


The Regulation of MMP2 and MMP9 in Radiotherapy-Induced Oral Mucositis

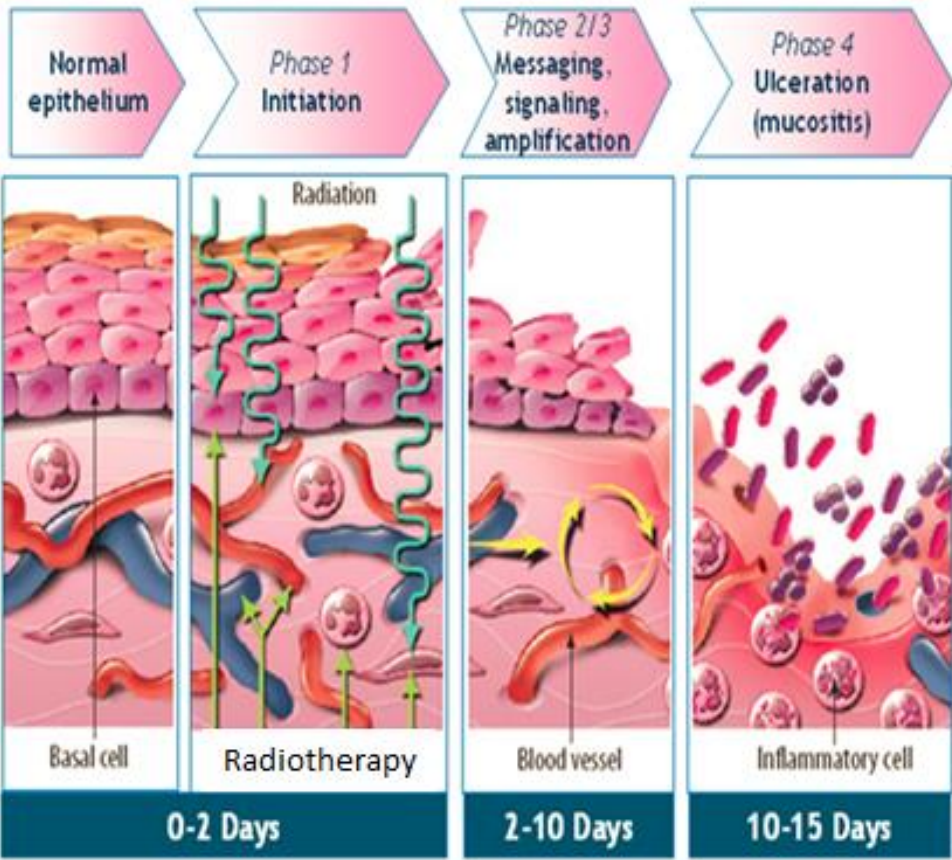


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USRCAP 2018

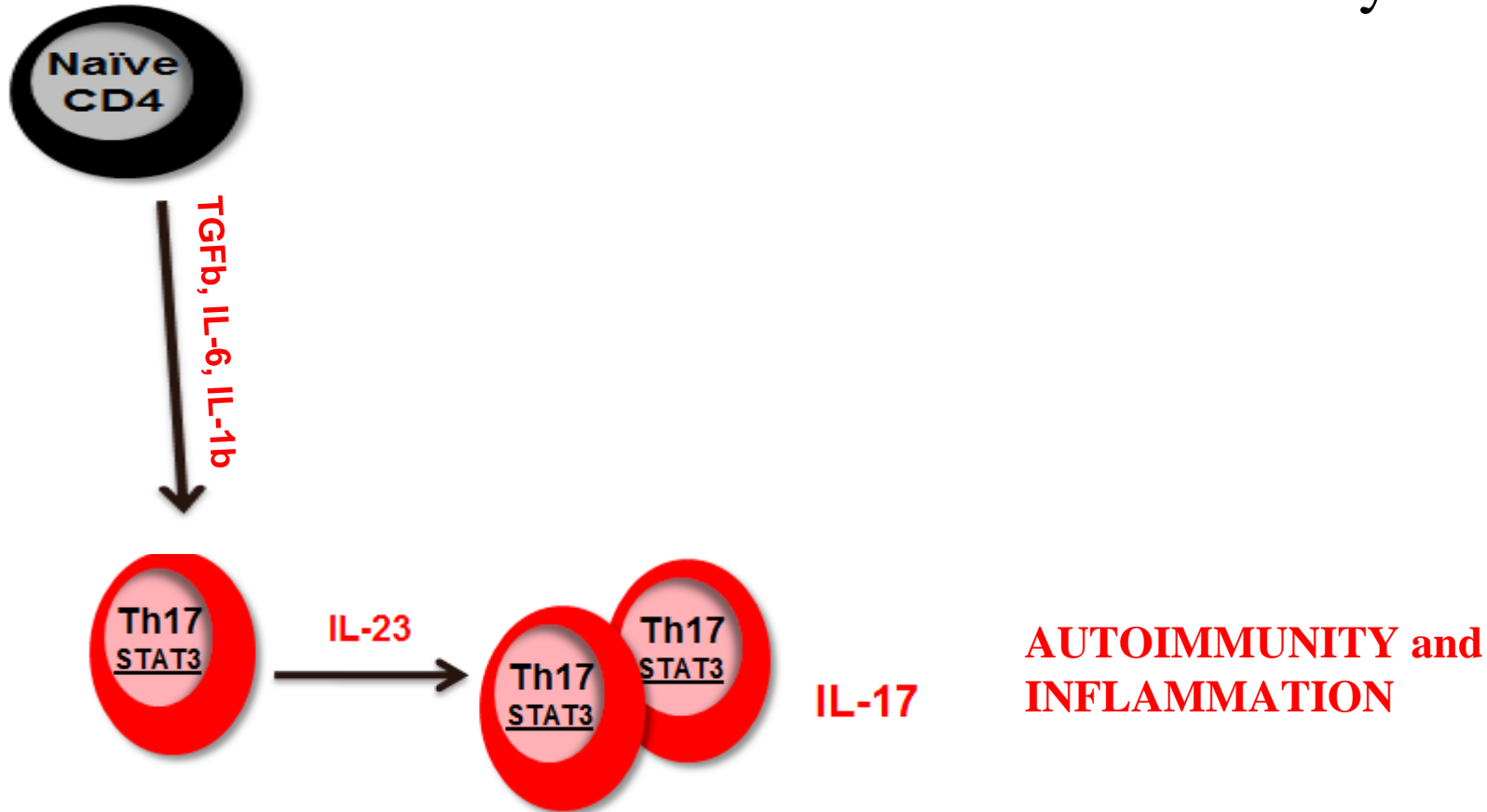
Oral Mucositis (OM)

- Caused by damage to oral epithelial tissue
 - Ulcers and sores in the mouth
 - Swelling
- All patients receiving head and neck irradiation as a form of cancer treatment develop oral mucositis

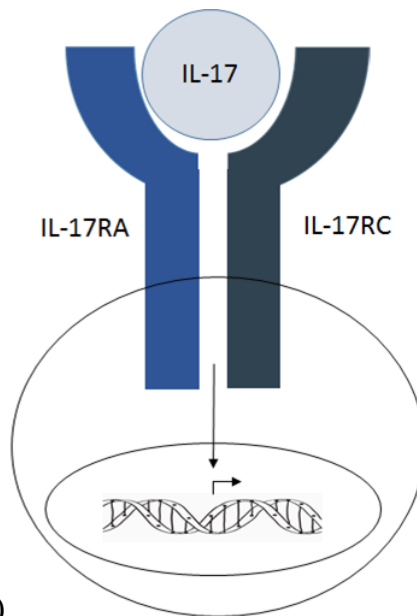
Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
No change				
	Soreness/ erythema	Erythema, ulcers; can eat solid food	Ulcers; requires liquid diet only	Alimentation (nourishment) not possible



Inflammation and the IL-17 Pathway



IL-17 Signals through the IL-17 Receptor



**Is IL-17 involved in oral
mucositis-associated
inflammation?**

Neutrophils chemokines (CXCL1 and CXCL5)
Antimicrobial peptides (AMPs) (beta-defensin 3)
Matrix metalloproteinases (MMP2 and MMP3)
Proinflammatory cytokines (IL-6)

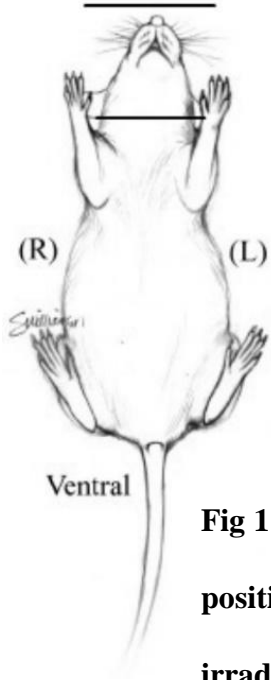
Are Matrix Metalloproteinases (MMPs) Involved in the Damage Associated with OM?

- Enzymes
 - Degrade extracellular matrix proteins
 - ECM holds cells together to form tissue
- Expression in adults is usually low
- Often upregulated in inflammatory disease

Hypothesis

Head and neck irradiation will cause upregulation of MMP2 and MMP9, resulting in damage to the oral mucosa

Experimental Model of Head-Neck Irradiation



**Fig 1: Mouse
positioning during
irradiation**

Radiation dose: 22.5 Gy

Elekta Precise Linear Accelerator

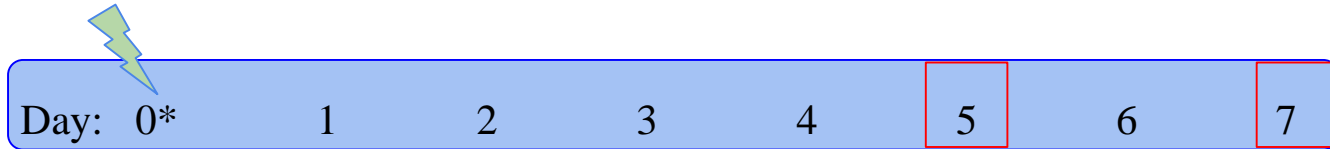




WT Sham
(3)



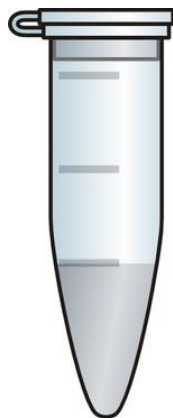
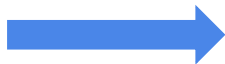
WT + HNI
(8)



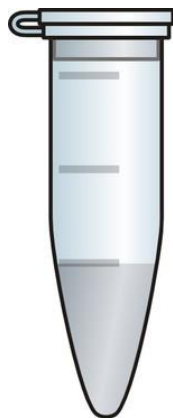
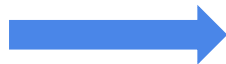
* saline injection



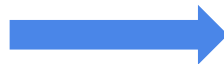
Harvested tongue



RNA extraction



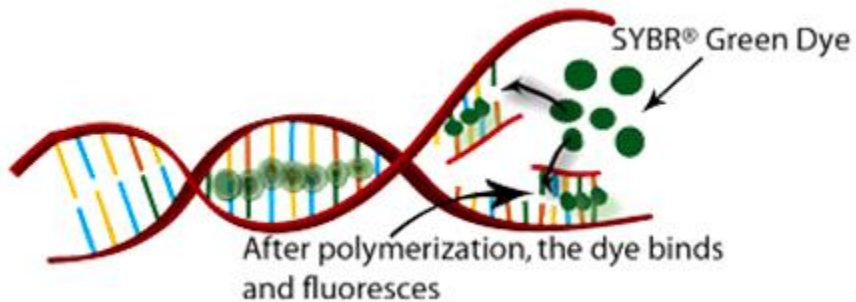
cDNA



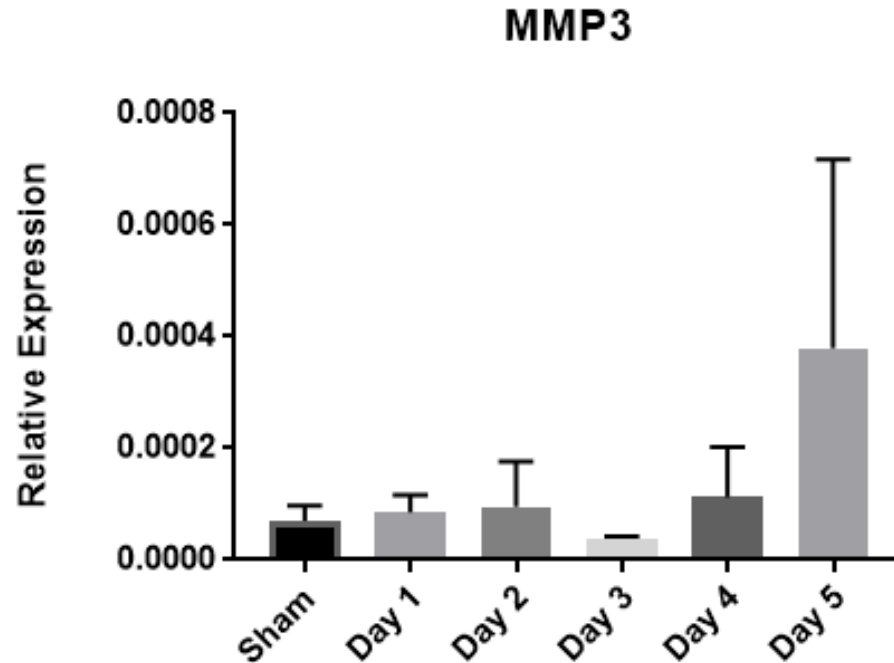
qPCR

qPCR (Quantitative Real-time PCR)

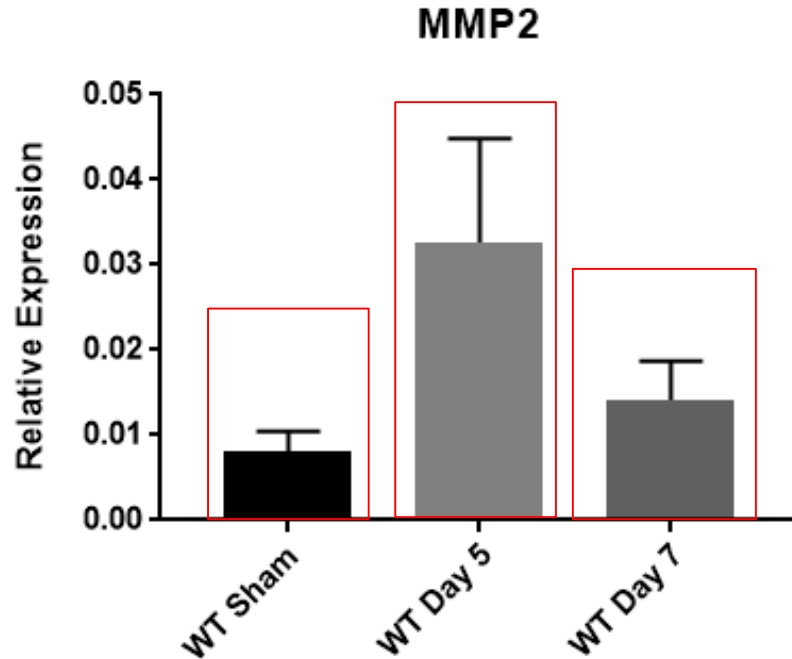
- Amplification of a target sequence (gene)
- Monitors amplification as reaction progresses



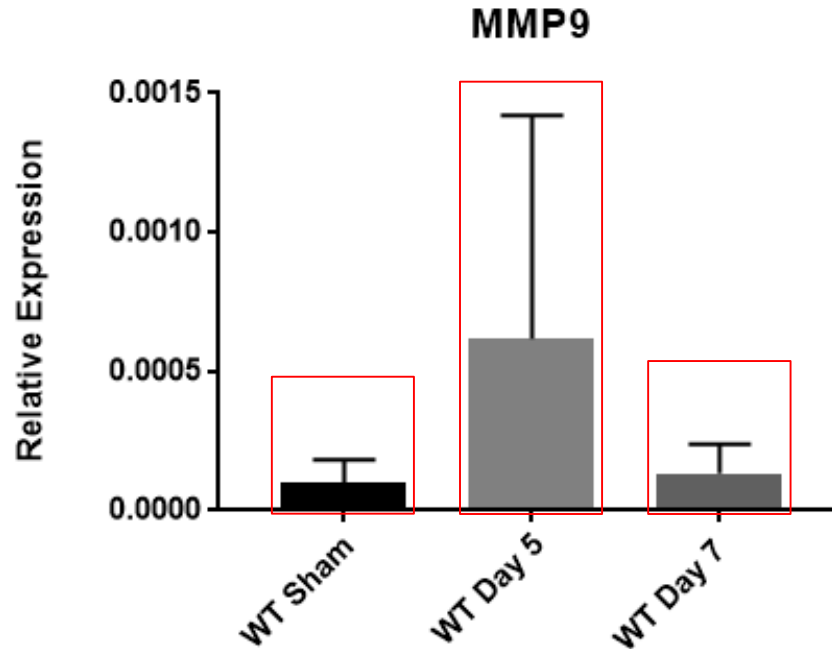
MMP3 Regulation in Tongue Tissue during OM



Expression of MMP2 Trends Towards Upregulation on Day 5 in Radiotherapy-Induced Oral Mucositis



Expression of MMP9 Trends Towards Upregulation on Day 5 in Radiotherapy-Induced Oral Mucositis



Conclusion

- MMP2 and MMP9 expression trends towards upregulation on Day 5 post-irradiation but is not statistically significant
- More research needs to be done to quantify damage done to the tongue for Day 5 and Day 7

Future Plans

- Quantify tongue damage to look for an association between MMP expression and tissue destruction
- Run qPCR for MMP3 and MMP12
- Run a longer experimental timeline (Day 11 or 12)
- Continue working with MMPs and look upstream in the IL-17 pathway



Acknowledgements

Advisor

Dr. Heather Conti

Graduate students

Jackie Kratch

Dylan Launder

Katie McKeone

Cole White

Undergraduate students

Dan O'Shea

Nicky Salas

Grace Michalski

Summer students

Shreyas Banerjee

Funded by

The University of Toledo Office
of Undergraduate Research

Lab tech

Nate Schmidt

Other thanks

Dana Cancer Center at
the University of
Toledo Medical Center



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Thank you!

Questions?

