Genomic Adaptation of *Moraxella catarrhalis* During Persistence in the Airways of COPD Patients

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Introduction

Chronic Obstructive Pulmonary Disease (COPD) is the 3rd leading cause of death worldwide[1].

Moraxella catarrhalis (*M. cat*) persists in the airways of COPD patients and contributes to progressive decline in lung function[2].

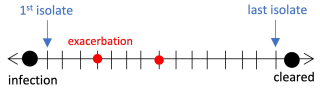
Ubiquitous surface proteins UspA1, UspA2, and UspA2H are virulence factors that mediate adherence, aggregation and complement adherence[3].

Hypothesis

M. cat adapts by altering its genome during persistence in the airways of COPD patients.

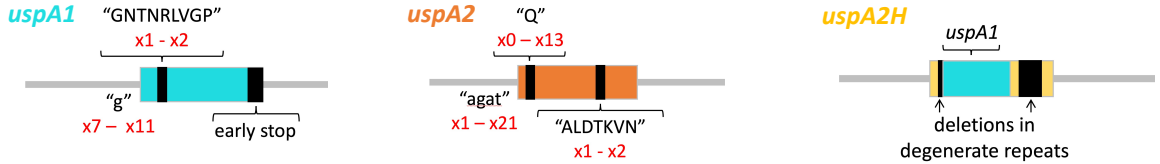
Methods

1. Isolated 78 persistent *M. cat* strains from COPD patients during a 20-yr prospective study at Buffalo VA Medical Center.



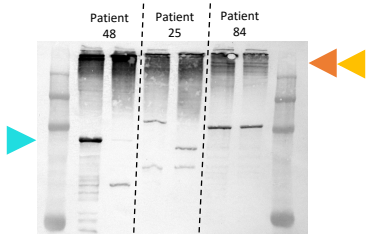
2. Sequenced complete genomes of sequential isolates of selected *M. cat* strains.
3. Genomic, protein and phylogenic analysis using bioinformatic tools.
4. Western Blots of whole cell lysates probed with a pan-UspA antibody.

1. Genes altered during persistence



2. Trends in genomic adaptation and expression

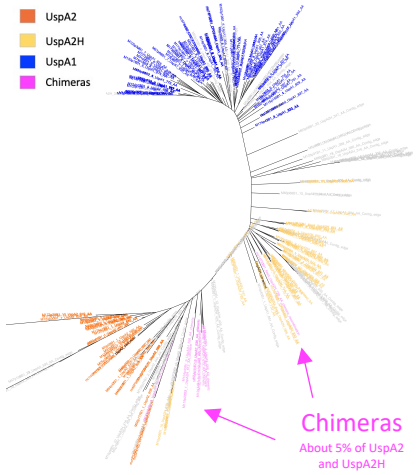
Repeat	Change	# of strains	Effect on expression	Western Blot example
"g" upstream *uspA1*	No changes	24		
	x12 --> x8	13	Decreases	Patient 48
	Increase	4		
"agat" upstream *uspA2*	No changes	8		
	x16 --> x11	9	No change	Patient 25
	x16 --> x21	11	No change	Patient 84
"Q" in *uspA2*	x4 --> x4	9	No change	Patient 84
	Decrease	0		
	Increase	0		
"ALDTKVN" in *uspA2* & *upsA2H*	x2 --> x2	63	No change	Patient 25
	Decrease	0		
	Increase	0		



Immunoblot of whole cell lysates of first and last isolates of 3 persistent strains probed with a pan-UspA antibody. Arrows indicate regions where UspA1, UspA2, and UspA2H are found.

3. Mechanism for genomic adaptation

Intragenomic recombination generates chimeric UspAs.



Conclusions

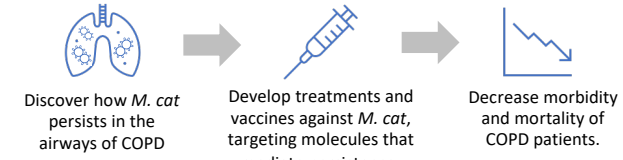
Overall:

Genomic repeat variations of *uspA1*, *uspA2*, and *uspA2H* alter expression of their encoded surface proteins and facilitate *M. cat* persistence in the airways of COPD patients.

Specific novel findings:

- "Q" and "ALDTKVN" are novel repeats identified in *uspA2* that may be crucial for immunogenicity.
- *M. cat* reduces the expression of *uspA1* by altering the "g" repeat in the promoter.
- Contrary to prior reports, changes in upstream "agat" repeats don't alter *uspA2* expression *in-vivo*.
- First report of intragenomic recombination as a mechanism that gives rise to chimeric UspAs.

Significance



Acknowledgements

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References

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