

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

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

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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

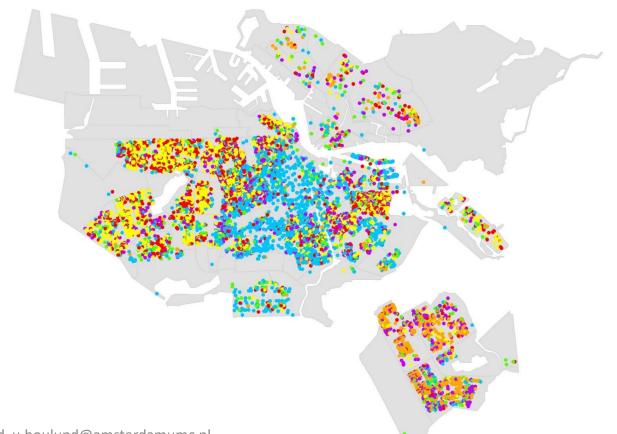


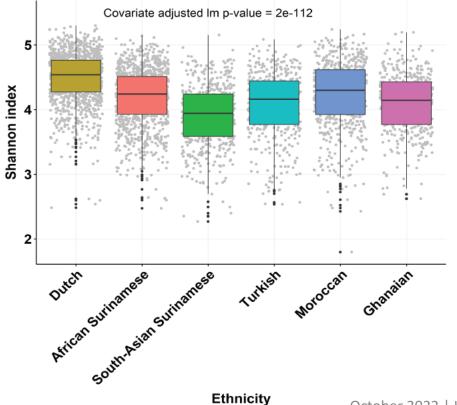


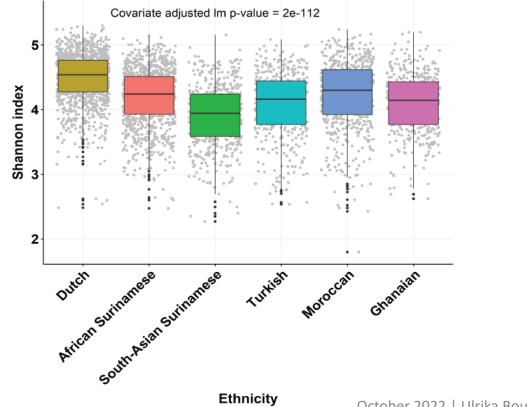
Healthy Life in an urban setting

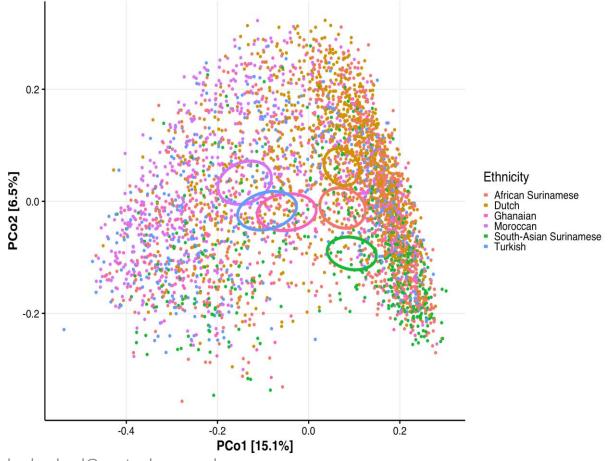
First data collection: 2011-2015

25.000 participants6 different ethnicitiesAge 18-70 years





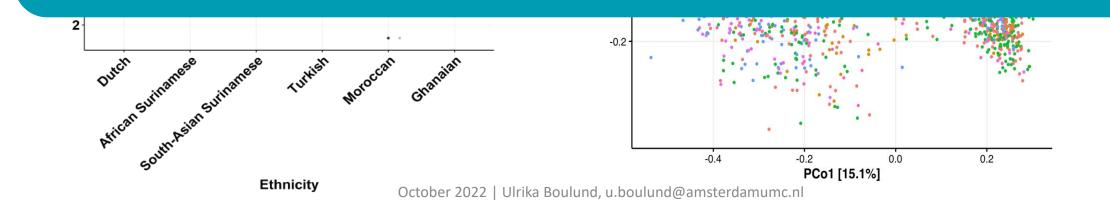




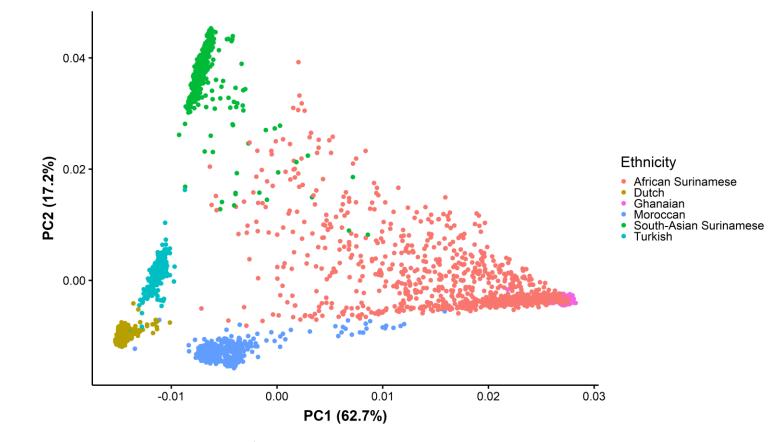
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Covariate adjusted Im p-value = 2e-112

What about 'ethnicity' influences the gut microbiome composition?



Ethnicity is many things, including genotype

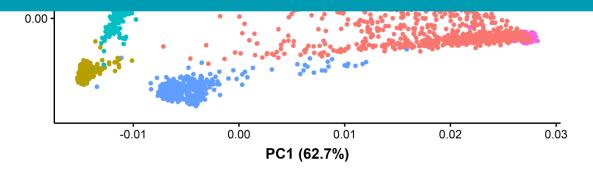


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Ethnicity is many things, including genotype

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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



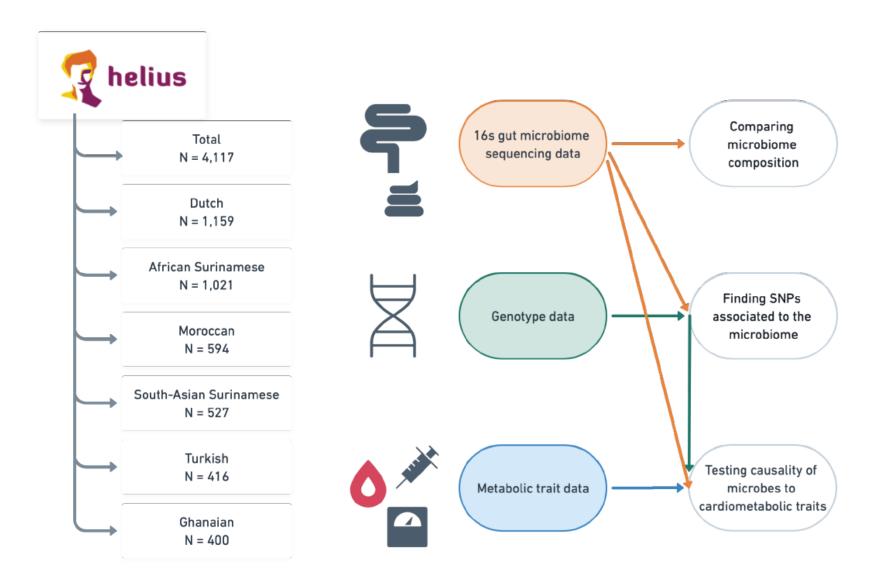
Microbe-associated loci are related to:

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

What associations are seen in other ethnicities?



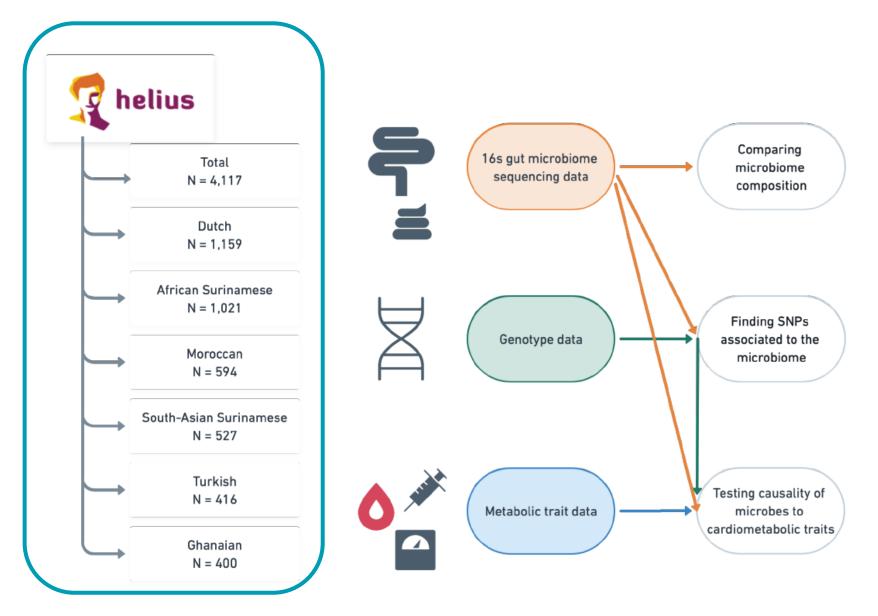
Study design



Study design

Largest single-cohort study: N = 8,000

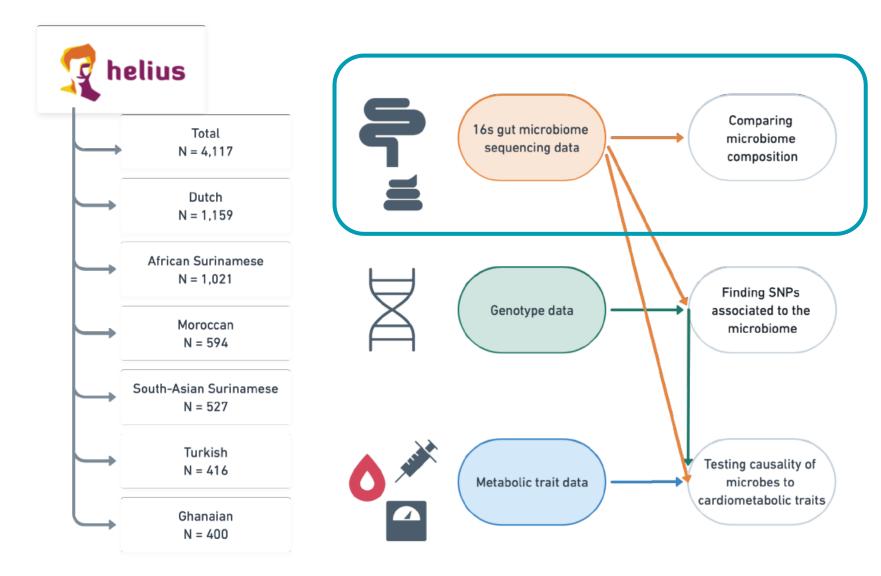
Largest multi-ethnic study: N = 18,000





Largest single-cohort study: N = 8,000

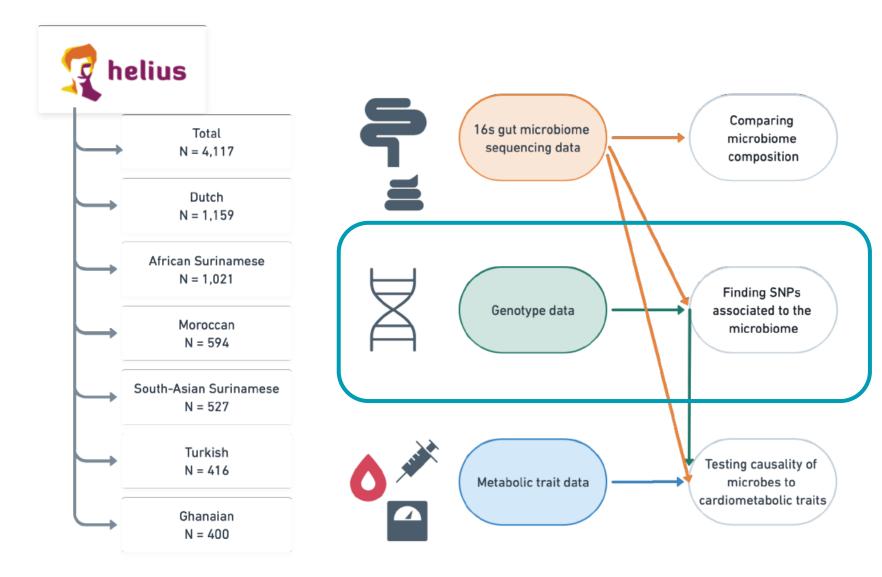
Largest multi-ethnic study: N = 18,000





Largest single-cohort study: N = 8,000

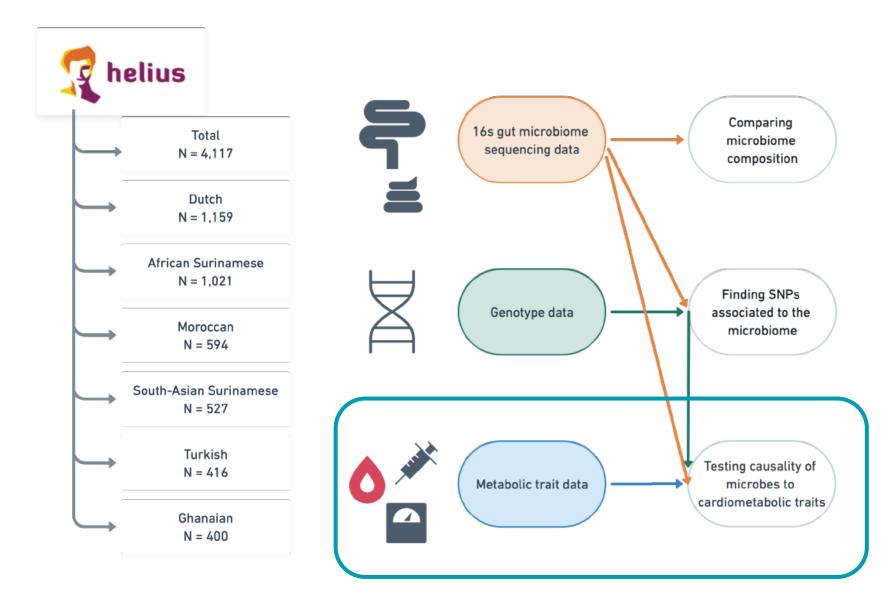
Largest multi-ethnic study: N = 18,000





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?

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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						
	Sanagalimassilia apagrahia						
	Senegalimassilia anaerobia Senegalimassilia						
	Ruminococcus 2 bromii-						
	Ruminococcus 1	•					
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	Ruminococcaceae UCG-0051		•				
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	Ruminococcaceae NK4A214 group						
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	Rikenellaceae RC9 gut group Prevotellaceae NK3B31 group						
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	Prevotella 2						
	Paraprevotella						
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	Olsenella						
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2	Lachnoclostridium						
	Intestinimonas						
	Gastranaerophilales	•					
	Fournierella						
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	Desulfovibrio	-					
	Coriobacteriales Eggerthellaceae						
	Coprococcus 2 eutactus	•					
	Coprococcus 2						
	Clostridium sensu stricto 1						
	Clostridiales Lachnospiraceae Clostridiales						
	Christensenellaceae R-7 group						
	Christensenellaceae R-7 group Christensenellaceae						
	Blautia faecis						
	Blautia	•					
	Bacteroides uniformis						
	Bacteroides massiliensis						
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	Alloprevotella						
	Actinobacteria						
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Gut microbes exhibit varying heritability

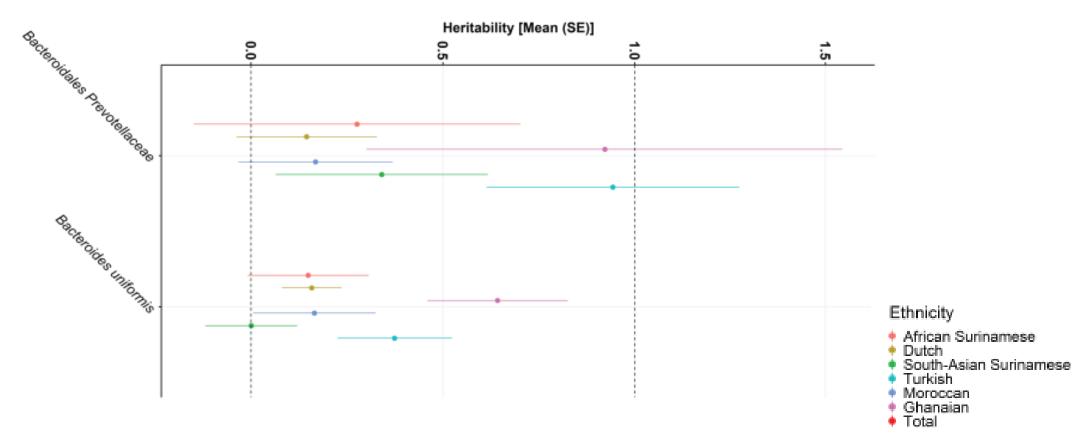
	Victivallales vadinBE97						
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	Sutterella						
	Subdoligranulum-		•				
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	Senegalimassilia						
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	Prevotella 9-						
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	Paraprevotella						
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Microbial taxa	Libanicoccus						
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	Intestinimonas						
	Gastranaerophilales						
	Fournierella						
	Flavonifractor plautii-						
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	Coriobacteriales Eggerthellaceae Coprococcus 2 eutactus						
	Coprococcus 2						
	Clostridium sensu stricto 1						
	Clostridiales Lachnospiraceae						
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	Bacteroidales Muribaculaceae						
	Anaerostipes hadrus					-	
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Which microbes are influenced by the human genome?

Gut microbes exhibit varying heritability

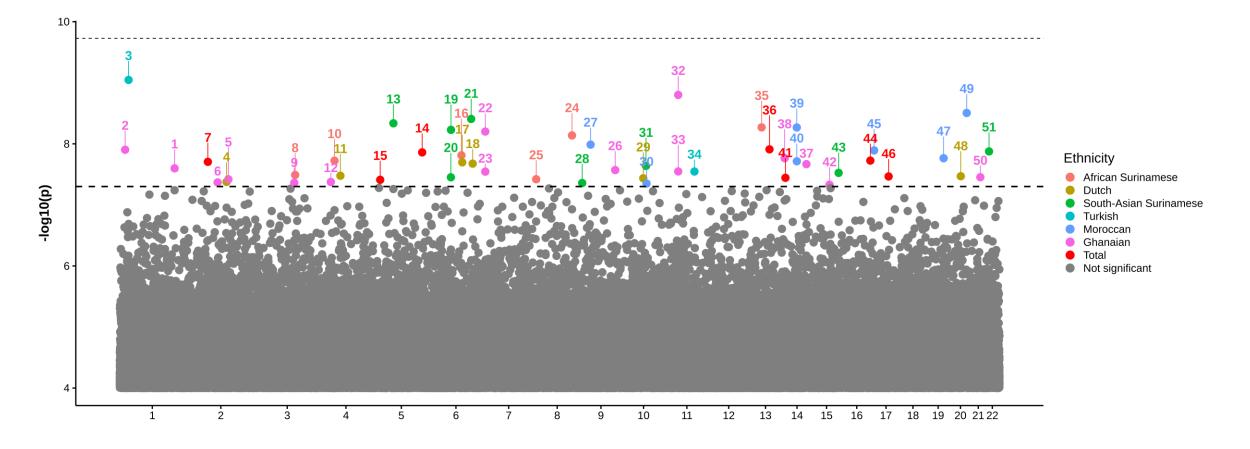
	Victivallales vadinBE97- Tenericutes-	*
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	Sutterella Subdoligranulum	
	Subdoligranulum	
	Solobacterium- Slackia-	
	Senegalimassilia anaerobia-	
	Seneralimassilia	
	Senegalimassilia- Ruminococcus 2 bromii-	
	Ruminococcus 1-	•
	Ruminococcaceae UCG-008-	-
	Ruminococcaseae UCG-008 Ruminococcaseae UCG-008 Ruminococcaseae UCG-005 Ruminococcaseae UCG-004 Ruminococcaseae UCG-004	
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	Rikenellaceae RC9 gut group Prevotellaceae NK3B31 group	
	Prevotellaceae	-
	Prevotella 9-	
	Prevotella 2-	
	Paraprevotella	-
	Parabacteroides distasonis-	•
	Parabacteroides	
	Oscillibacter-	•
	Olsenella-	
	Muribaculaceae	
50	Mogibacterium	
ă	Mitsuokella multacida-	
4	Marvinbryantia-	
.00	Libanicoccus	
9	Lachnospiraceae UCG-001 Lachnospiraceae NK4A136 group	
Microbial taxa	Lachnospiraceae	
₿	Lachnospira	
2	Lachnoclostridium-	**
	Intestinimonas-	
	Gastranaerophilales-	•
	Fournierella	
	Flavonifractor plautii Flavonifractor	
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	Coprococcus 2-	
	Clostridium sensu stricto 1-	
	Clostridiales Lachnospiraceae	•
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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	•
		0.0 0.1 0.2 0.2 0.1 0.5
	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



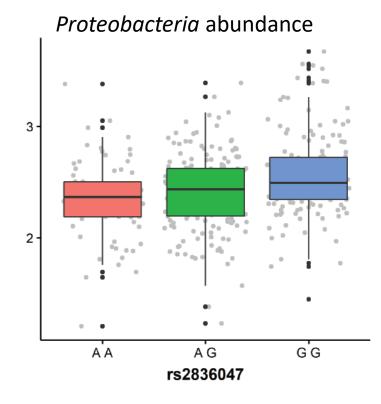
How can the genome influence the human gut microbiome?

Human genetic loci associated with various gut microbes across ethnic groups



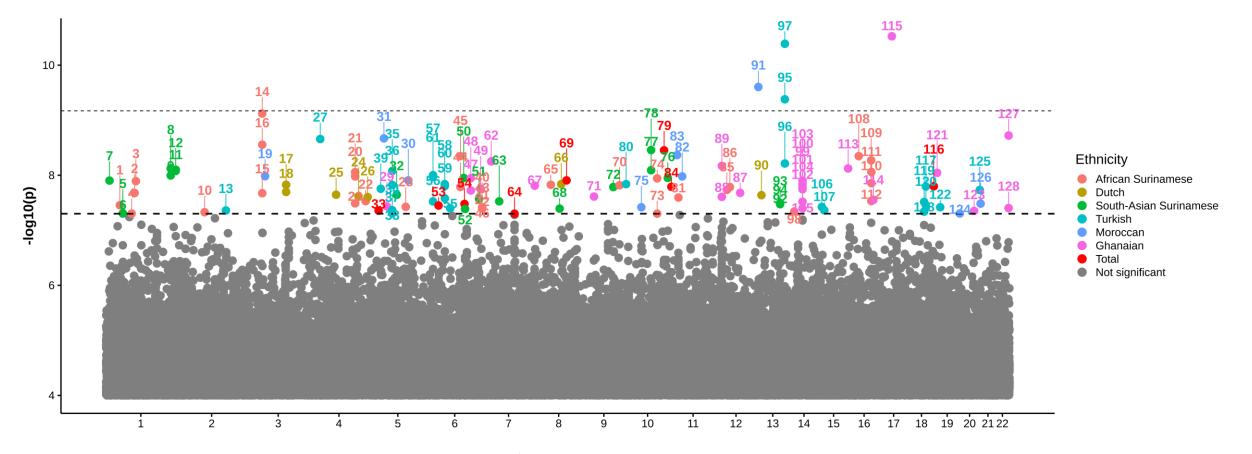
How can the genome influence the human gut microbiome?

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

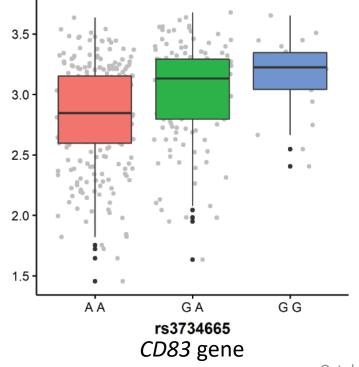
Human genetic loci associated with various gut microbial pathways across ethnic groups



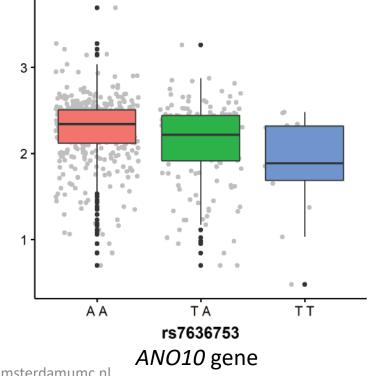
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Loci associated with microbial pathways are involved in the immune system and expressed in the gut

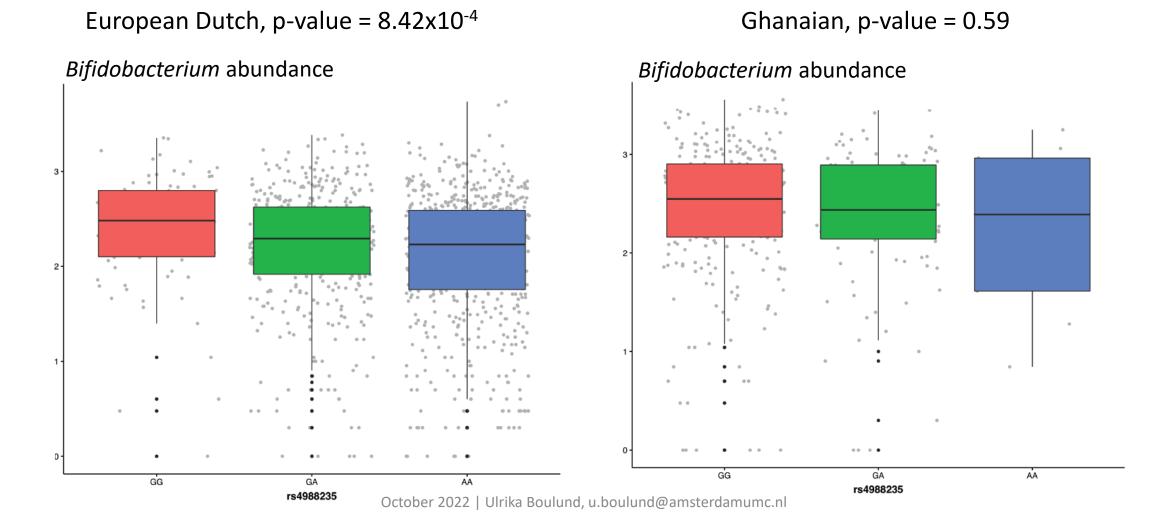
Superpathway of pyridoxal 5'-phosphate biosynthesis and salvage

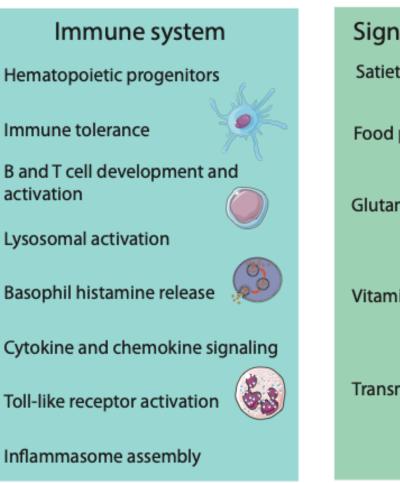


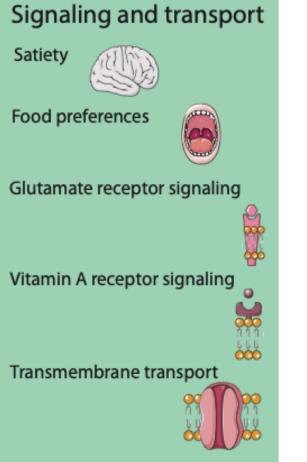
Lactose and galactose degradation

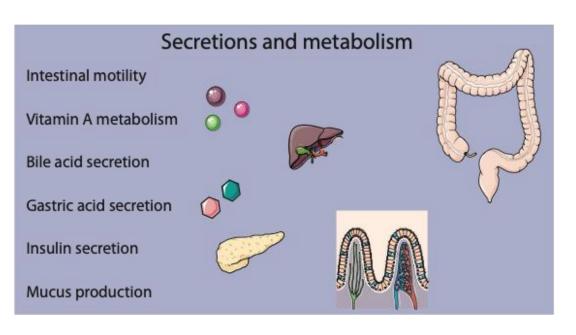


Bifidobacterium is associated with the LCT locus, but this may be ethnicity specific



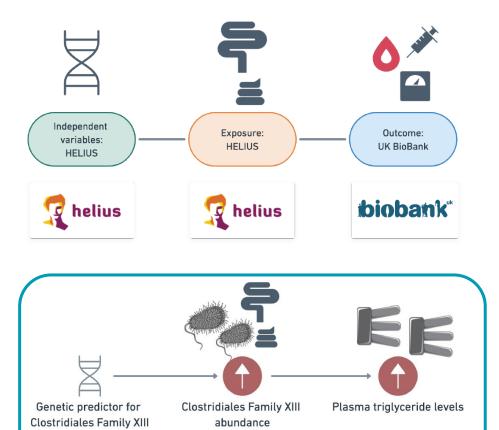




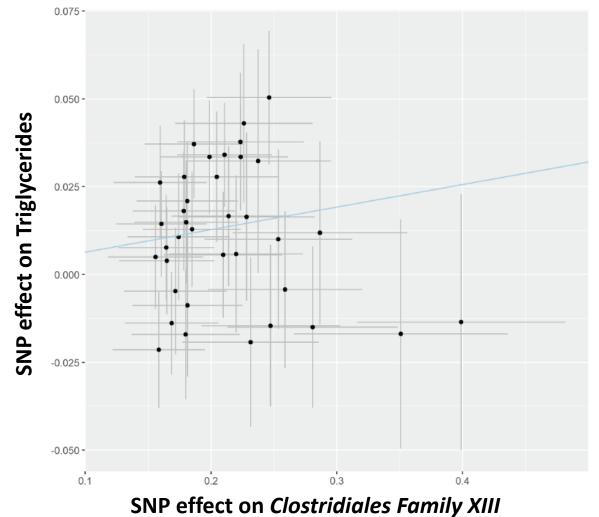


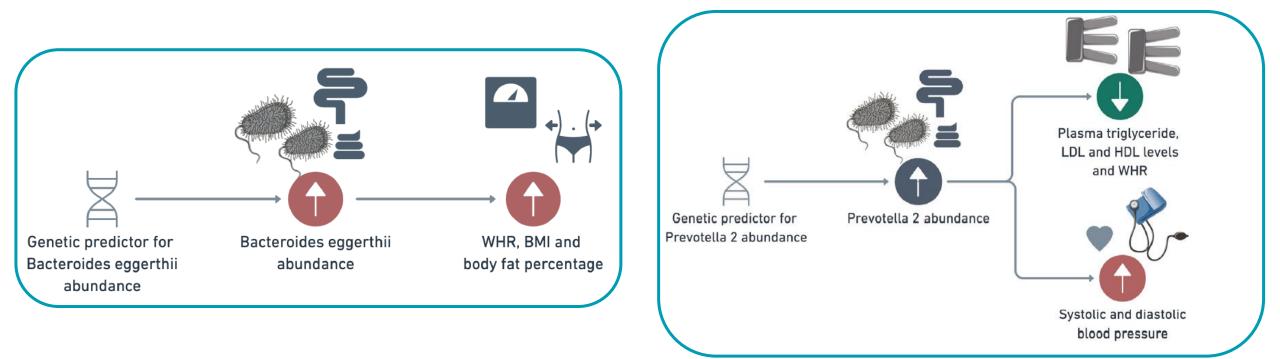
Which gut microbes are potentially causal in cardiometabolic phenotypes?

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

Bart Ferwerda

Bert-Jan van den Born

Sara Joan Pinto-Sietsma

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Evgeni Levin

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Max Nieuwdorp





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