Lipid composition of circulating extracellular vesicles as a biomarker for head and neck cancer

Wyatt Wofford, BS[1]; Lauren Howser, MD[1]; Besim Ogretmen, PhD[1]; Alexandra Kejner, MD[1]
[1]Medical University of South Carolina

MUSC Medical University of South Carolina

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Introduction

- Oral cavity squamous cell carcinoma (**OCSCC**) is a highly **aggressive** cancer with poor outcomes, primarily due to **late-stage diagnoses** and **frequent recurrence**.
- Current diagnostic methods **lack reliable tools** for early detection and recurrence monitoring.[1]
  - In comparison, **HPV-driven** head and neck cancers benefit **several reliable tools**.[2,3]
- Extracellular vehicles (**EVs**) are lipid bilayer coated particles shed from cancer cells that carry **tumor-specific information**:
  - Protein
  - Genetic (RNA)
  - Metabolic (lipids)
- EVs have been investigated for their potential in cancer diagnostics; however, **the role of lipidomics in this context remains limited**.[4]
- This study aims to **characterize EV lipid profiles** using **lipidomics** to identify **OCSCC biomarker** signatures.

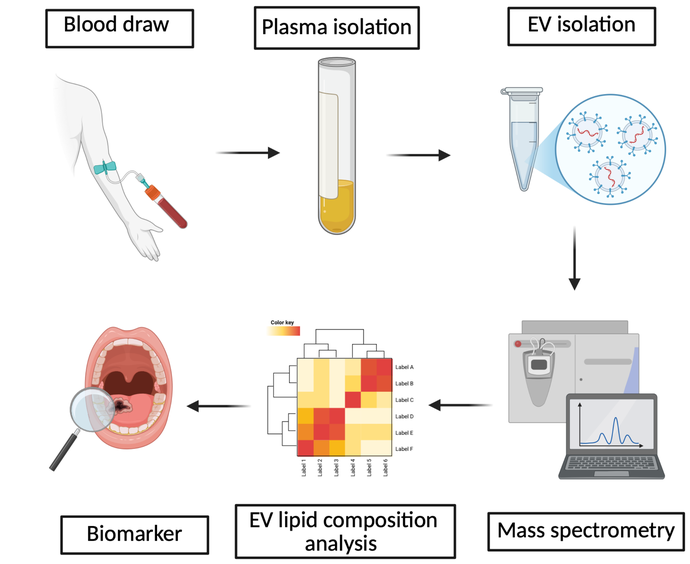

Figure 1. Workflow schematic

Methodology

- Plasma samples from **10 OCSCC** patients (T4) and **10 controls** with benign head and neck pathology were used for the analysis.
- **EVs were isolated** using magnetic bead positive selection from Miltenyi.
- Corresponding **lipid profiles** were quantified using **liquid chromatography mass spectrometry** at the MUSC Lipidomics Shared Resource.
- Three separate **sphingolipid-focused lipid profiles** were quantified:
  - **Ceramide/Sphingosine** (Cer-Sph)
  - **Hexosyl-Ceramide** (Hex-Cer)
  - **Lactosyl-Ceramide** (Lac-Cer)
- Group comparisons were performed using two-way ANOVA and, while associations with clinical data were evaluated using ANOVA.

Patient population

ID	Group	Diagnosis	Location	T stage	N status	Recurrence
1	Cancer	SCC	FOM	T4	N0	N
2	Cancer	SCC	Buccal	T4a	N2c	N
3	Cancer	SCC	Ventral tongue	T4a	N2c	N
4	Cancer	SCC	Buccal	T4a	N2b	Y
5	Cancer	SCC	FOM	T4	N2c	Y
6	Cancer	SCC	FOM	T4a	N0	Y
7	Cancer	SCC	Maxilla	T4a	N0	N
8	Cancer	SCC	Maxilla	T4a	N0	N
9	Cancer	SCC	Buccal	T4a	N2b	N
10	Cancer	SCC	Retromolar Trigone	T4a	N2b	Y
11	Control	pleomorphic adenoma				
12	Control	pleomorphic adenoma				
13	Control	pleomorphic adenoma				
14	Control	fibrous dysplasia				
15	Control	parotid inflammation				
16	Control	thyroid hyperplasia				
17	Control	thyroid hyperplasia				
18	Control	thyroid hyperplasia				
19	Control	parotid inflammation				
20	Control	thyroid hyperplasia				

Table 1. Patient population included in this work. For figure 2, all patients were included, and cancer vs. control was the comparison. For figures 3-4, only the cancer group was included, and recurrence or nodal status were the comparisons.

OCSCC vs Control Lipid Profiles

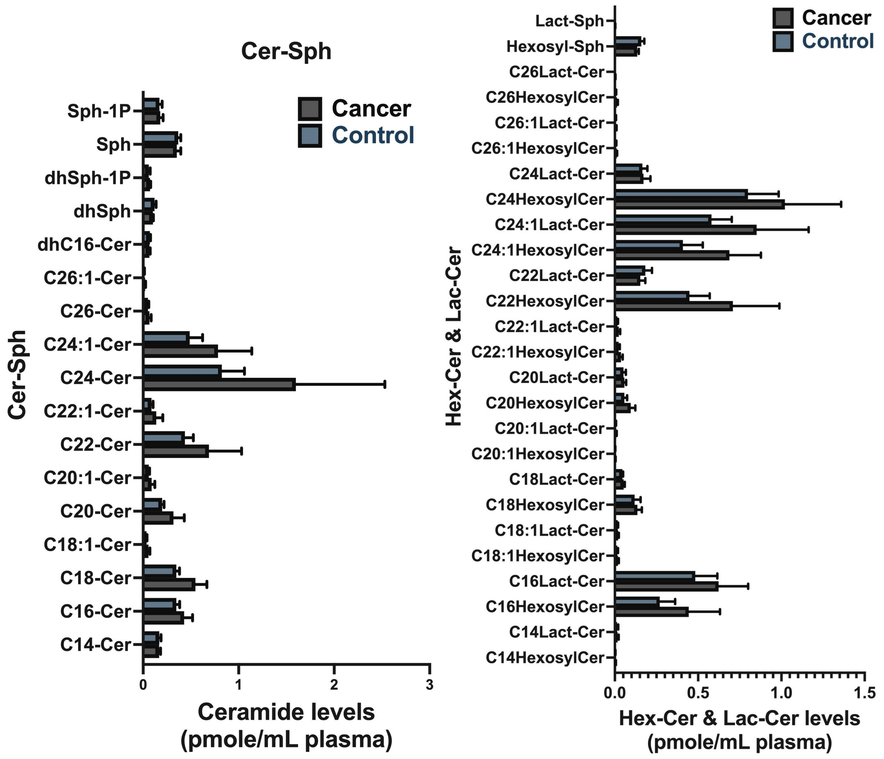

Figure 2. OCSCC and non-cancerous controls demonstrates differential lipid patterns in circulating EVs. Preliminary findings revealed 18 specific lipids elevated 1.5-fold in OCSCC EVs compared to control, with C24-ceramide (C24-Cer) showing the most significant difference. Data are means +/- SEM.

Lipid profiles and OCSCC recurrence

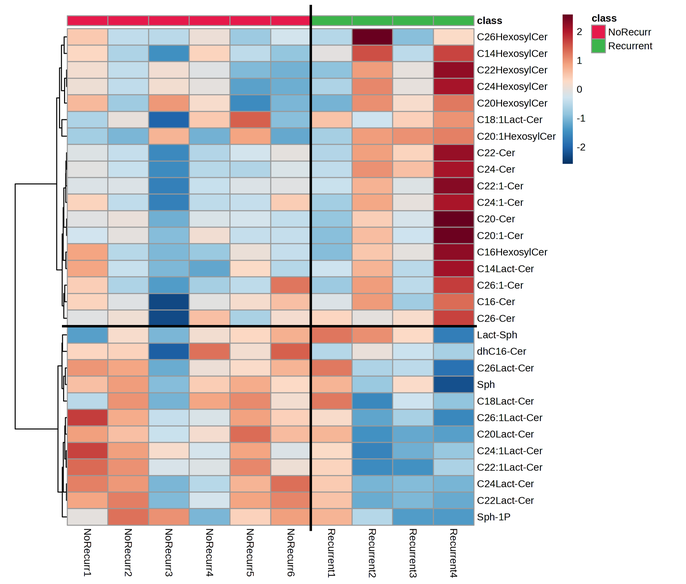

Figure 3. OCSCC recurrence demonstrates a unique lipidomic signature.

Lipid profiles and OCSCC nodal status

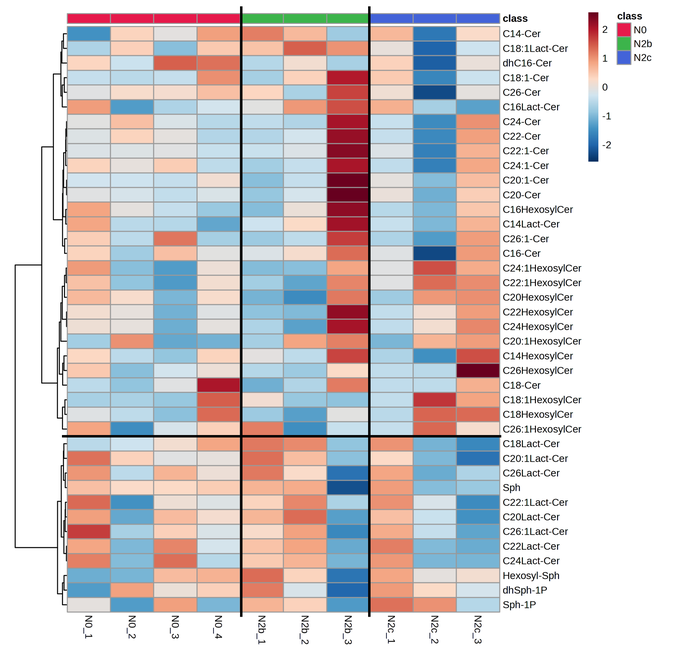

Figure 4. OCSCC nodal status demonstrates a unique lipidomic signature.

Conclusions

- This study identifies **EV lipidomics** as a promising approach for non-invasive biomarker discovery in OCSCC
- Future research will **expand on these findings**, using **larger cohorts** and **paired post-operative samples** to validate lipid-based diagnostic strategies.
- Additionally, **EV-specific features** will be better explored (number, size, etc.) and **complete plasma lipidomics** will be performed in conjunction with EV lipidomics

Contact

Wyatt Wofford, BS
MD/PhD Candidate (MSTP7, MS3)
Medical University of South Carolina
woffordw@musc.edu

LinkedIn

NCBI

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