Blood Diagnosis of HNSCC

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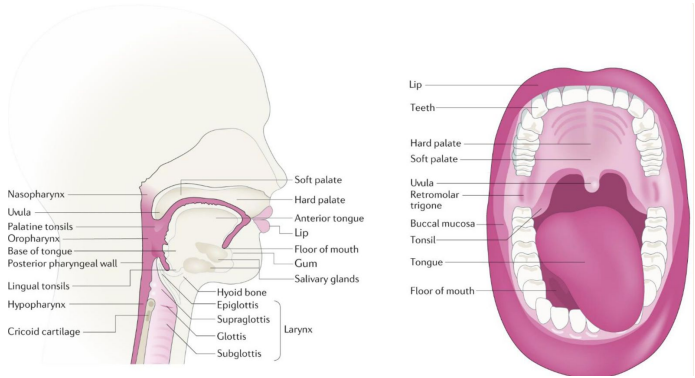
Background: HNSCC

- Head and Neck Squamous Cell Carcinoma
- Cancer of the mucosal epithelium in the oral cavity, larynx and pharynx
- Strongly correlated to various etiological factors
- 6th most common cancer worldwide
- Later stage diagnosis
    - Lower survival rate compared to other major cancers



Background: HNSCC Diagnosis

- Tissue biopsy
- Lymph node biopsy
- Ultrasound
- Immunochemistry
- Computed tomography (CT), Magnetic resonance imaging (MRI), Positron emission tomography (PET)

Project Goal

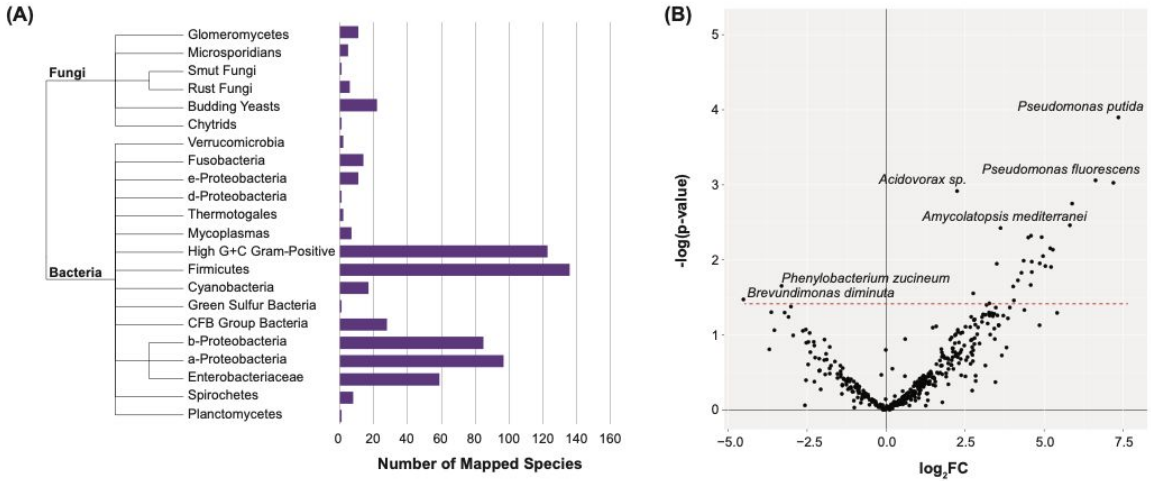
The goal of this project is to be able to use a blood sample from a patient to diagnose if they have HNSCC. This test should be less invasive and more cost effective. It should utilize the microbiome and genomics to effectively diagnose patients in early stages.

Methods

RNA-Seq for Tissue and Whole Exome Sequencing for Blood Samples

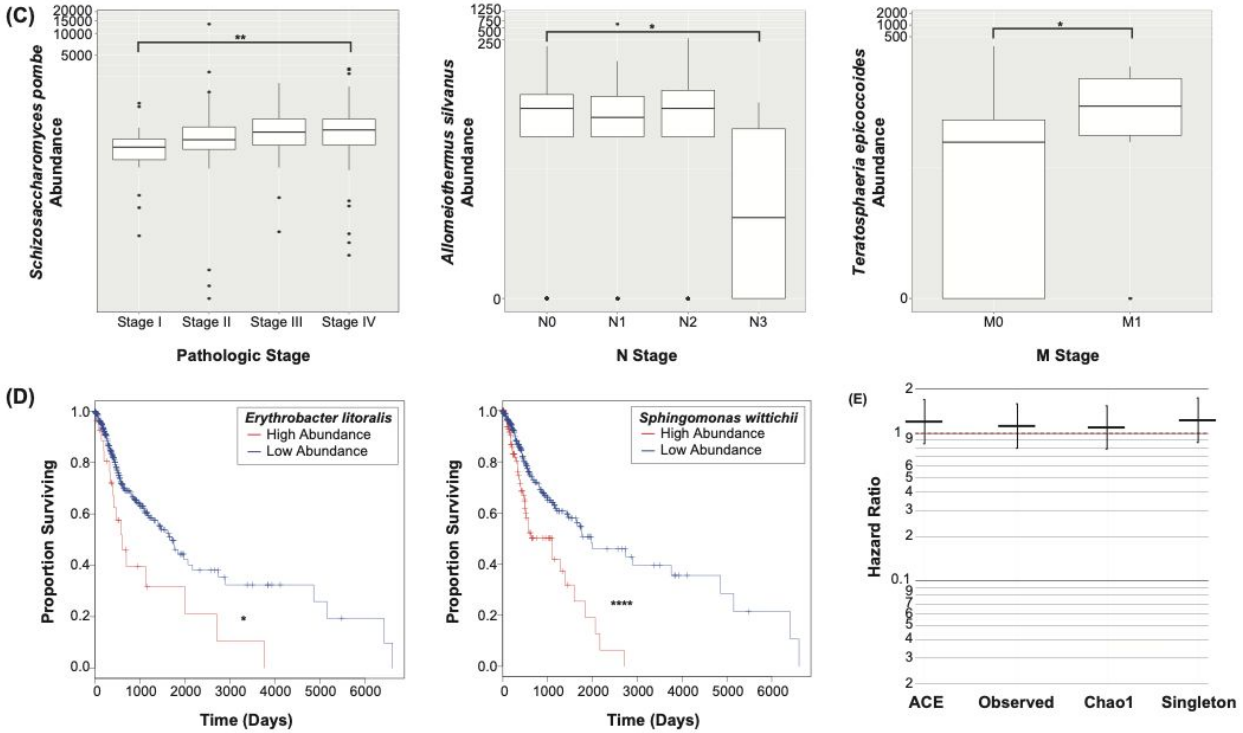
Source	TCGA Tissue	TCGA Blood	GTEX Normal	UCSD
# of Samples	443 Cancer 44 Normal	117 Cancer	117 Normal	20 HNSCC Blood Samples 10 Normal Blood Samples

Differentially Abundant/Kruskal Wallis Test



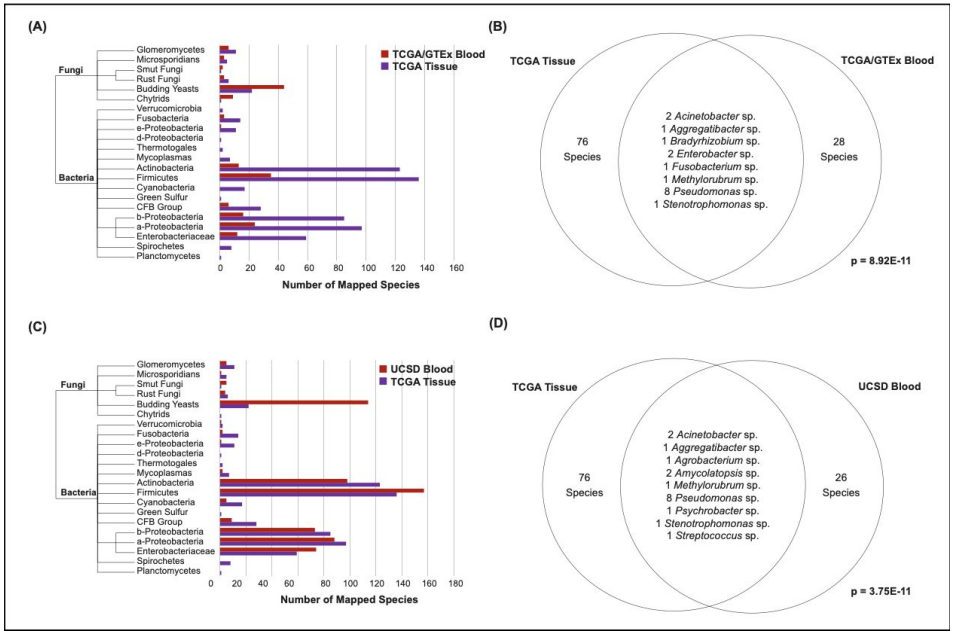
A) Phylogenic tree of all mapped bacterial and fungal species in HNSCC tissue samples, following contamination correction. **(B)** Volcano plot of species differentially abundant between cancerous and non-cancerous samples. Points represent species, and heights represent significance.

Association of Clinical Variables



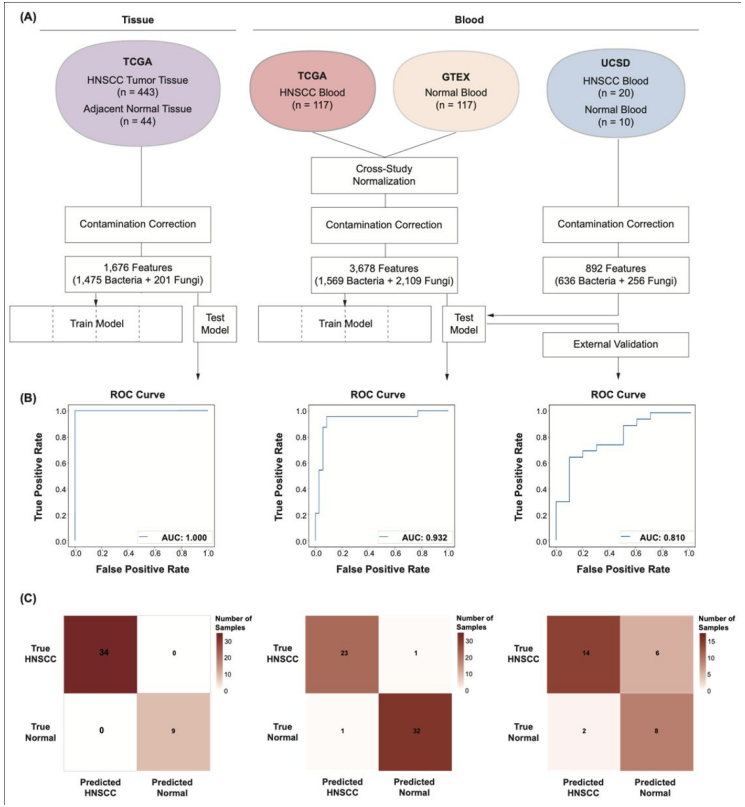
(C) Box plots of select species found to be differentially abundant between patients of different pathologic stages (left), N stages (middle), and M stages (right). **(D)** Survival plots of select species that correlate significantly to survival length. **(E)** Logarithmic plot showing the hazard ratios of patients with low diversity for each of the following metrics: ACE, observed OTUs, Chao1, and Singleton observations. Greater hazard ratios indicate greater likelihoods of death in patients with low microbial diversity.

Differences/Similarities Between Blood and Tissue Samples



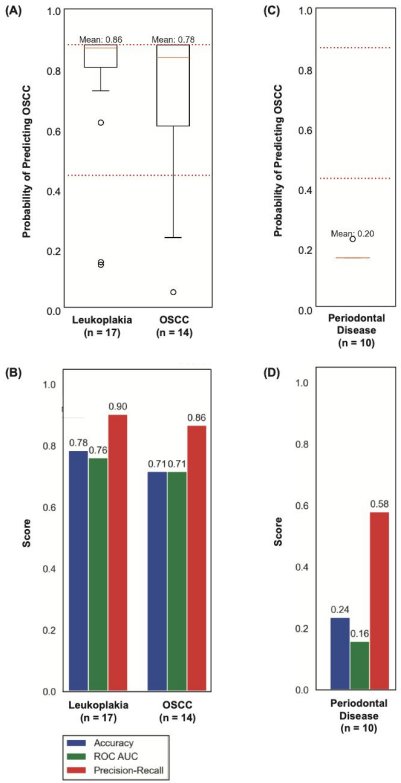
(A) Phylogenic tree showing the number of species mapped in the TCGA tissue and TCGA/GTEX blood cohorts. **(B)** Venn diagram showing the number of species differentially abundant between cancerous and non-cancerous samples.

Diagnostic Model Ability to Predict Cancerous Samples



(A) Overview schematic. A diagnostic model was created for both the TCGA tissue cohort (left) and the TCGA/GTEx blood cohort (middle). Our UCSD blood cohort was used to validate the performance of the TCGA/GTEx blood model. **(B)** ROC curves showing the internal validation performance of the TCGA tissue model (left), and both the internal (middle) and external (right) validation performances of the TCGA/GTEx blood model. The AUCs were found to be 1.000, 0.932, and 0.810 respectively. **(C)** Confusion matrices showing the internal validation performance of the TCGA tissue model (left), and both the internal (middle) and external (right) validation performances of the TCGA/GTEx blood model. The tissue model correctly classified all cases. The blood model correctly classified all but two internal cases, and all but eight external cases.

Model's Ability to Distinguish Between Cancer and Other Oral Diseases



(A) Box plot showing the scores predicted of each leukoplakia and OSCC sample by the TCGA tissue model. Predicted scores range from 0 to 1, with 1 corresponding to OSCC and 0 corresponding to normal. The tissue model was of even greater sensitivity to leukoplakia than OSCC. **(B)** Bar chart showing the accuracy, AUC, and precision-recall scores of the tissue model for the leukoplakia and OSCC samples. Accuracy is a simple metric describing the number of correctly predicted cases, while AUC and precision-recall scores consider false positive and false negative rates. **(C)** Box plot showing the scores predicted of each periodontal disease sample by the TCGA tissue model. The model was minimally sensitive to periodontal disease **(D)** Bar chart showing the accuracy, AUC, and precision-recall scores of the tissue model for the periodontal disease samples.

Conclusions

- The HNSCC blood microbiome shows many species to be differentially abundant between cancer and normal samples
- The HNSCC blood microbiome shows much overlap between the HNSCC tissue microbiome
- The microbiome shows promising potential as a diagnostic tool in blood samples
- The diagnostic test can be further expanded to include more markers to create a more comprehensive test

Acknowledgements

PI/Mentor: Dr. Weg Ongkeko

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