

# Mining the infant gut microbiota for therapeutic targets against atopic disease

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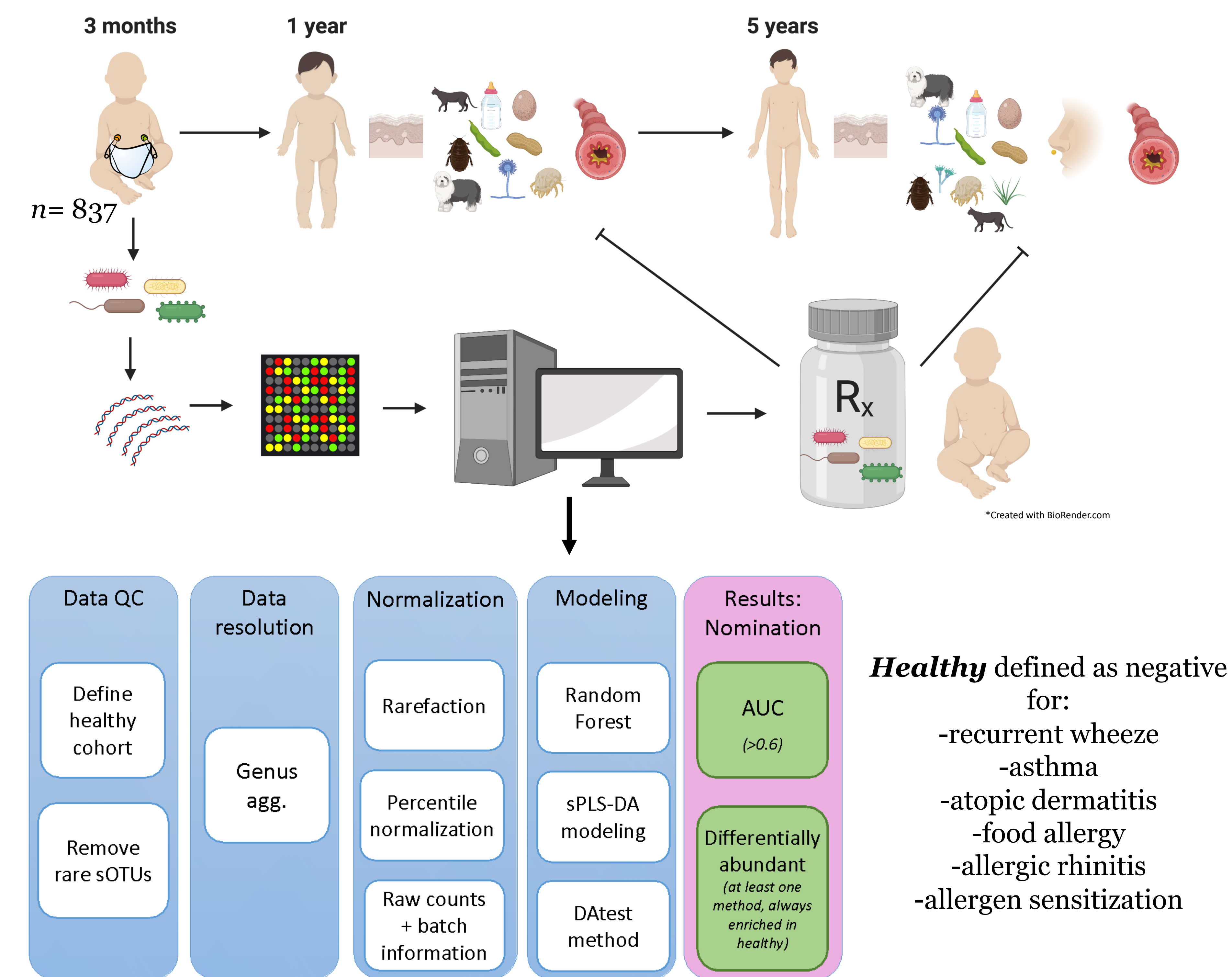
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## Background

- Atopic disease prevalence has risen dramatically in recent decades<sup>1,2</sup>
- Many atopic diseases are considered incurable
- Gut microbial dysbiosis in early life may precede atopic disease onset<sup>1-4</sup>
- Supplementation with 'missing' microbes in early life as a live biotherapeutic product (LBP) may represent a novel means of treating, curing, and/or preventing atopic diseases<sup>1-3,5</sup>

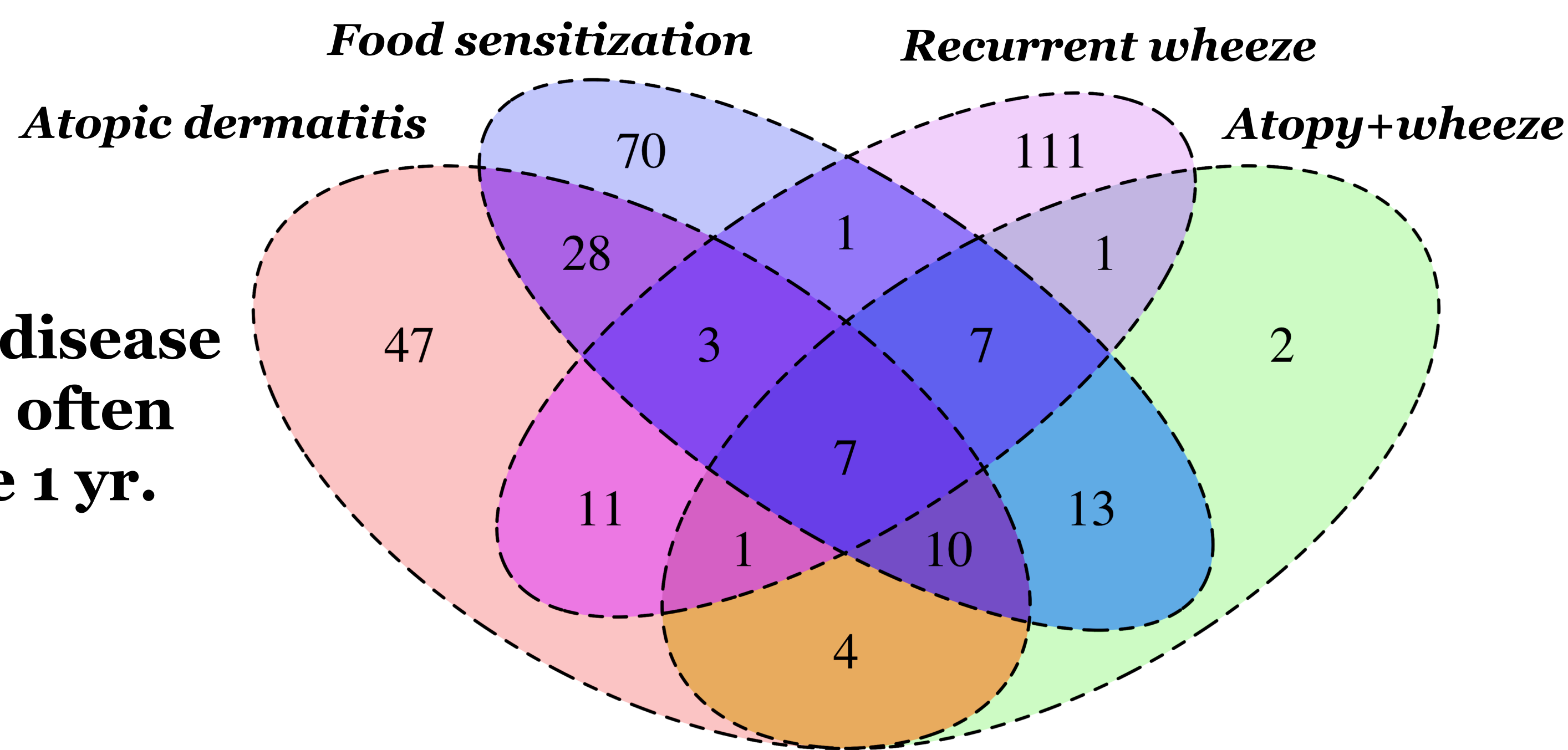
## Experimental design & methods

**Figure 1:** Bacterial taxa were nominated for inclusion in an atopic disease-preventative LBP using a series of complementary machine learning approaches to integrate clinical data with 16S rDNA amplicon sequencing data from stool samples collected at 3 months of age.



Subsequently nominated taxa were filtered for prevalence greater than 15% in the healthy children and relative abundances greater than 0.2%.

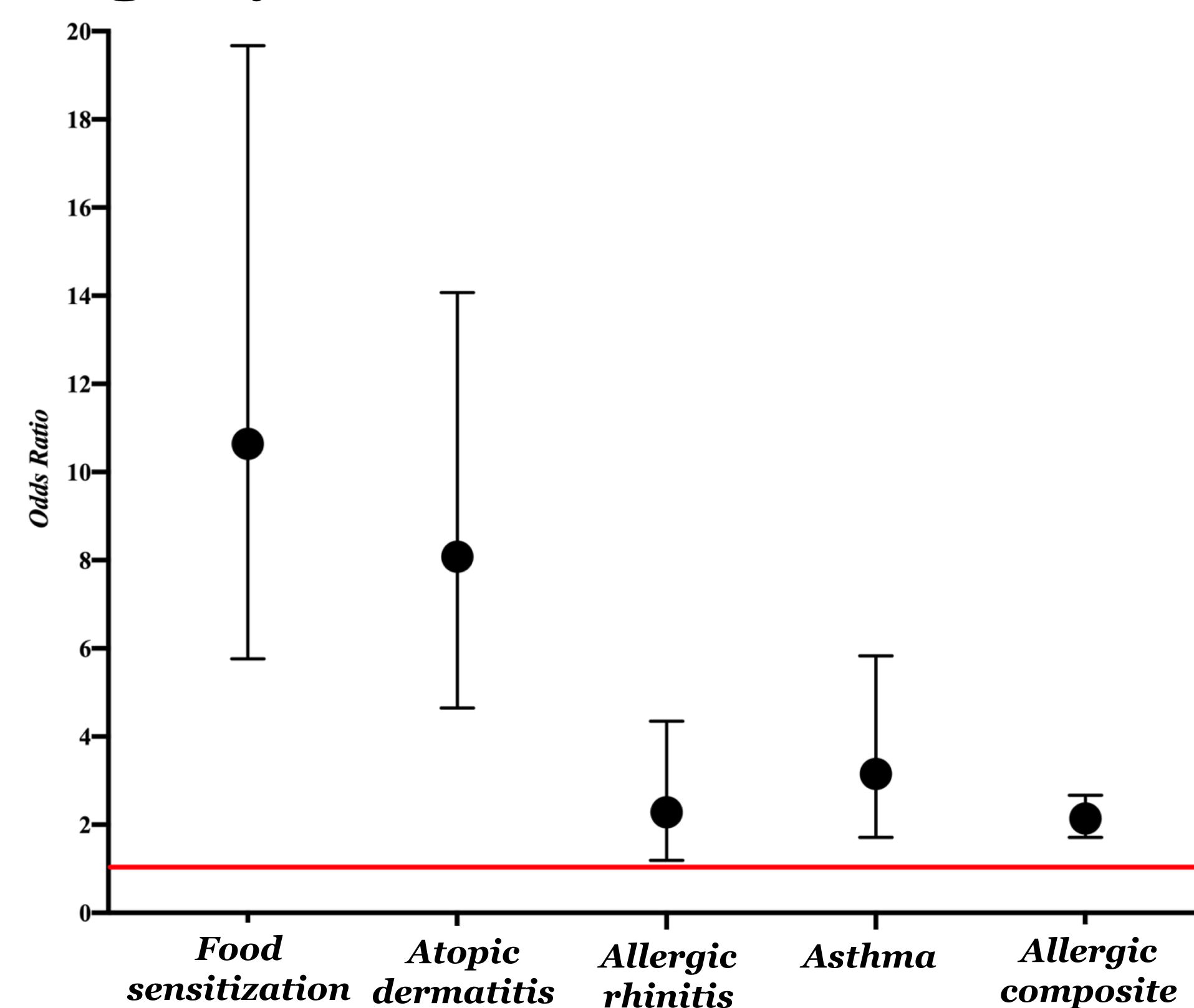
**Figure 2: Atopic disease manifestations often co-occur at age 1 yr.**



## References

<sup>1</sup>Stiemsma LT, Turvey SE. *Allergy, Asthma Clin Immunol.* 2017;13:1-9.; <sup>2</sup>Boutin RCT, Finlay BB. *Curr Treat Options Allergy.* 2016;3:292-309.; <sup>3</sup>Arrieta MC, Stiemsma LT, et al. *Sci Transl Med.* 2015;7:307ra152.; <sup>4</sup>Bokulich NA, et al. *Sci Transl Med.* 2016;8:343-82.; <sup>5</sup>Gilbert JA, et al. *Nature.* 2016;535:94-103. \*Now published: Boutin RCT<sup>†</sup>, Sbihi H<sup>†</sup>, Dsouza M<sup>†</sup>, Malhotra R,<sup>‡</sup> et al. *Allergy.* DOI: 10.1111/all.14244\*

**Figure 3: Children with a positive atopic composite score at age 1 yr are at increased risk of allergic disease at age 5 yrs.**



- 1 yr atopic manifestations predict allergic outcomes at age 5 yrs
- 1 yr outcomes can be used as a proxy for later allergic disease outcomes and represent a realistic target for clinical trials

- Atopic composite: two or more atopic indications at age 1 yr
- Allergic composite: two or more of asthma, allergic rhinitis, atopic dermatitis, and food sensitization at age 5 yrs

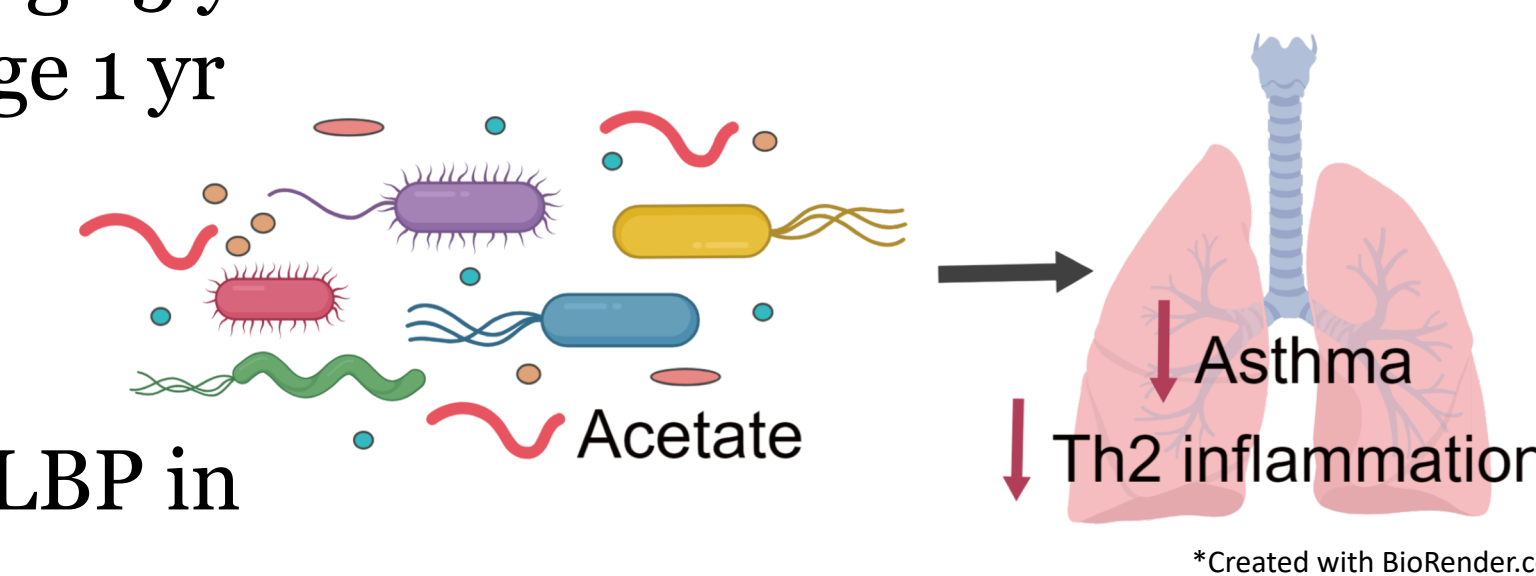
**Table 1: Bacterial genera nominated for inclusion in a live biotherapeutic product protective against atopic disease.**

Nominated genera	Atopic dermatitis	Food sensitization	Recurrent Wheeze	Atopy + Wheeze
<i>Faecalibacterium</i> *	✓	✓	✓	✓
<i>Lachnospira</i> <sup>†</sup>		✓	✓	✓
<i>Coprococcus</i> <sup>†</sup>	✓	✓	✓	✓
<i>Oscillospira</i> *	✓	✓	✓	
<i>Roseburia</i> * <sup>◇</sup>	✓	✓	✓	✓
<i>Blautia</i> *	✓	✓		✓
<i>Dorea</i>	✓	✓		
<i>Parabacteroides</i>	✓			✓
<i>Ruminococcus</i> *	✓	✓		✓

\*=known butyrate producer; <sup>†</sup>=known acetate producer; <sup>◇</sup>=known propionate producer

## Conclusions & future directions

- Atopic phenotypes at age 1 yr predict those at age 5 yrs
- Infants with 2+ atopic disease indications at age 1 yr lack certain gut bacteria
- Supplementation with a LBP in infancy may prevent/treat allergic disease
- Future work: determine safety and efficacy of LBP in mice and humans



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