The Sinonasal Microbiome in Chronic Rhinosinusitis

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BACKGROUND

Sequencing of the 16S and 18S bacterial and fungal ribosomal subunits by state of the art molecular techniques allows for the study of the complex sinus microbial community. These techniques are able to identify low-abundance and unculturable bacteria and fungi, and compare the relative abundance of taxa between samples. In the setting of chronic rhinosinusitis (CRS), these molecular techniques allow scientists and clinicians to address problems inherent in culture-based bacteriology and have the potential to revolutionize the understanding of the impact of microbes on CRS.

OBJECTIVES

1) Compare the experimental designs, analytic techniques, and results of the extant literature utilizing molecular techniques to study CRS using ribosomal subunits.
2) Identify and discuss successes and limitations of the previously published studies and discuss best-practice strategies to maximize the potential of molecular techniques in advancing the understanding of the role of bacteria and fungi in chronic rhinosinusitis.

Search Strategy

SEARCH TERMS	AND Microbiome	AND 16S
Chronic rhinosinusitis	15	12
Sinusitis	14	30
Sinus	18	41
Unique PubMed Results	**72**	

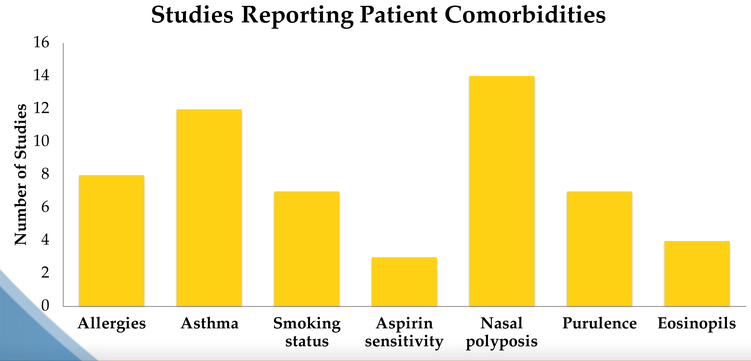
INCLUSION CRITERIA
1): Human study
2): Study design involved CRS
a) CRS
b) CRS Molecular vs Culture
c) CRS vs Healthy
3) English language journal

Included: 18
Excluded: 59

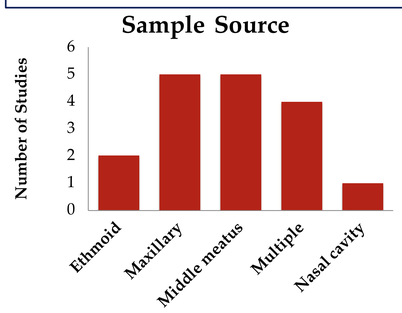
RESULTS: Demographics

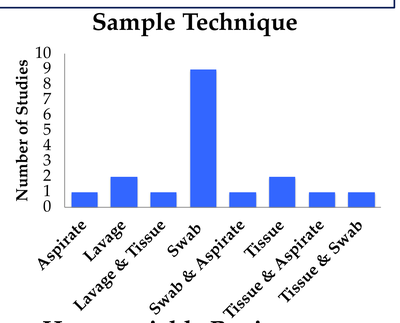
- 514 total patients, average of 29.7 patients per study.
- Average age of patients was 47.6
- Where gender was reported, there were an average of 9.6 males, and 9.4 females per study

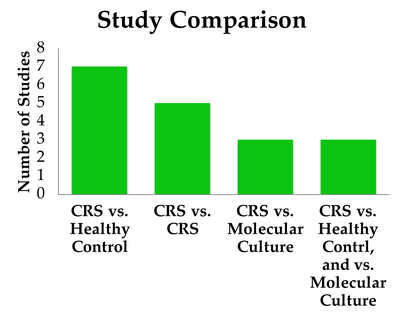
RESULTS: Patient Characteristics

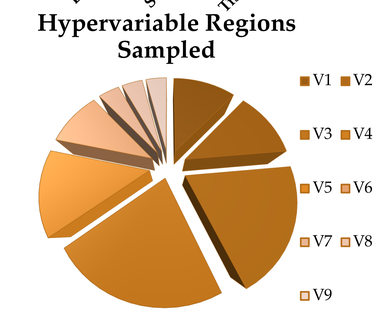


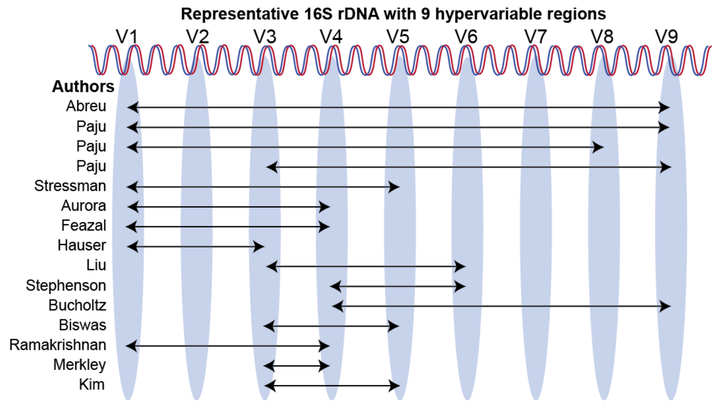
RESULTS: Study Design











RESULTS: Sequencing vs Culture

Author	Group	N	%positive samples	Reads / specimen	Unique OTUs	Taxa / sample	Most Abundant Taxa	% Speciated
Paju, 2003	Molecular	11	36%	NA	12	1.1	No repeats	70
	Culture		36%	NA	3	0.5	*S. aureus*	80
Power, 2005	Molecular	6	100%	NA	7	3.2	Mitis-sanguinis group *Streptococci*	32
	Culture		100%	NA	6	2	*S. aureus, S. pneumoniae*	100
Hauser, 2014	Molecular	54	98%	1068.5	NR	21.5	*Corynebacterium corynebacterium*	54.5
	Culture		100%	NR	NR	3	CNS	NR

RESULTS: CRS vs Control; Molecular vs Culture

Author	Group	N	%positive samples	Reads / specimen	Unique OTUs	Taxa / sample	Most Abundant Taxa	% Speciated
Stephenson, 2010	CRS	18	100	NR	NR	10	*Propionibacterium*	NR
	Control	9	100			NR	*Staphylococcus sp.*	
	Culture	17	82	NA	NR	1.4	CNS	
Feazel, 2012	CRS	15	100	1485	34	11.6	*S. aureus*	NR
	Control	5	100		49	14.6	*Proprionibacterium sp.*	
	Culture	20	100	NA	NR	2.8	CNS	
Boase, 2013	CRS	38	100	298	30	3	*S. aureus*	90
	Control	6	100	67.8	5	2	*P. acnes*	
	Culture	44	74	NA	12	1.3	*S. aureus*	NR

RESULTS: CRS Comparisons

Author	Group	N	Reads / specimen	Unique OTUs	Taxa / sample	Most Abundant Taxa	% Speciated
Bucholtz, 2002	Polyp	26	NA	2	0.05	*Streptococcus sp*	50%
	Sinus	6				NA	
	Turbinate	7				*P. aeruginosa*	
Stressman, 2013	Polyp	28	35	48	8.7	*P. aeruginosa*	100%
	Mucous	15	25		5.9	*P. aeruginosa*	
	Turbinate	30	42		8.3	*P. aeruginosa*	
Liu, 2013	Pre-Abx	6	2939	>60	NR	Varied by patient	NR
	Post-Abx					Varied by patient	
Kim, 2015	Swab	9	2510	756	42	*Staphylococcus*	NR
	Tissue					*Staphylococcus*	
Merkley, 2015	Pre-Abx	8	93,517	320	3.9	*Staphylococcus*	27%
	Post-Abx		35,535		15.9	*Proprionibacterium*	

RESULTS: CRS vs Healthy Control (molecular)

Author	Group	N	Reads / specimen	Unique OTUs	Taxa / sample	Most Abundant Taxa	% Speciated
Abreu, 2012	CRS	7	NA	NR	950	*Corynebacterium tuberculostearicum*	NA
	Control	7			1200	*Lactobacillus sakei*	
Aurora, 2013	16S CRS	30	18,363	3780	126	*Cyanobacteria sp.*	NR
	16S Control	12		2333	194	*Cyanobacteria sp.*	
	18S CRS	30	18,228	132	4.4	*Cryptococcus neoformans*	NR
	18S Control	12		106	8.8	*Cryptococcus neoformans*	
Cleland, 2014	18S CRS	23	NR	207	12.14	*Malassezia sp.*	NR
	18S Control	11			8.18	*Malassezia sp.*	NR
Choi, 2014	Lavage CRS	8	5154	NR	225	*Staphylococcus sp.*	NR
	Lavage Control	3	1982		325	*Streptococcus sp.*	
	EV CRS	8	5431		200	*Staphylococcus sp.*	
	EV Control	3	2195		300	*Staphylococcus sp.*	
Biswas, 2015	CRS	9	NR	NR	NR	*Corynebacterium sp.*	NR
	Control	6					
Ramakrishnan, 2015	CRS	56	1662	NR	19.4	*Staphylococcus sp.*	NR
	Control	26	1779		21.4	*Staphylococcus sp.*	
Liu, 2015	Control, NI	18	4856	76	18.3	*Proprionibacterium sp.*	13.2
	Control, I	10			14.5		
	CRSwNP, NI	7			22.4		
	CRSwNP, I	7			18.7		

CONCLUSIONS

- DNA Sequencing techniques have proven to be more effective than traditional culture methods in identifying the total bacterial community present in patients with CRS.
- Molecular techniques have also demonstrated a difference in the composition and the relative of abundance of the microbiome in CRS patients and healthy control patients.
- Molecular techniques are being further used to characterize different CRS states, response to irrigation, response to antibiotics, etc.

Future Directions

- Majority of studies are from a single time-point: **more longitudinal studies are needed.**
- Sampling technique and sampling site may contribute to experimental variability: **continue to study and refine sampling techniques to maximize yield and reduce contamination.**
- Comorbidities may contribute to variation in CRS and control patients: **consistently report comorbidities**
- Experimental data included in results is heterogeneously reported: **standardization of included data will allow comparison of experimental quality**