially expressed genes

Microarray Assays

- Detects the expression of thousands of genes at the same time.
- Can show differentially expressed genes between healthy and cancerous cells



red is "hot" or high expression

Research Goals:

Identify Potential Diagnostic Biomarkers of OSCC

Analyze the Determined Biomarkers' Roles (Functional Analysis)

Data Collection and Cleaning

- **Microarray Data was collected from NCBI GEO**
  - expression data from a genome-wide analysis of transcription of 79 samples between patients with OSCC and patients without

Data Collection and Cleaning

Data was normalized in Rusing quantile normalization

	ID	GSM616583	GSM616584	GSM616585	GSM616586	GSM616587	GSM616588
1	2315554	5.22558	5.88321	6.43585	6.49950	5.35155	6.69381
2	2315633	5.93447	6.56393	6.79998	7.01917	6.16583	6.66688
3	2315674	5.78948	6.29855	6.66782	6.83117	5.72356	6.64923
4	2315739	6.69112	6.44189	7.15693	7.14195	6.48628	7.32783
5	2315894	8.53834	9.17154	9.57810	9.87447	8.09890	9.65277
6	2315918	4.83979	4.72540	5.91972	5.51478	4.06058	5.80428
7	2315951	7.76094	7.71483	8.15706	8.52111	6.95680	7.93065
8	2316218	5.14405	6.00817	7.10223	6.36627	5.08488	6.32311
9	2316245	7.53523	7.65137	7.84077	8.01794	7.60192	7.74430
10	2316379	7.84576	8.08522	8.07019	8.44277	7.45154	8.32158
11	2316558	9.33612	9.01487	8.97805	8.92788	9.29024	9.04247
12	2316605	6.45565	6.57696	7.11231	7.31975	6.20564	7.10786
13	2316746	6.94854	7.15727	7.52113	7.89495	7.09920	7.71053
14	2316905	4.83053	5.62484	6.17838	6.40761	4.91707	6.26290

Determine differentially expressed genes

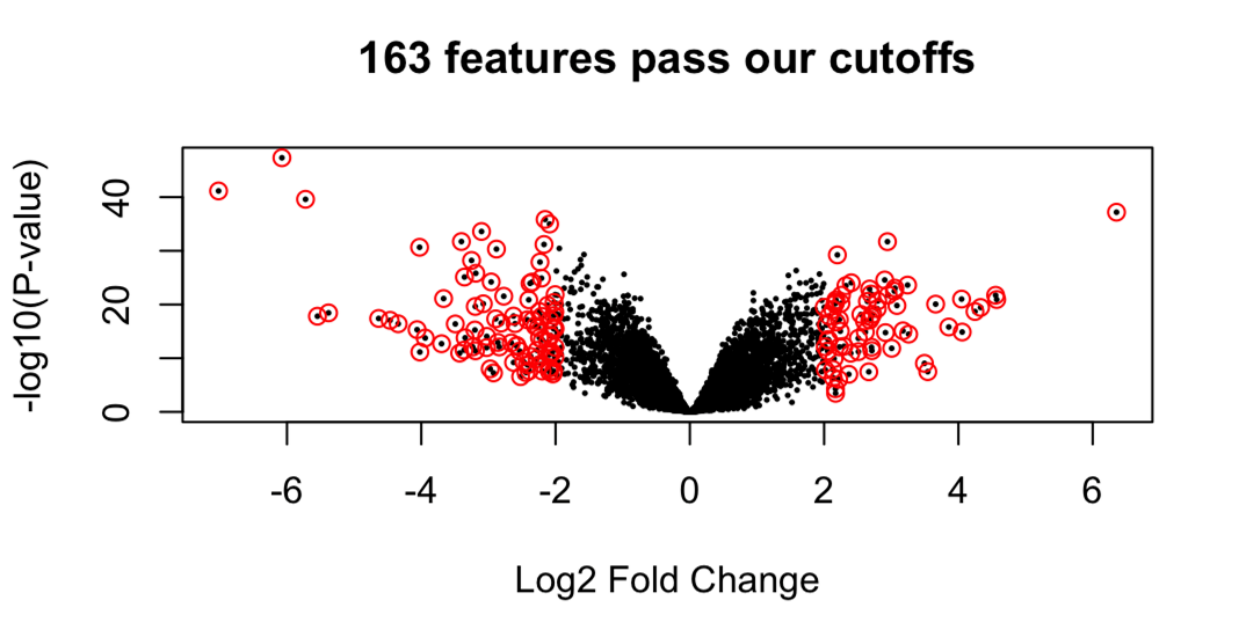
Using limma, a moderated t-test identified significant differences in biomarker expression.

Table I. Sorted table of genes with a positive log fold change value.

probe_id	logFC	AveExpr	P.Value	adj.P.Val	gene_assignment
3388807	6.354774933	8.770374108	6.46E-38	3.55E-34	MMP1
3388830	4.570398794	7.598941287	1.18E-21	2.88E-19	MMP3
3388785	4.554129576	7.322304996	1.90E-22	5.51E-20	MMP10
2773958	4.330296051	8.418709443	3.58E-20	5.84E-18	CXCL10
2731332	4.246756595	7.98302588	2.03E-19	2.65E-17	IL8
2773972	4.056157737	7.159238817	1.33E-15	8.00E-14	CXCL11
3388859	4.047199119	8.023728497	9.76E-22	2.44E-19	MMP12
2773947	3.856334397	7.287738484	1.55E-16	1.10E-14	CXCL9
2422035	3.660777005	7.573664765	8.49E-21	1.61E-18	GBP5
4028512	3.543598475	7.386712848	3.22E-08	3.58E-07	RPS4Y1
3388893	3.494236919	7.640560368	9.21E-10	1.50E-08	MMP13

Distinguish genes that are significantly differentially expressed

163 genes were identified as significant and 68 genes upregulated in OSCC tissue—indicated by a positive log2-fold change—were determined.



Results

The 11 most upregulated genes were determined to be MMP1, MMP3, MMP10, CXCL10, IL8, CXCL11, MMP12, CXCL9, GBP5, RPS4Y1, and MMP13. The majority of these genes (IL8, CXCLs, MMPs) were immune system genes, and a large portion were MMPs.

Matrix Metalloproteinases

- MMPs (matrix metalloproteinases) are a gene family
- Code for MMP endopeptidases
  - tissue remodeling and degradation of the extracellular matrix (ECM) in normal physiological processes
  - immune system function, regulating inflammatory processes
- A lot of previous research also corroborates the role of MMPs

Matrix Metalloproteinases

- Surface of metastatic cancer cells → cell migration
- Unregulated cell growth and proliferation in many tumors
- Blocking receptor-transmitted or lymphocyte-mediated apoptosis
- Deregulating signaling pathways responsible for controlling cell growth, inflammation, and angiogenesis
    - Unregulated tumor growth, inflammation, and metastasis

Matrix Metalloproteinases

- Complex role of MMPs hinders the use of widespread matrix metalloproteinase inhibitors as an effective tool against cancer
  - MMPs can generate both angiogenesis-inhibiting and angiogenesis-promoting signals
  - In mice, can generate ECM fragments like tumstatin, which suppress tumor vasculature formation
  - In one study, mice that were MMP9 deficient had increased tumor growth compared to those with normal MMP9 levels

Limitations and Future Research

- Limited Sample Size
- Only Data from Transcriptional Level
- Only looked for diagnostic biomarkers
- Salivary MMPs

Conclusions

KEY FINDINGS

- Comparative analysis of genome-wide transcriptomic expression data of OSCC and normal tissues
- 163 significant genes and 68 upregulated genes were identified as potential diagnostic biomarkers for OSCC
- In particular, MMPs were identified as especially promising diagnostic biomarkers and therapeutic targets for OSCC
    - MMPs, along with other immune genes, may play important roles in the metastatic, angiogenic, and immunosuppressive abilities of OSCC

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