

#### Gut microbe associations with host genotype vary across ethnicities and potentially influence cardiometabolic traits

Ulrika Boulund, PhD Student at Experimental Vascular Medicine department Supervisor: Max Nieuwdorp



### Cell Host & Microbe

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Gut microbiome associations with host genotype vary across ethnicities and potentially influence cardiometabolic traits

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Ulrika Boulund • Diogo M. Bastos • Bart Ferwerda • ... Albert K. Groen • Aeilko H. Zwinderman • Max Nieuwdorp  $2^{5}$   $\sim$  • Show all authors • Show footnotes

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#### Poster # 2

Longitudinal study on the variation of the human gut microbiome composition in a multi-ethnic cohort and its predictive relationship with metabolic health

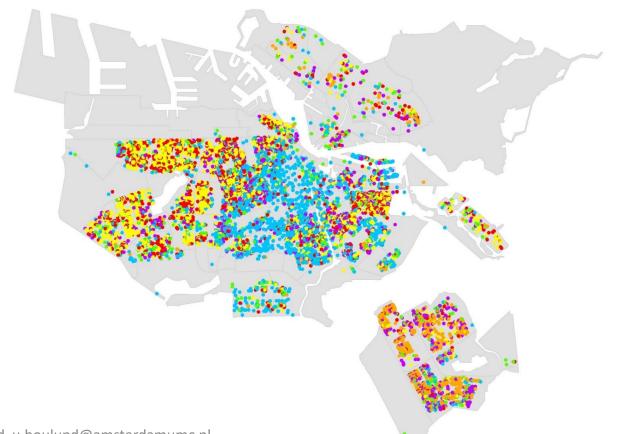


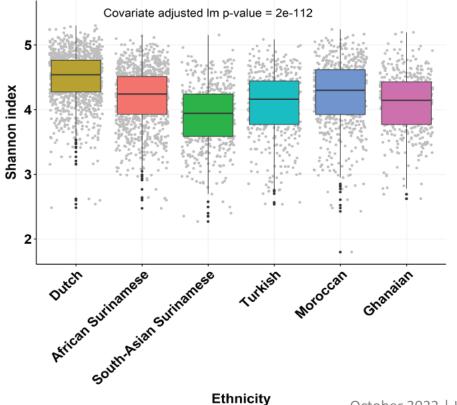


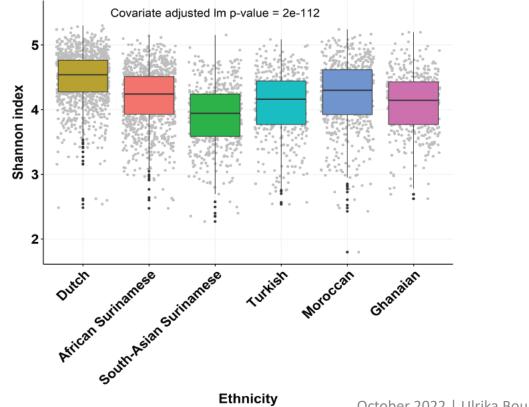
### Healthy Life in an urban setting

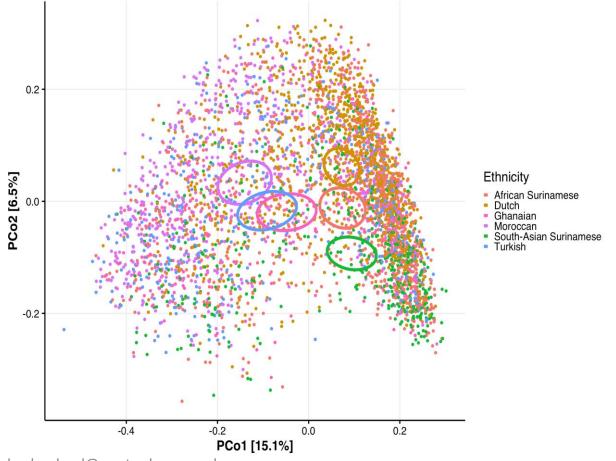
First data collection: 2011-2015

25.000 participants6 different ethnicitiesAge 18-70 years





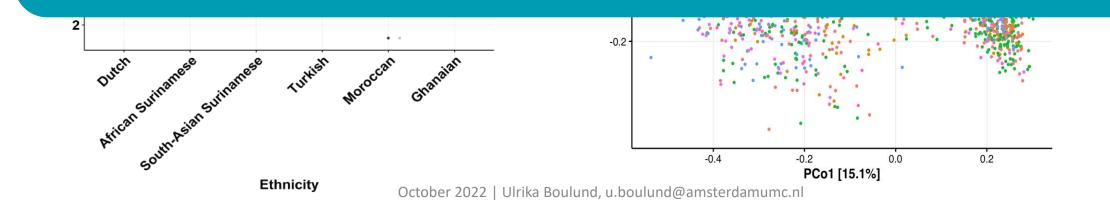




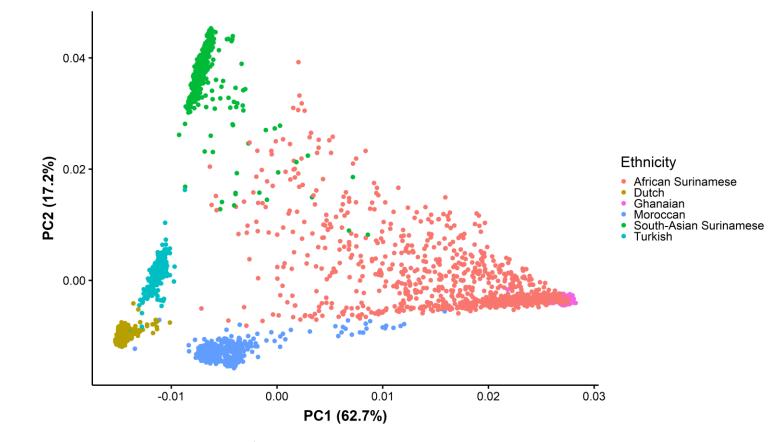
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Covariate adjusted Im p-value = 2e-112

What about 'ethnicity' influences the gut microbiome composition?



### Ethnicity is many things, including genotype

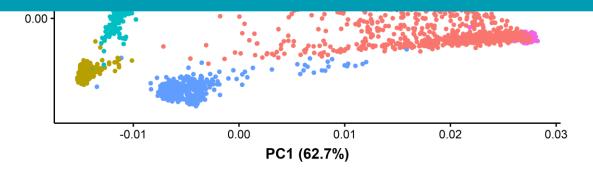


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### Ethnicity is many things, including genotype

0.04

Does the human genome influence the gut microbiome composition?





Microbe-associated loci are related to:

- Immune system
- ABO/FUT2 gene
- Vitamin D receptor
- Mucus genes



Microbe-associated loci are related to:

- Immune system
- ABO/FUT2 gene
- Vitamin D receptor
- Mucus genes
- Small, mainly European cohorts



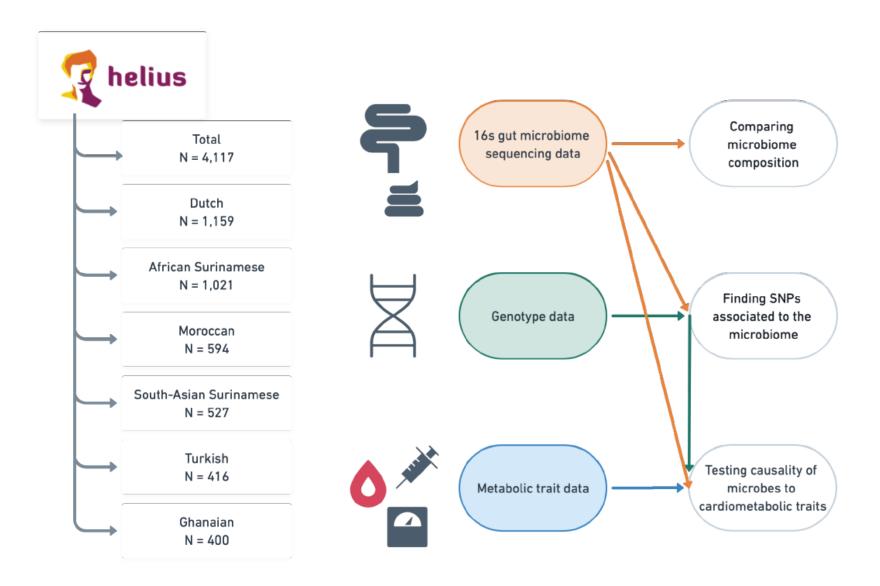
Microbe-associated loci are related to:

- Immune system
- ABO/FUT2 gene
- Vitamin D receptor
- Mucus genes
- Small, mainly European cohorts

What associations are seen in other ethnicities?



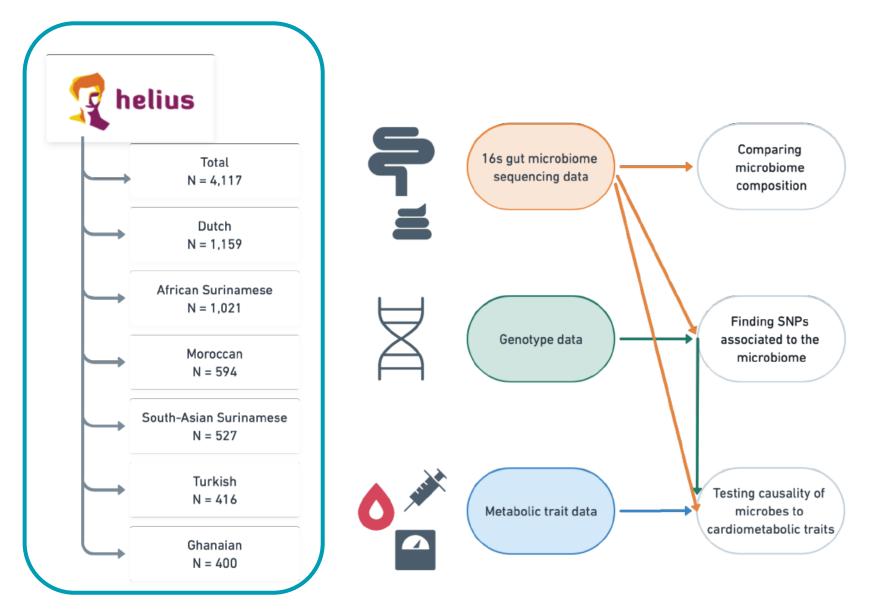
## Study design



### Study design

Largest single-cohort study: N = 8,000

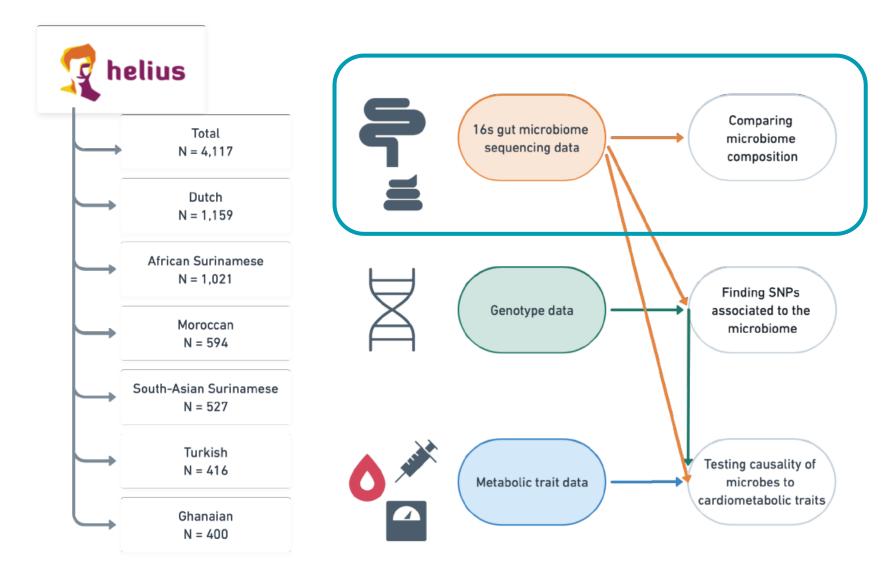
Largest multi-ethnic study: N = 18,000





Largest single-cohort study: N = 8,000

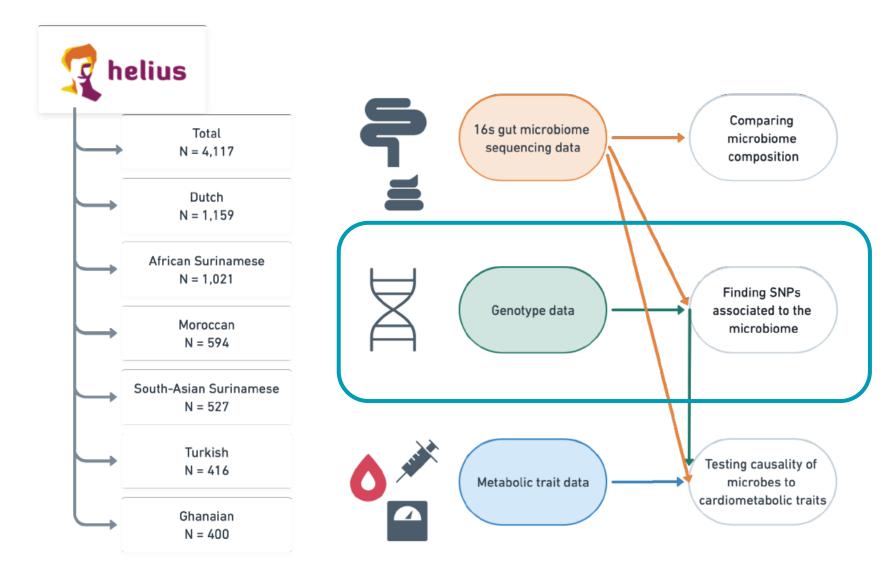
Largest multi-ethnic study: N = 18,000





Largest single-cohort study: N = 8,000

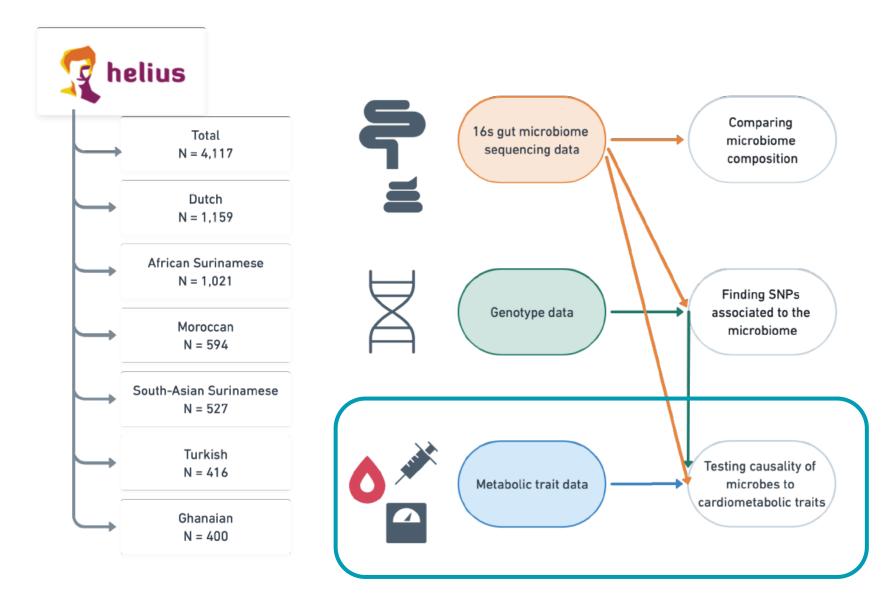
Largest multi-ethnic study: N = 18,000





Largest single-cohort study: N = 8,000

Largest multi-ethnic study: N = 18,000



Which microbes are influenced by the human genome?

Which microbes are influenced by the human genome?

How can the genome influence the human gut microbiome?

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Which gut microbes are potentially causal in cardiometabolic phenotypes?

Which microbes are influenced by the human genome?

How can the genome influence the human gut microbiome?

Which gut microbes are potentially causal in cardiometabolic phenotypes?

Are these effects ethnicity specific?

# Gut microbes exhibit varying heritability

	Victivallales vadinBE97						
	Tenericutes						
	Sutterella						
	Subdoligranulum		•				
	Solobacterium						
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	Senegalimassilia anaerobia Senegalimassilia						
	Ruminococcus 2 bromii-						
	Ruminococcus 1	•					
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	Ruminococcaceae UCG-003						
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	Rikenellaceae RC9 gut group Prevotellaceae NK3B31 group						
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	Prevotella 2						
	Paraprevotella						
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	Mogibacterium						
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ta	Marvinbryantia						
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	Clostridium sensu stricto 1						
	Clostridiales Lachnospiraceae Clostridiales						
	Christensenellaceae R-7 group						
	Christensenellaceae R-7 group Christensenellaceae						
	Blautia faecis						
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	Bacteroides massiliensis						
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	Bacteroidales Muribaculaceae	-					
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	Actinobacteria						
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# Gut microbes exhibit varying heritability

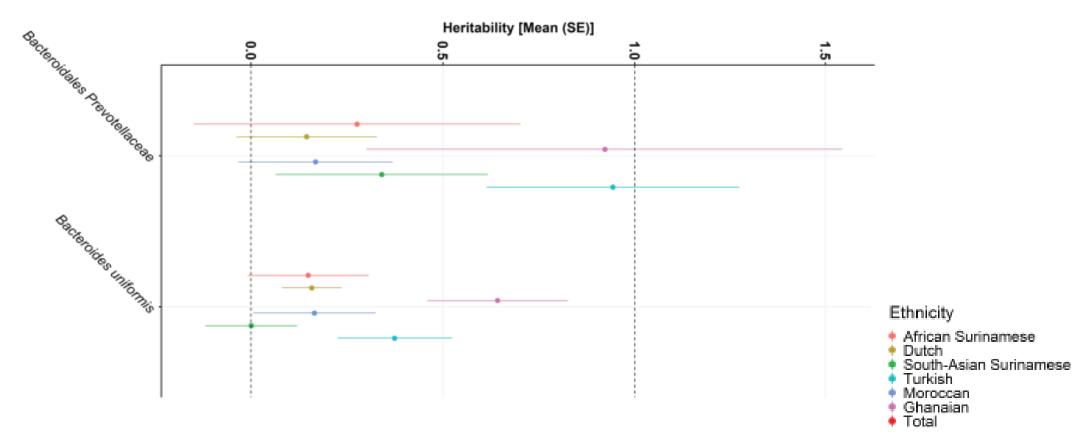
	Victivallales vadinBE97						
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	Subdoligranulum-		•				
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	Senegalimassilia						
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	Ruminiclostridium 6-						
	Rikenellaceae RC9 gut group Prevotellaceae NK3B31 group						
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	Prevotella 9-						
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2	Lachnoclostridium-						
	Intestinimonas						
	Gastranaerophilales						
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	Coprococcus 2						
	Clostridium sensu stricto 1						
	Clostridiales Lachnospiraceae						
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	Blautia faecis-						
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	Bacteroidales Muribaculaceae						
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Which microbes are influenced by the human genome?

# Gut microbes exhibit varying heritability

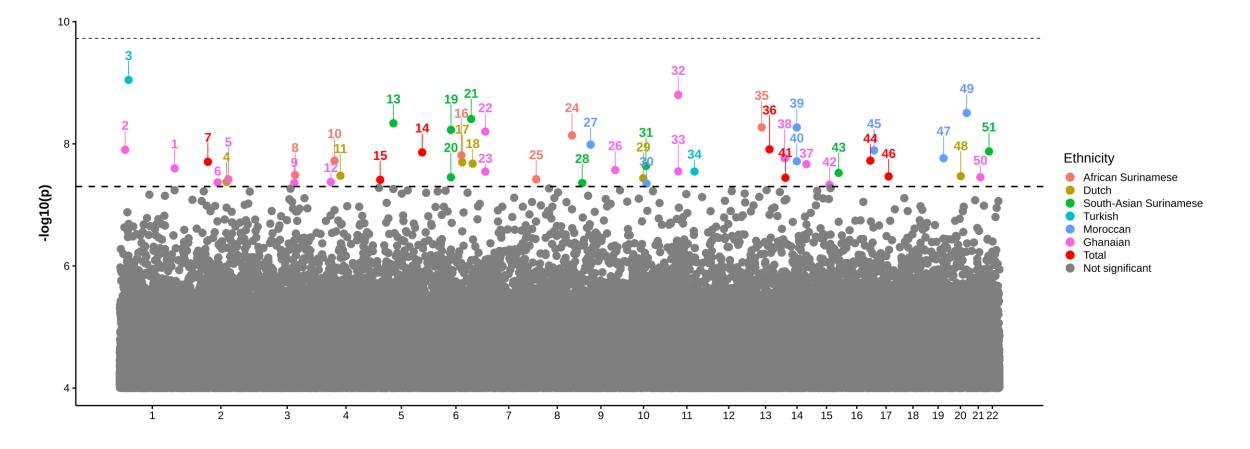
	Victivallales vadinBE97- Tenericutes-	*
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	Sutterella Subdoligranulum	
	Subdoligranulum	
	Solobacterium- Slackia-	
	Senegalimassilia anaerobia-	
	Seneralimassilia	
	Senegalimassilia- Ruminococcus 2 bromii-	
	Ruminococcus 1-	•
	Ruminococcaceae UCG-008-	-
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	Prevotellaceae	-
	Prevotella 9-	
	Prevotella 2-	
	Paraprevotella	-
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	Parabacteroides	
	Oscillibacter-	•
	Olsenella-	
	Muribaculaceae	
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ă	Mitsuokella multacida-	
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.00	Libanicoccus	
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	Gastranaerophilales-	•
	Fournierella	
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	Christensenellaceae R-7 group	
	Christensenellaceae R-7 group Christensenellaceae	+
	Blautia faecis	+
	Blautia	
	Bacteroides uniformist	-
	Bacteroides massiliensis	
	Bacteroides coprocola Bacteroides caccae	
	Bacteroides caccae	
	Bacteroides uniformis-	
	Bacteroidales Prevotellaceae	
	Bacteroidales Muribaculaceae	
	Appemetings hadrus	
	Anaerostipes hadrus Alloprevotella	+
	Actinobacteria	•
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	l.	0.0 0.1 0.2 0.3 0.4 0.5
nc.nl		Heritability [Mean (SE)]
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# Gut microbe heritability differs between ethnicities



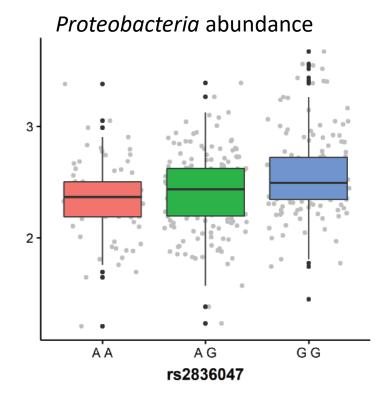
How can the genome influence the human gut microbiome?

# Human genetic loci associated with various gut microbes across ethnic groups



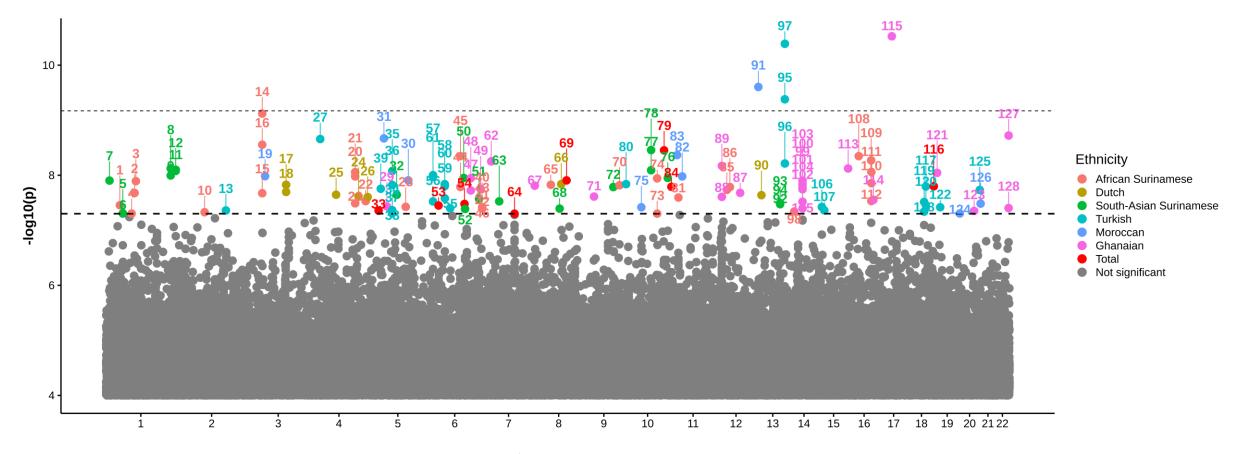
How can the genome influence the human gut microbiome?

# Loci associated with gut microbes are expressed in the pancreas and gut



The *KCNJ6* gene encodes a potassium channel Expressed in the pancreas Regulates insulin secretion

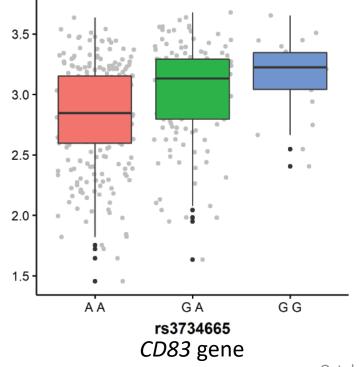
# Human genetic loci associated with various gut microbial pathways across ethnic groups



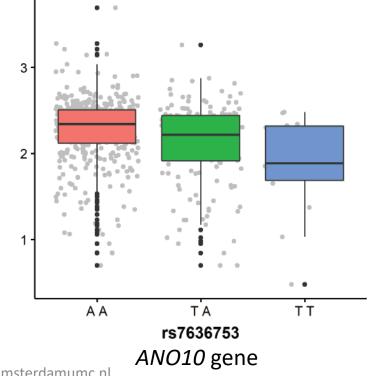
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### Loci associated with microbial pathways are involved in the immune system and expressed in the gut

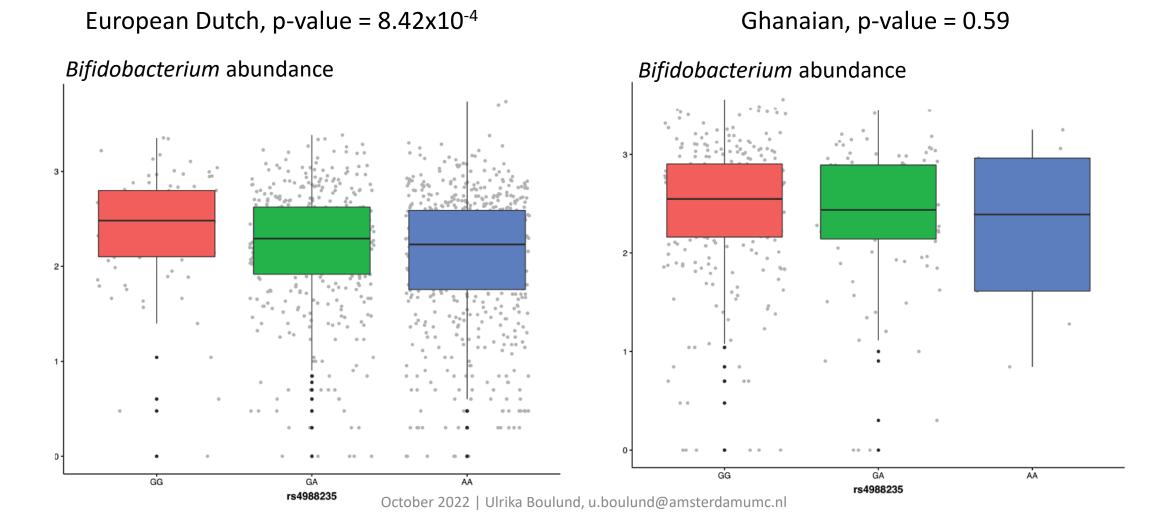
#### Superpathway of pyridoxal 5'-phosphate biosynthesis and salvage

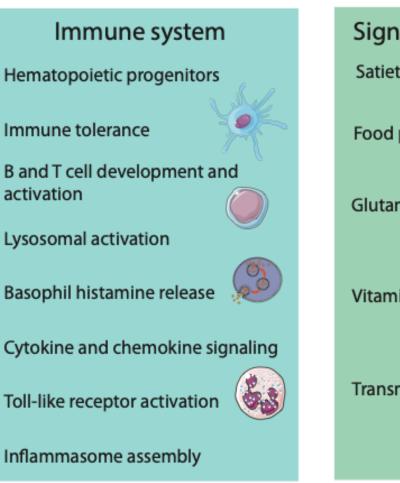


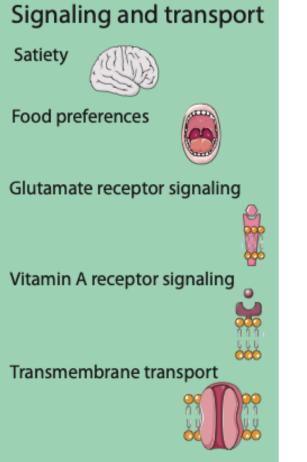
#### Lactose and galactose degradation

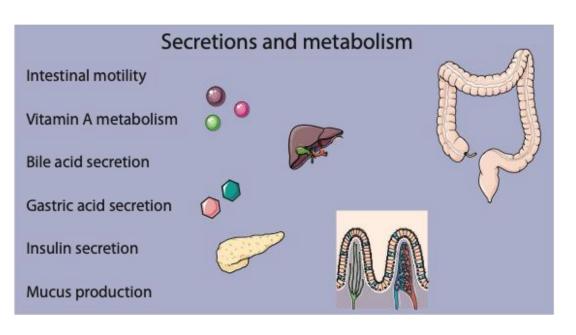


# *Bifidobacterium* is associated with the LCT locus, but this may be ethnicity specific



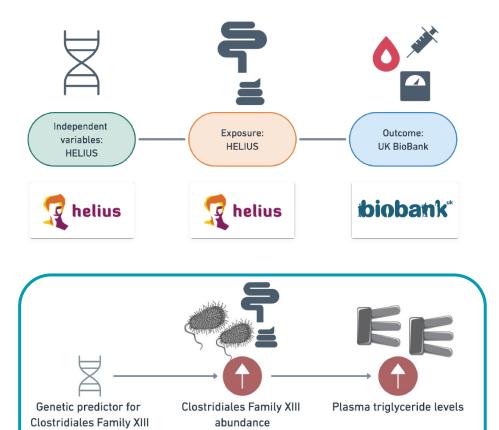




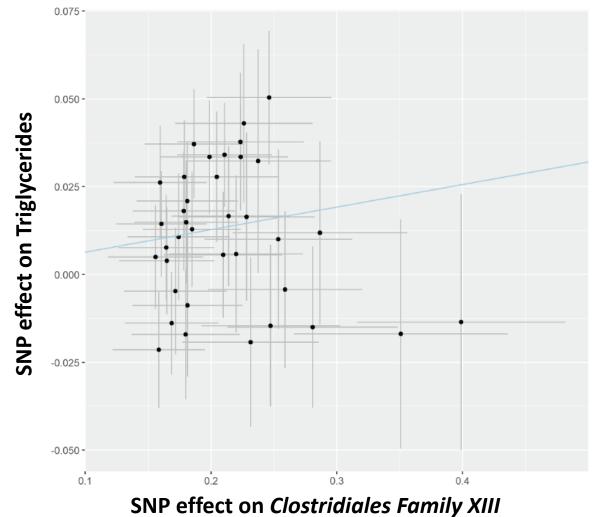


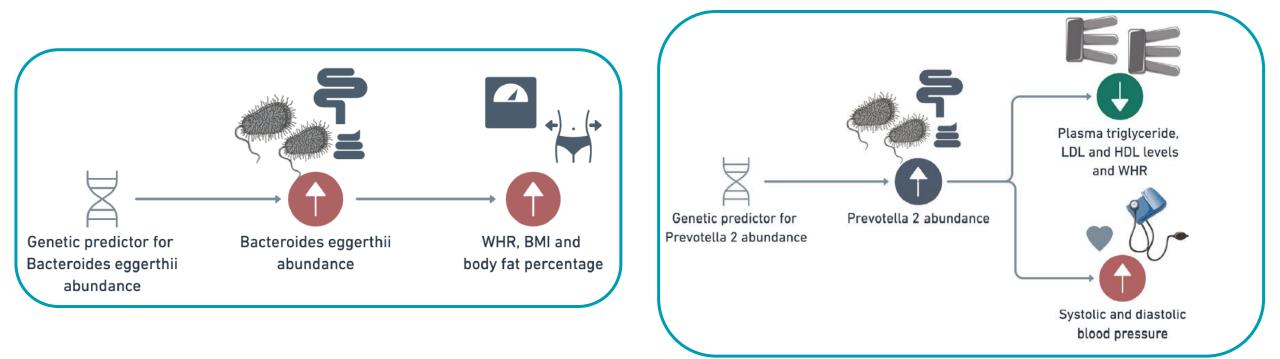
Which gut microbes are potentially causal in cardiometabolic phenotypes?

### Clostridiales Family XIII potentially increases triglycerides



abundance





#### **Ethnicities exhibit different gut-microbe-to-genotype associations**

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Microbe-associated loci are involved in immune functions or intestinal secretions

**Ethnicities exhibit different gut-microbe-to-genotype associations** 

Microbe-associated loci are involved in immune functions or intestinal secretions

Microbe-associated loci are located in genes expressed in the gut and pancreas

**Ethnicities exhibit different gut-microbe-to-genotype associations** 

Microbe-associated loci are involved in immune functions or intestinal secretions

Microbe-associated loci are located in genes expressed in the gut and pancreas

Gut microbes may influence cardiometabolic health factors

#### Future prospects

**Expanding cohorts in size and diversity** 

#### Future prospects

**Expanding cohorts in size and diversity** 

**Characterize genome associated microbes** 

#### Future prospects

**Expanding cohorts in size and diversity** 

**Characterize genome associated microbes** 

Mechanistic studies of potentially causal microbes

### Acknowledgements

**Diogo Mendes Bastos** 

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Henrike Galenkamp

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Max Nieuwdorp





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