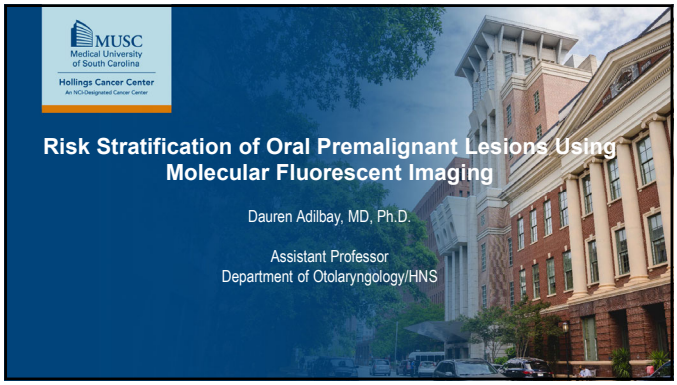


1

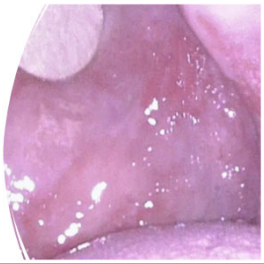
Disclosures

- Evergreen Theragnostics – consultant
- Nonfinancial: The presenter has no relevant nonfinancial relationship to disclose

2

Background

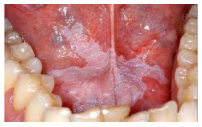
- *"OPMDs – are any oral mucosal abnormality that is associated with a statistically increased risk of developing oral cancer."*
- Leukoplakia,
- Erythroplakia
- Proliferative verrucous leukoplakia
- Oral lichen planus,
- And others: oral submucous fibrosis, palatal lesions in reverse smokers, lupus erythematosus, epidermolysis bullosa, and dyskeratosis congenita.

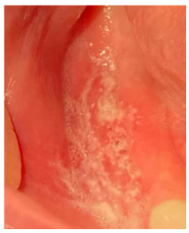


3

Definition

- leukoplakia: white plaques of questionable risk, having excluded other known diseases or disorders that carry no increased risk for cancer





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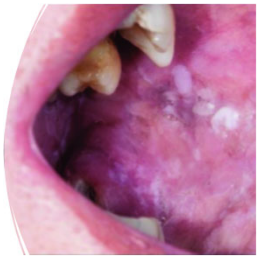
Classification (consensus report)

- Homogenous
- Non-homogenous
  - Nodular leukoplakia: Small polypoid or rounded outgrowths, red or white excrescences.
  - Verrucous leukoplakia: The surface is raised, exophytic, wrinkled, or corrugated
  - Erythroleukoplakia



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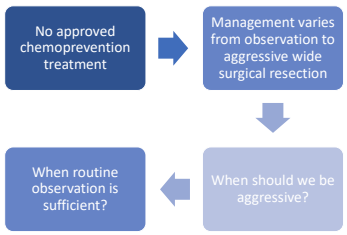
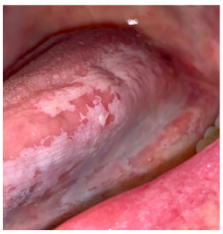
Current management issues





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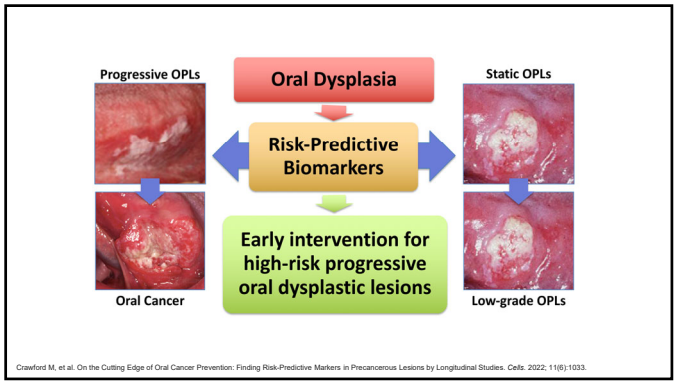

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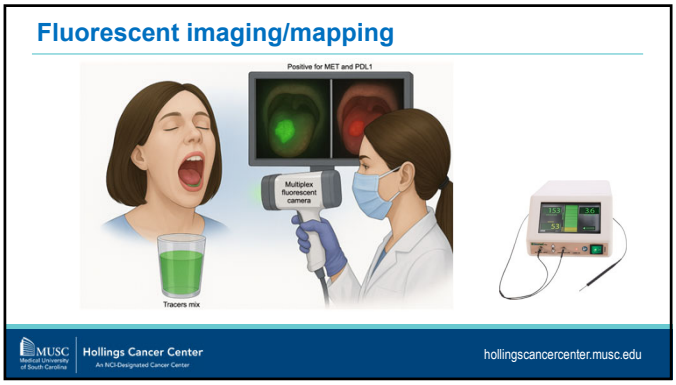

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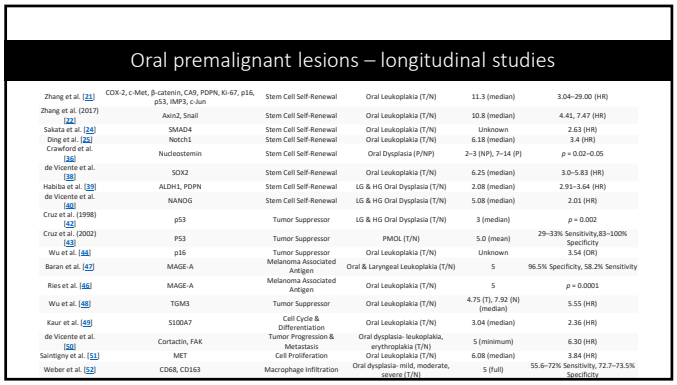

Zhang et al. [21]	COX-2, c-Met, β-catenin, CA9, PDPN, Ki-67, p16, p53, JMP3, c-Jun	Stem Cell Self-Renewal	Oral Leukoplakia (T/N)	11.3 (median)	3.04–29.00 (HR)
Zhang et al. (2017) [22]	Axin2, Snail	Stem Cell Self-Renewal	Oral Leukoplakia (T/N)	10.8 (median)	4.41, 7.47 (HR)
Sakata et al. [24]	SMAD4	Stem Cell Self-Renewal	Oral Leukoplakia (T/N)	Unknown	2.63 (HR)
Ding et al. [25]	Notch1	Stem Cell Self-Renewal	Oral Leukoplakia (T/N)	6.18 (median)	3.4 (HR)
Crawford et al. [26]	Nucleostemin	Stem Cell Self-Renewal	Oral Dysplasia (P/NP)	2–3 (NP), 7–14 (P)	$p = 0.02–0.05$
de Vicente et al. [38]	SOX2	Stem Cell Self-Renewal	Oral Leukoplakia (T/N)	6.25 (median)	3.0–5.83 (HR)
Hablba et al. [39]	ALDH1, PDPN	Stem Cell Self-Renewal	LG & HG Oral Dysplasia (T/N)	2.08 (median)	2.91–3.64 (HR)
de Vicente et al. [40]	NANOG	Stem Cell Self-Renewal	LG & HG Oral Dysplasia (T/N)	5.08 (median)	2.01 (HR)
Cruz et al. (1998) [42]	p53	Tumor Suppressor	LG & HG Oral Dysplasia (T/N)	3 (median)	$p = 0.002$
Cruz et al. (2002) [43]	P53	Tumor Suppressor	PMOL (T/N)	5.0 (mean)	29–33% Sensitivity,83–100% Specificity
Wu et al. [44]	p16	Tumor Suppressor	Oral Leukoplakia (T/N)	Unknown	3.54 (OR)
Baran et al. [47]	MAGE-A	Melanoma Associated Antigen	Oral & Laryngeal Leukoplakia (T/N)	5	96.5% Specificity, 58.2% Sensitivity
Ries et al. [46]	MAGE-A	Melanoma Associated Antigen	Oral Leukoplakia (T/N)	5	$p = 0.0001$
Wu et al. [48]	TGM3	Tumor Suppressor	Oral Leukoplakia (T/N)	4.75 (T), 7.92 (N) (median)	5.55 (HR)
Kaur et al. [49]	S100A7	Cell Cycle & Differentiation	Oral Leukoplakia (T/N)	3.04 (median)	2.36 (HR)
de Vicente et al. [50]	Cortactin, FAK	Tumor Progression & Metastasis	Oral dysplasia- leukoplakia, erythroplakia (T/N)	5 (minimum)	6.30 (HR)
Saintigny et al. [51]	MET	Cell Proliferation	Oral Leukoplakia (T/N)	6.08 (median)	3.84 (HR)
Weber et al. [52]	CD68, CD163	Macrophage Infiltration	Oral dysplasia- mild, moderate, severe (T/N)	5 (full)	55.6–72% Sensitivity, 72.7–73.5% Specificity

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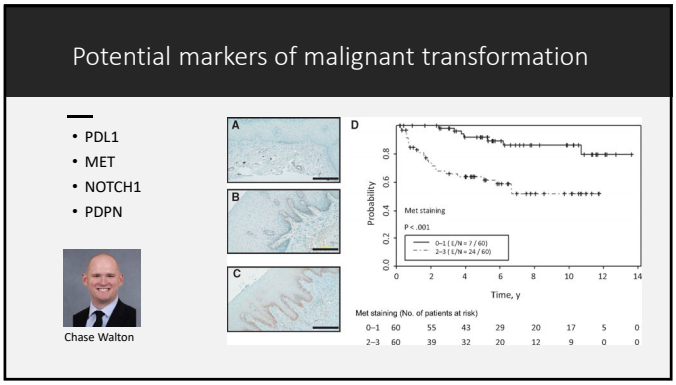

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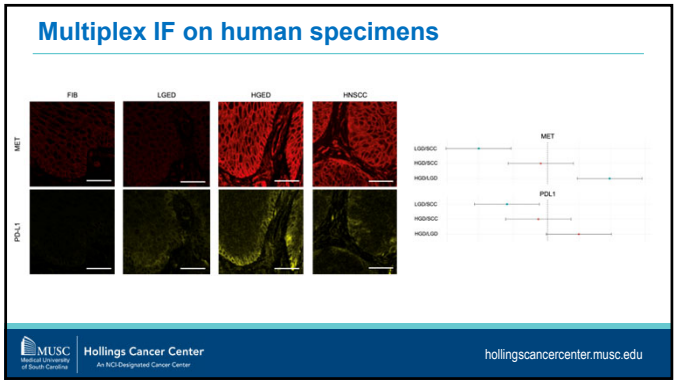

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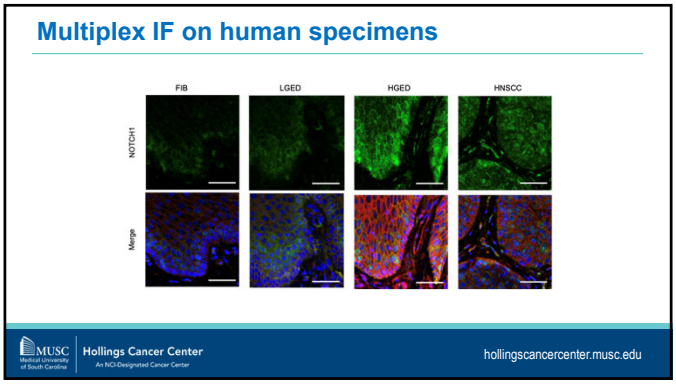

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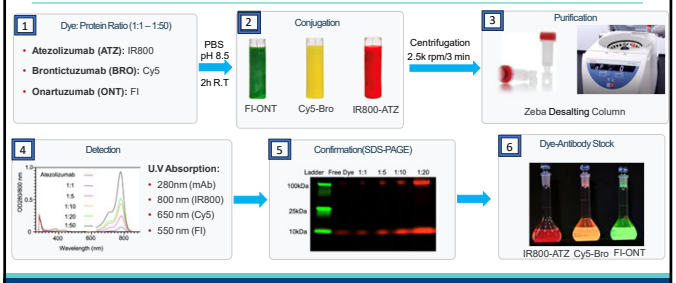
Formulation Method



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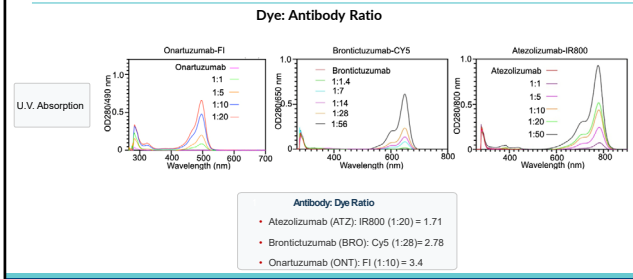
Results



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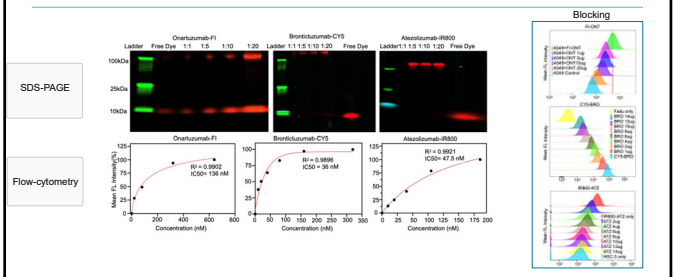
SDS-PAGE/Binding Efficacy(IC50)



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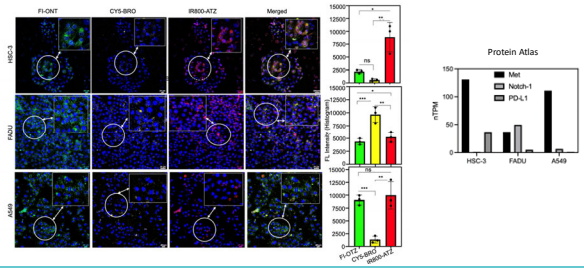
Live Cells Multispectral Imaging



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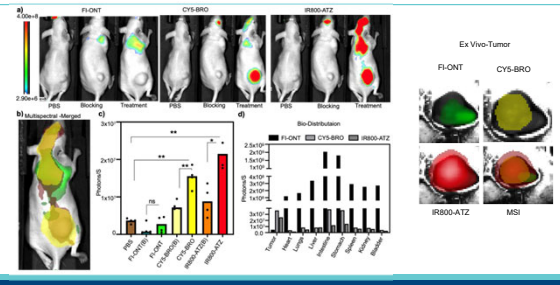
In vivo Multispectral Imaging



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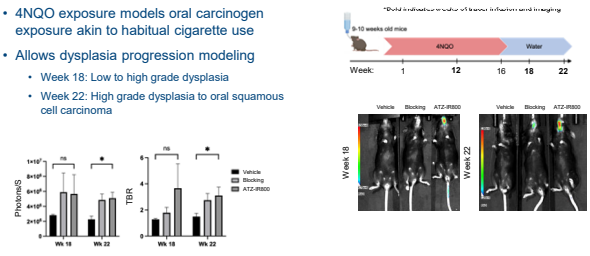
In vivo MSI in Oral Epithelial Malignancy

- 4NQO exposure models oral carcinogen exposure akin to habitual cigarette use
- Allows dysplasia progression modeling
  - Week 18: Low to high grade dysplasia
  - Week 22: High grade dysplasia to oral squamous cell carcinoma



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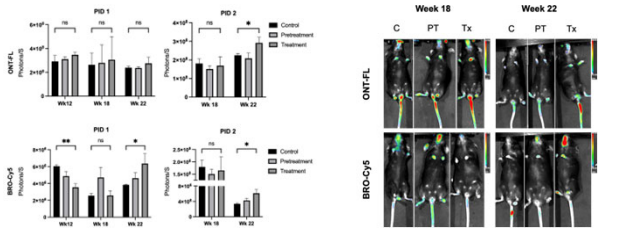
In vivo MSI in Oral Epithelial Malignancy



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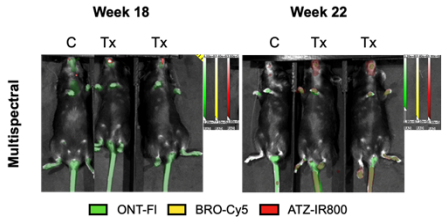
In vivo MSI in Oral Epithelial Malignancy



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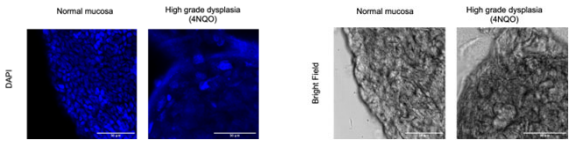
Mucosal lesion organoids



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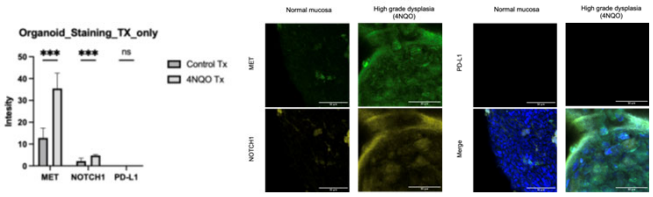
Mucosal lesion organoids - MSI



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Conclusion

- We have successfully formulated and quantified the FI-OTZ, Cy5-BRO, and IR800-ATZ through the U.V absorption and SDS-PAGE
- These conjugates successfully target MET, NOTCH-1, and PD-L1, respectively—all of which are highly expressed in head and neck mucosal cancer cells.
- In vitro MSI imaging and blocking studies (flow cytometry) showed specificity towards respective antigens.
- In vivo MSI showed precise tumor uptake and specificity of FI-OTZ, Cy5-BRO, and IR800-ATZ

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FUTURE DIRECTIONS

- Tracers has shown promise in early studies, but further exploration of clinical relevance is warranted
- Future study will address the following questions:
  - Sensitivity and specificity of the tracers for low grade, high grade, and malignant lesions
  - Optimal administration route, dose, and timing
  - Safety profile per route of administration

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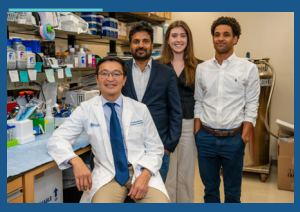
Acknowledgment



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Core Facility (MUSC)

Cell & Molecular Imaging Shared Resource
Drug Discovery Core (DDC)
Flow Cytometry & Cell Sorting
Division of Lab Animal Resources
Biorepository & Tissue Analysis

MUSC Medical University of South Carolina | Hollings Cancer Center
An NCI-Designated Cancer Center

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