

5TH World Congress of Cutaneous Lymphomas



Enhancing the Ability to Diagnose, Interpret and Apply Best Treatment Options for Cutaneous Lymphomas

Gut microbiome of cutaneous T-cell lymphoma of cutaneous T cell lymphoma patients is altered following narrowband ultraviolet-B phototherapy and exhibits profiles that predict treatment responsiveness

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Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

CTCL and Association with Microbiome

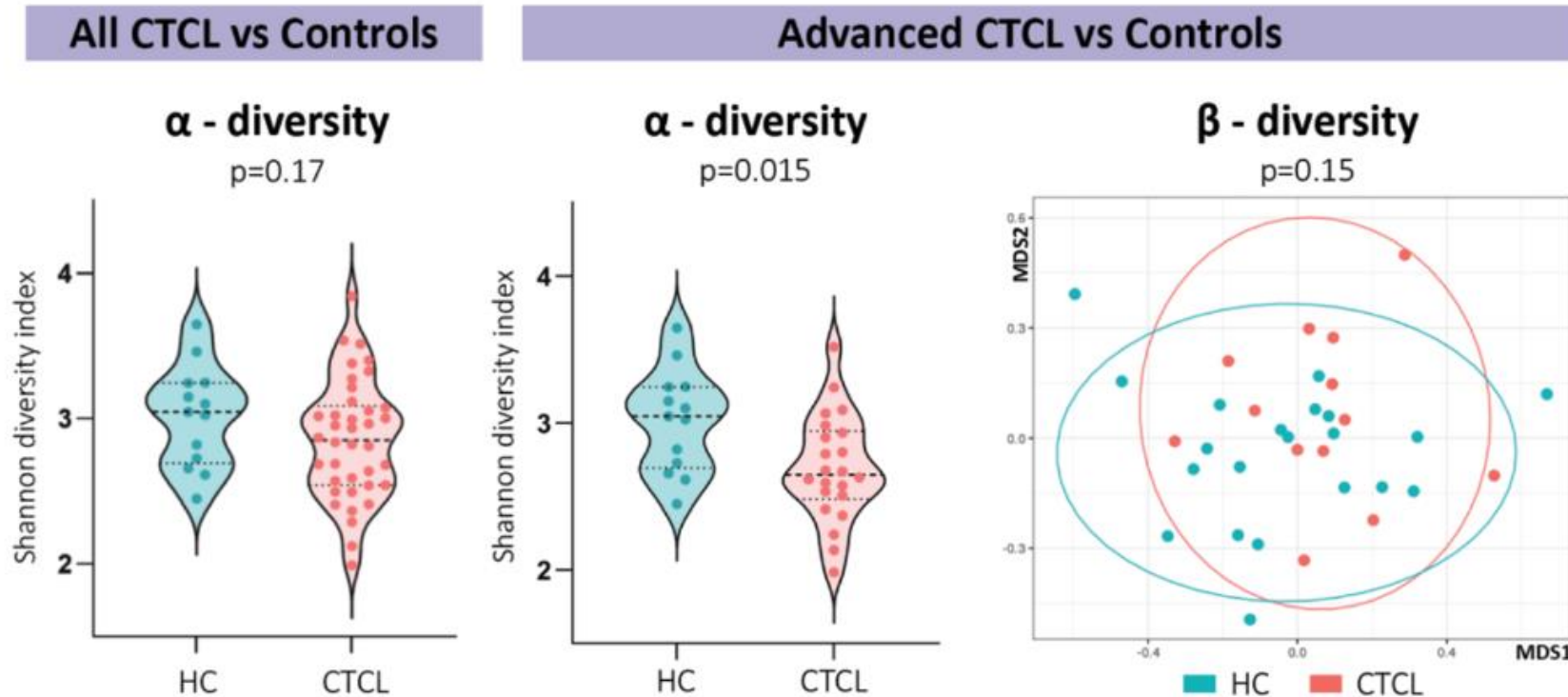
- Increasing evidence suggests that CTCL is closely tied to host microbiome
 - Aggressive antibiotic treatment inhibits malignant T cells in lesional skin
 - CTCL mouse models exhibit mild, indolent disease when housed in germ free isolators but have rapid disease progression when moved to traditional housing



Lindahl et al, Blood 2019
Fanok et al., JID 2018

Previous Findings from Our Group

- CTCL patients exhibit gut dysbiosis, particularly in advanced disease



n=38 CTCL
n=13 HC

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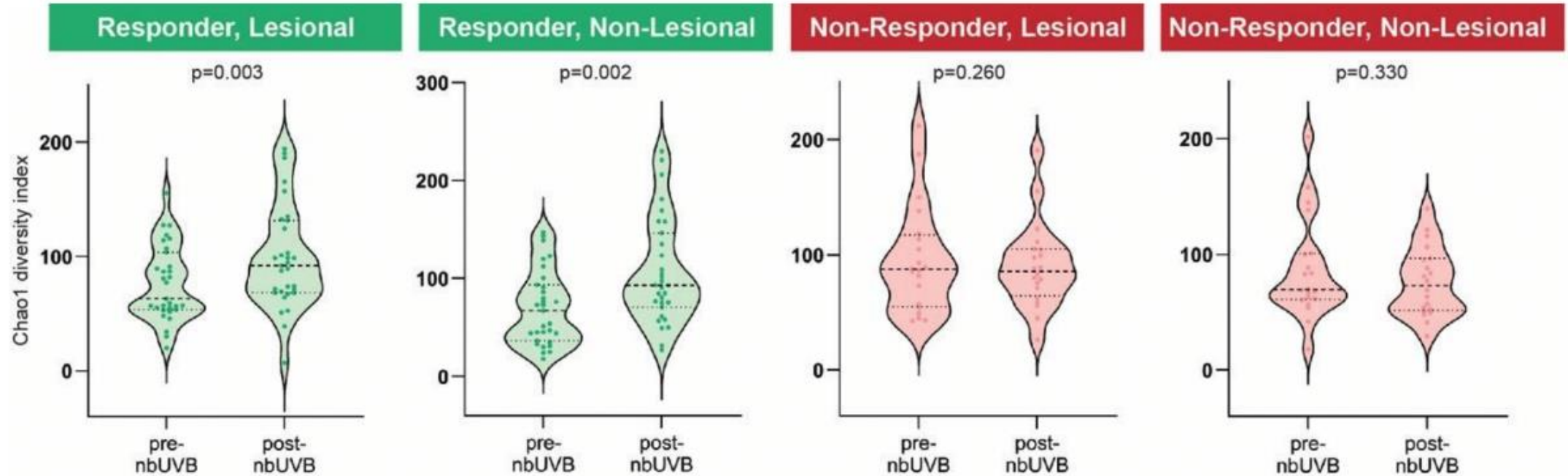
Previous findings from our group - Bacterial shifts mirror immune axis

Taxon	CTCL	Atopic Dermatitis	Psoriasis
Bifidobacteriaceae		Not seen	↑
Bifidobacterium	↓	↓	
Coriobacteriaceae		↓	↑
Collinsella	↓		<i>C. aerofaciens</i> ↑
Eggerthellaceae	Unclassified ↓	<i>Eggerthella</i> ↓	↑
Prevotellaceae	↑ / ↓ (advanced)		↑
Prevotella		<i>Paraprevotella</i> ↑	↑, <i>P. copri</i> ↓
Lactobacillaceae			↓
Lactobacillus	↓ (advanced disease)		
<u>Clostridiales</u>	Family XIII ↓ Unclassified Family XIII ↓	Clostridium cluster IV ↓	Family XIII ↑
Ruminococcaceae		↓	↑
	<i>Anaerotruncus</i> ↓ <i>Angelakisella</i> ↓		<i>Ruminococcus</i> ↑ <i>R. gnavus</i> ↑
Lachnospiraceae	Lachnospiraceae ND3007 group ↓ (advanced) <i>Sellimonas</i> ↑ (advanced)	<i>Blautia</i> ↓ / ↑ <i>Coprococcus</i> ↓	↑ <i>Coprococcus</i> ↓ <i>Dorea formicigenerans</i> ↑
Peptostreptococcaceae	<i>Romboutsia</i> ↓		↑

Gut microbial signature in CTCL is similar to that of atopic dermatitis, opposite psoriasis

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Previous Findings from Our Group



- When observing the skin microbiome, patients experienced a significant increase in alpha diversity in response to phototherapy
- Levels of *Staph aureus* and *Staph lugdenensis* significantly decreased

Hooper MJ...Zhou XA,
Frontiers in Immunology
Nov 2022

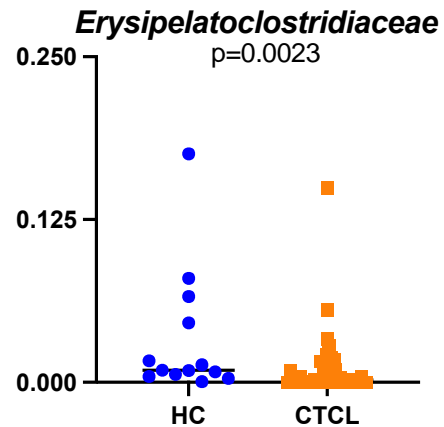
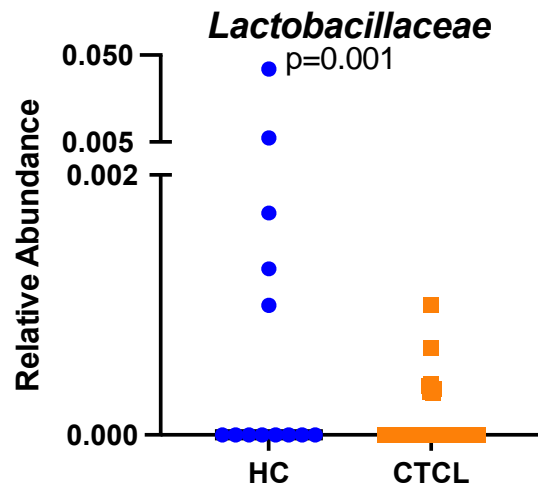
Big Questions

- Do the taxonomic differences in the gut for CTCL patients align with our previous paper?
- What changes can be observed pre vs post nbUVB?
- Are there differences in the gut microbiomes of nbUVB responders vs non-responders, as defined by mSWAT?

Patient Groups

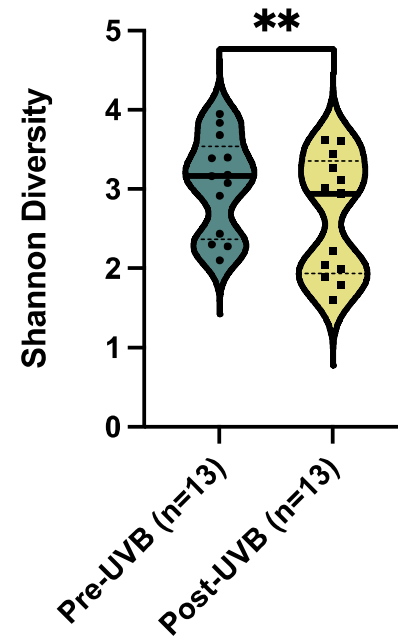
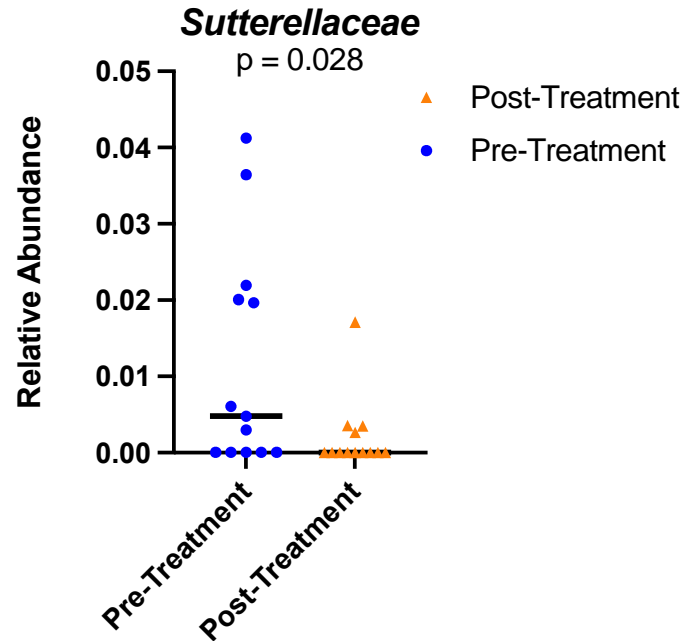
- 21 total CTCL patients
 - 13 patients underwent treatment regiment of nbUVB phototherapy
 - 6 responders and 7 non-responders
 - 8 patients used standard of care treatments but not nbUVB
- 13 Healthy Control patients (no CTCL or other active skin disease)
- Patients who utilized antibiotics within 4 weeks prior to collection were excluded

CTCL vs Healthy Controls



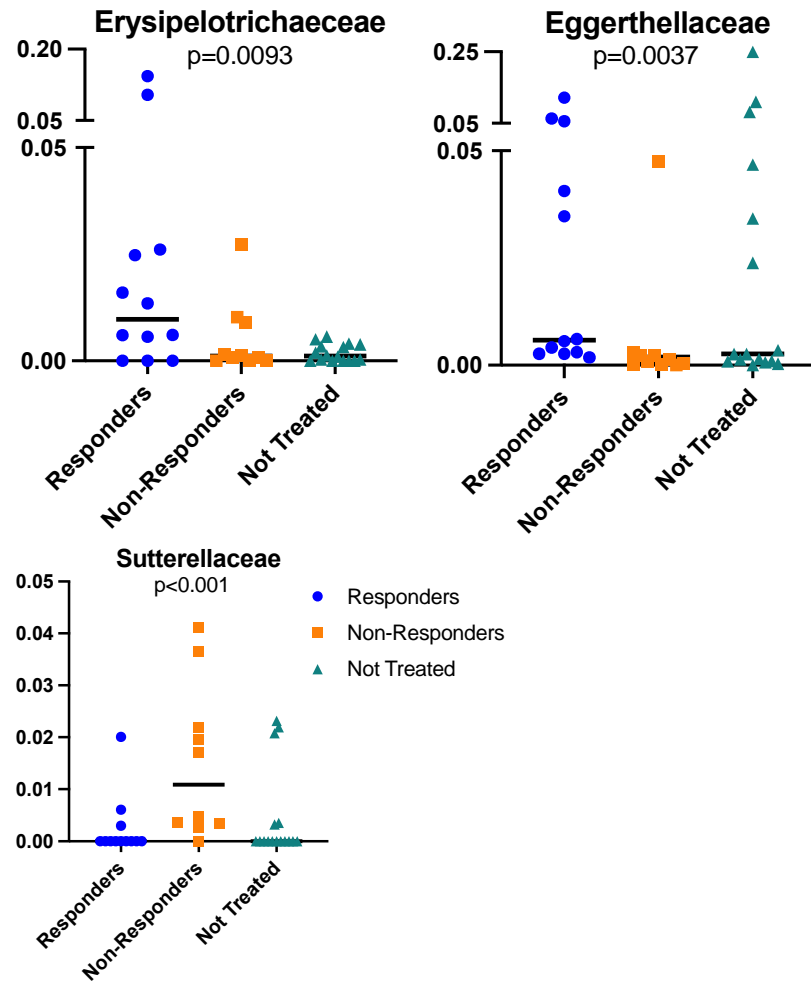
- Protective commensal bacteria including *Lactobacillaceae* and *Erysipelatoclostridiaceae* were significantly less abundant in CTCL
- Others higher in HC: *Ruminococcaceae*, *Streptococcaceae*, *Tannerellaceae*, *Anaerovoracaceae*, *Peptostreptococcaceae*, *Rikenellaceae*

Pre vs Post Phototherapy



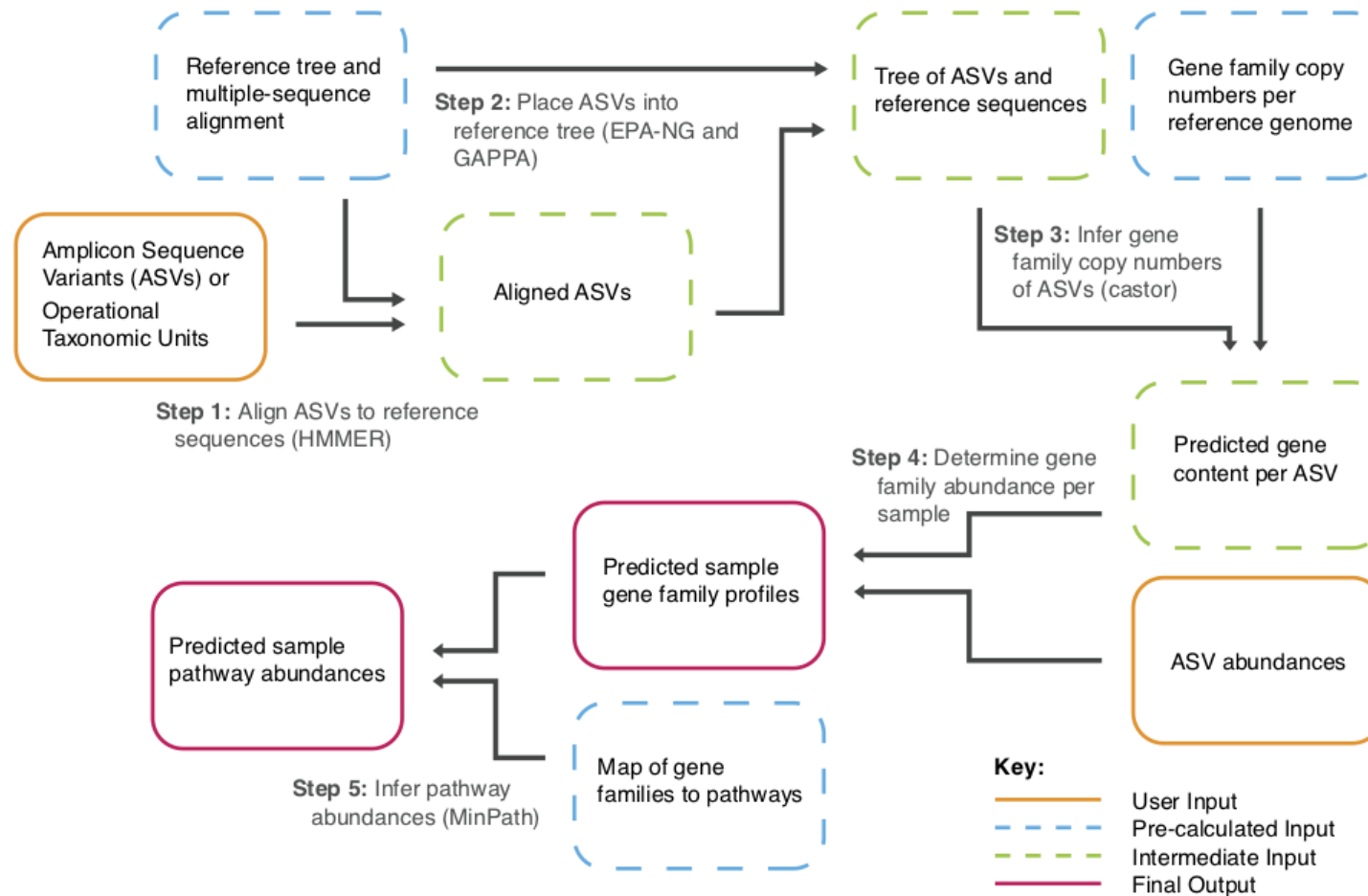
- Levels of proinflammatory *Sutterellaceae* (degrades IgA) decreased post-treatment
- Notably, alpha diversity decreased post treatment

Responders vs Nonresponders

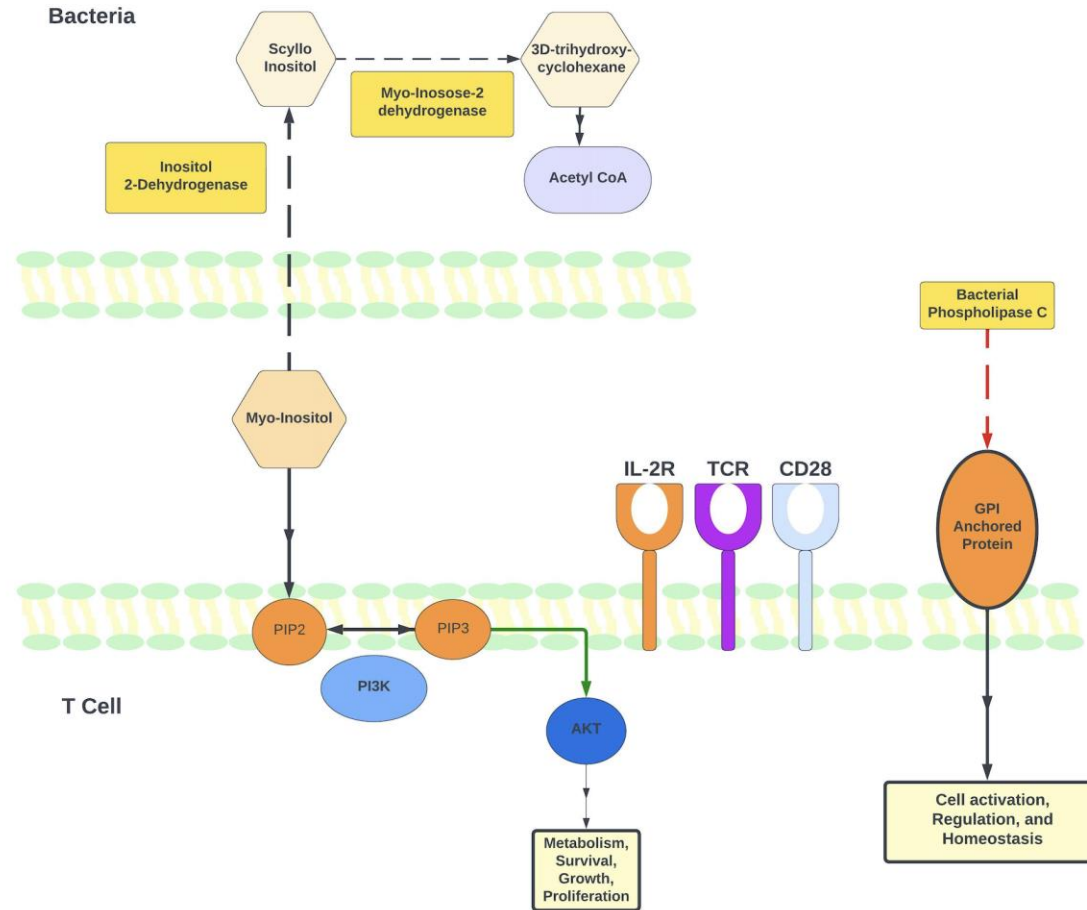


- *Sutterellaceae* is increased in non-responders
- Responders have higher levels of *Eggerthellaceae* and *Erysipelotrichaceae*,
 - *Eggerthellaceae* has anti-inflammatory properties
- *Lachnospiraceae* trended higher in responders
 - Produces butyrate, a potent histone deacetylase inhibitor
 - Mechanism of action for vorinostat and romidepsin

PICRUSt 2.0 Analysis



Myoinositol degradation increases and Phospholipase C decreases following phototherapy



- What is the functional consequence of the changes following nbUVB therapy?
- Taking the microbiome community as a whole, degradation of myo-inositol increases following phototherapy
- Phospholipase C is also decreased
- We propose a mechanism of action for how this effects T-cell activity here
- This will need to be confirmed with further study

Key Points

- CTCL patients have gut dysbiosis
- Bidirectional relationship between immune systems of gut and skin in CTCL – nbuVB leads to changes in the gut microbiome, and gut microbiome influences response to nbUVB (responders vs nonresponders)
- Levels of pro-inflammatory bacteria such as *Sutterellaceae* decrease following phototherapy
- Responders have higher levels of protective commensal bacteria such as *Erysipelotrichaceae* and *Eggerthellaceae*, while non-responders have higher levels of *Sutterellaceae*
- Myoinositol and Phospholipase C may decrease following phototherapy

Next Steps

- Shotgun metagenomic sequencing to analyze the microbiome at a strain level
- Functionally validating our theories in the inositol pathway (metabolomics)
- Investigating influence of *Lachnospiraceae* on butyrate levels in CTCL (metabolomics)
- The relationship between nbUVB, Vitamin D, and the gut microbiome in CTCL

Acknowledgements

Microbiome Project

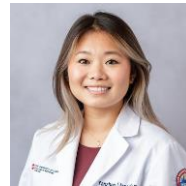
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Thank you!

