Dissecting complex traits in pigs: metabotypes illuminate genomics for practical applications

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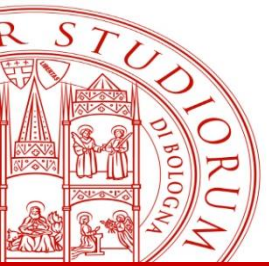
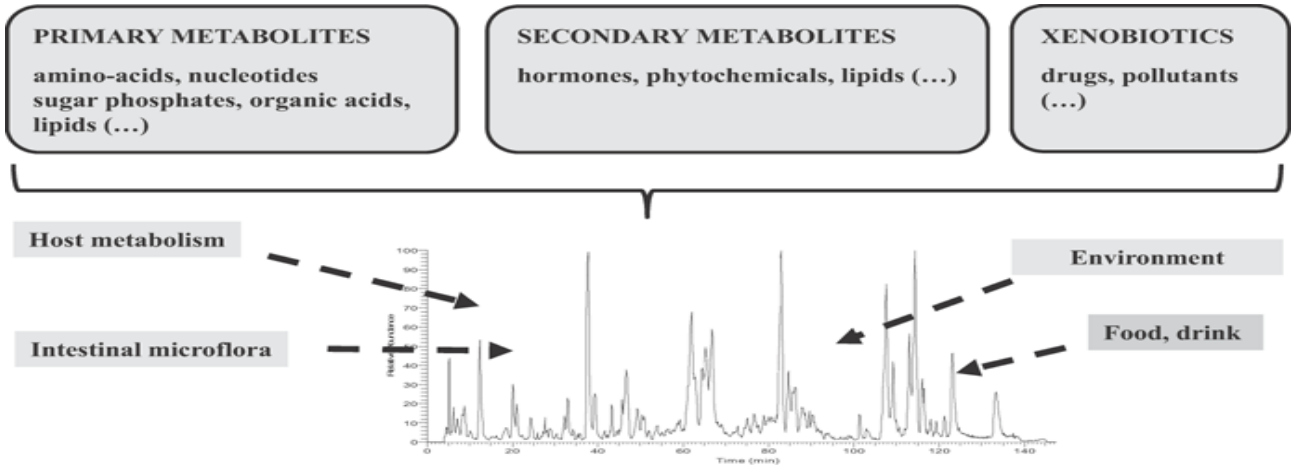
Metabolomics



Metabolomics measures all endogenous metabolites of a tissue or body fluid under given conditions



From Junot et al. 2014

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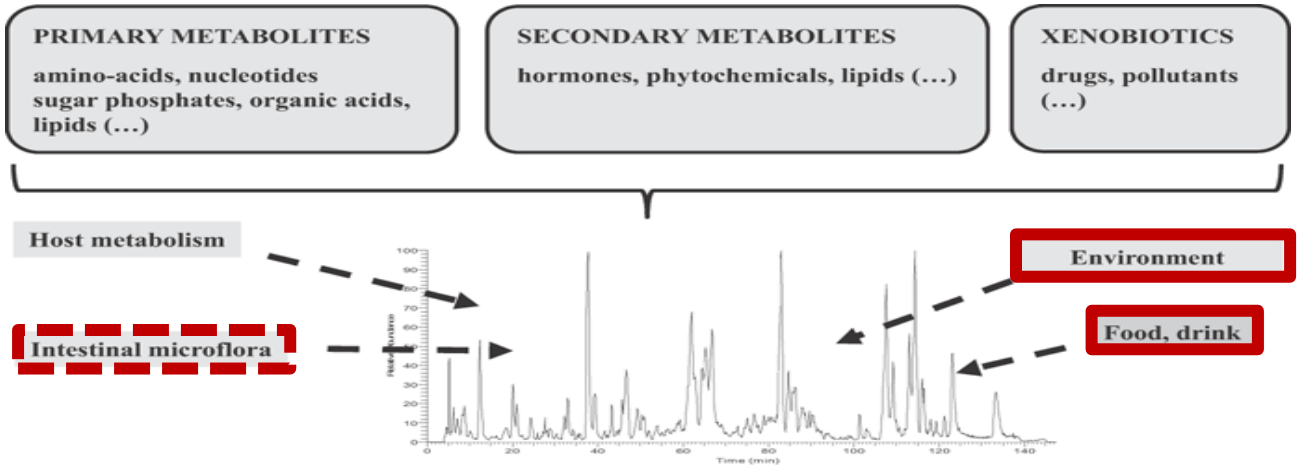

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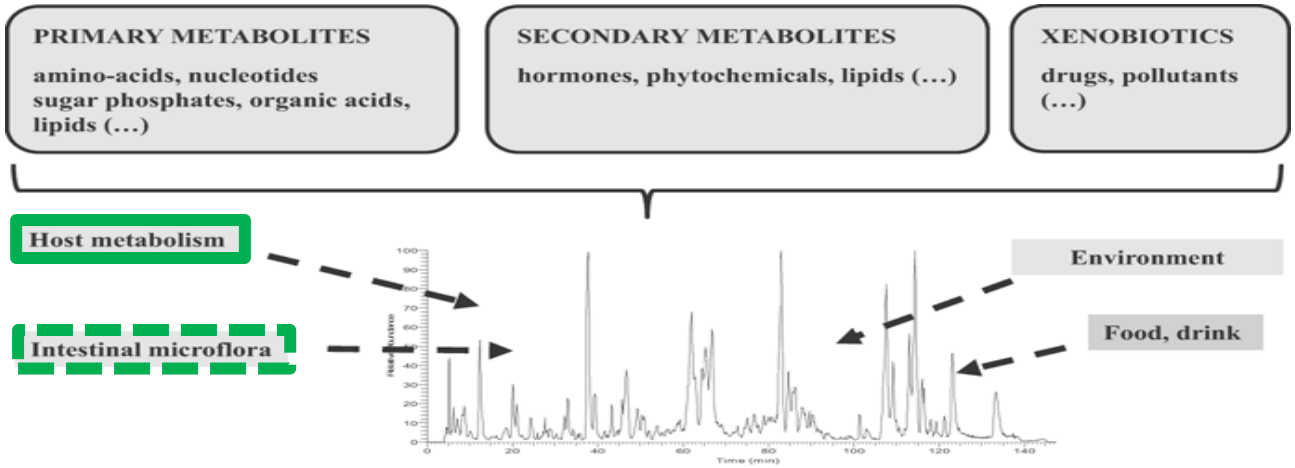

From Junot et al. 2014

Animal resources

~15,000 performance tested Italian Large White

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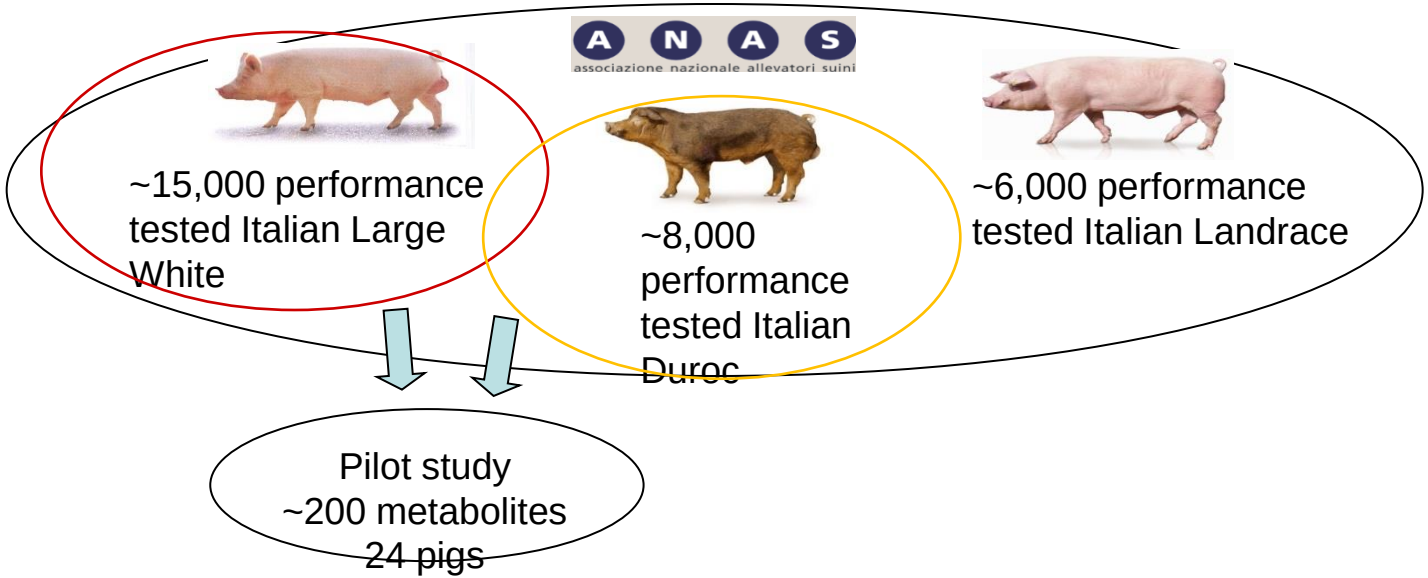
associazione nazionale allevatori suini

~8,000 performance tested Italian Duroc

~6,000 performance tested Italian Landrace

Animal resources



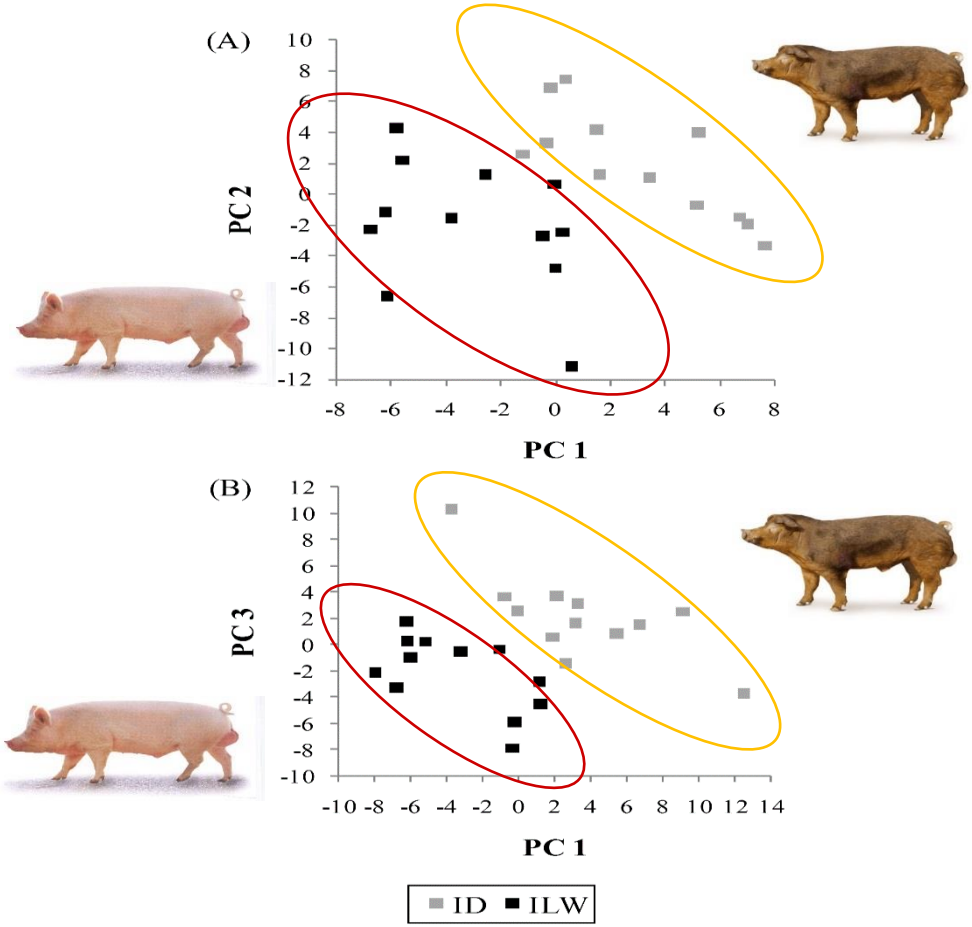
Metabolomic differences between two pig breeds

METABOTYPES

Metabolyte classes	No.	Biological relevance (selected examples)
Acylcarnitines	40	Energy metabolism, fatty acid transport and mitochondrial fatty acid oxidation, ketosis, oxidative stress, mitochondrial membrane damage (apoptosis)
Amino acids	21	Amino acid metabolism, urea cycle, activity of gluconeogenesis and glycolysis, insulin sensitivity/resistance, neurotransmitter metabolism, oxidative stress
Biogenic amines	19	Neurological disorders, cell proliferation, cell cycle progression, DNA stability, oxidative stress
Hexoses	1	Carbohydrate metabolism
Glycerophospholipids	90	
- lysoPhosphatidylcholine acyl – lysoPC a Cx:x	14	Degradation of phospholipids (phospholipase activity), membrane damage, signalling cascades, fatty acid profile
- Phosphatidylcholine diacyl – PC aa Cx:x	38	Dyslipidemia, membrane composition and damage, fatty acid profile, activity of desaturases
- Phosphatidylcholine acyl-alkyl – PC ae Cx:x	38	
Sphingolipids	15	Signalling cascades, membrane damage (e.g. neurodegeneration)

METABOTYPES

Metabolomic differences between **breeds**: Partial Least Square Discriminant Analysis (PLS-DA) on plasma and serum collected on pigs just after jugulation (slaughtering weight of about 160 kg)



METABOTYPES

sPLS results

Biofluid	Metabolic class	Metabolite	ID		ILW		Stability		Significance		Direction
			Mean	SD	Mean	SD	t	P	t	P	
Plasma	Sphingomyelins	SM (OH) C14:1	1.69E+00	1.79E-01	1.40E+00	1.47E-01	24	0.037	0.9066	0	ID
	Biogenic Amines	Ac.Orn	6.93E+00	3.62E+00	14.11E+00	3.07E+00	24	0.064	-1.0855	0.001	ILW
		Kynurenine	4.75E-01	2.53E-01	1.01E+00	2.72E-01	24	0.066	0.1169	0.177	ILW
Serum	Sphingomyelins	SM (OH) C14:1	1.74E+00	2.13E-01	1.37E+00	1.76E-01	24	0.029	0.2798	0.008	ID
		SM (OH) C16:1	2.43E+00	3.90E+00	1.82E+00	2.86E-01	22	0.084	0.2957	0.012	ID
		SM C 16:0	7.44+01	7.12E+00	6.17E+01	5.13E+00	24	0.021	0.3759	0.002	ID
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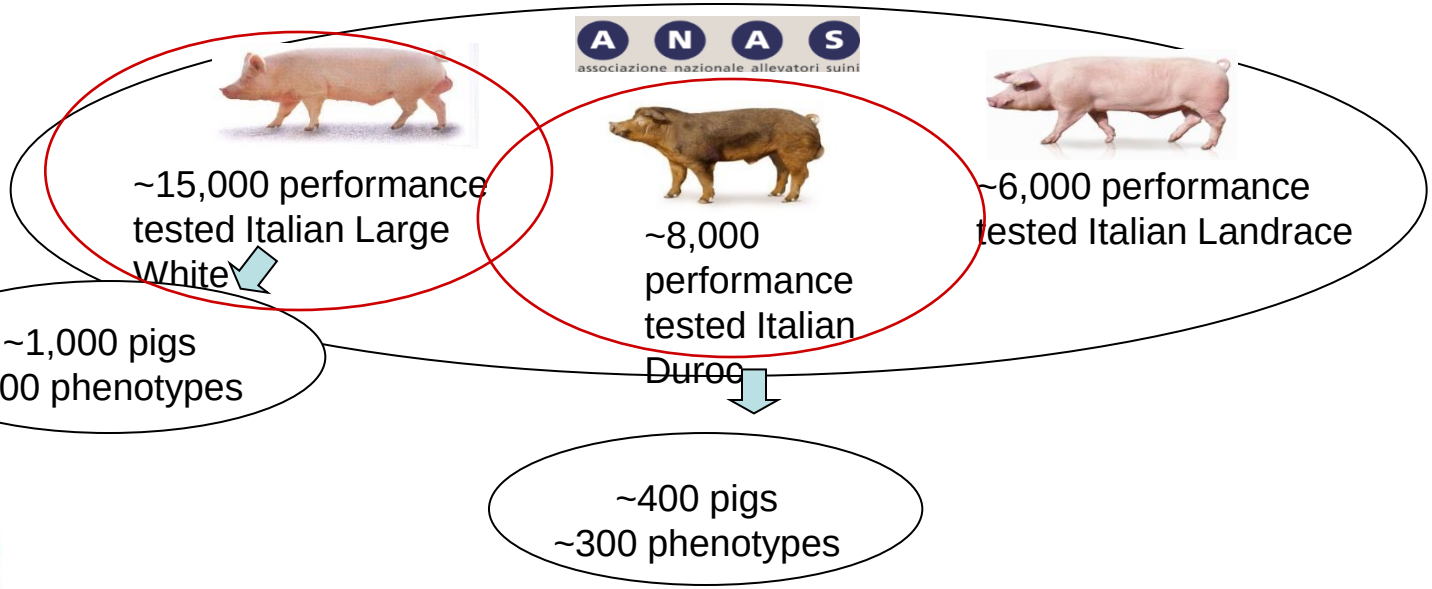
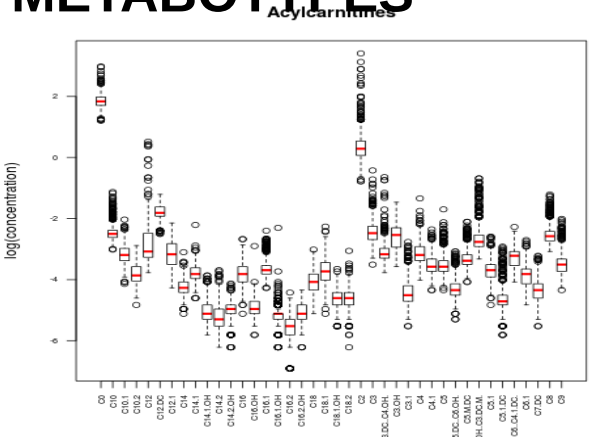
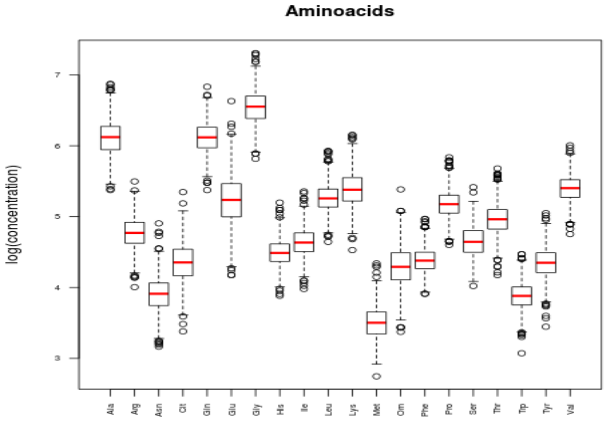
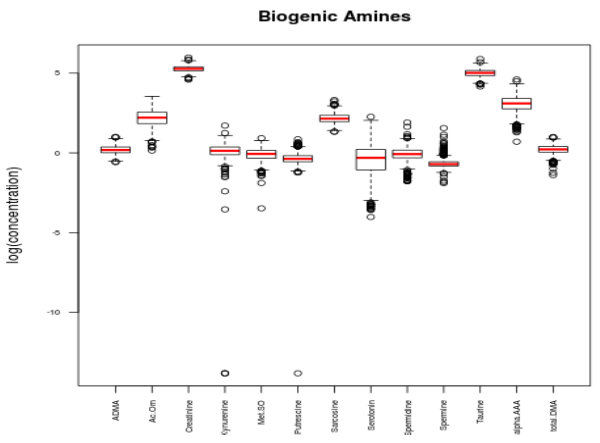
Animal resources

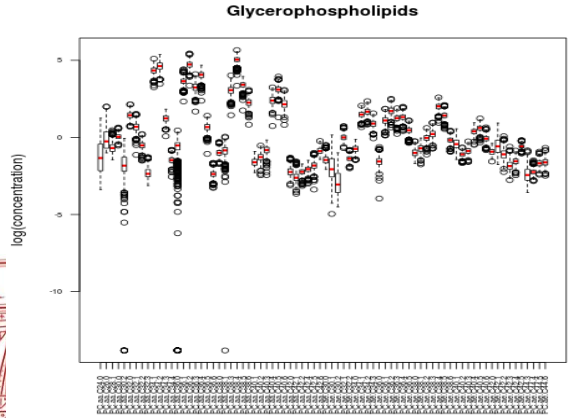


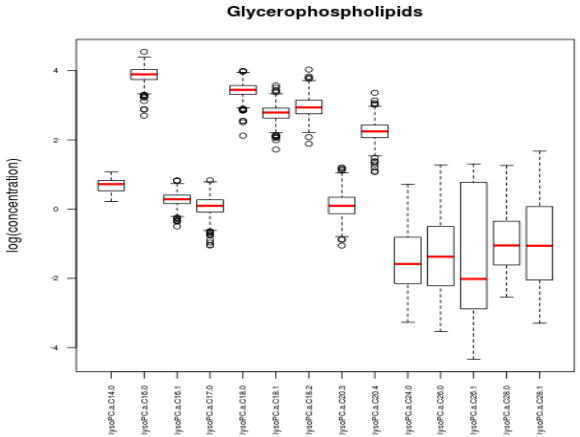
METABOTYPES

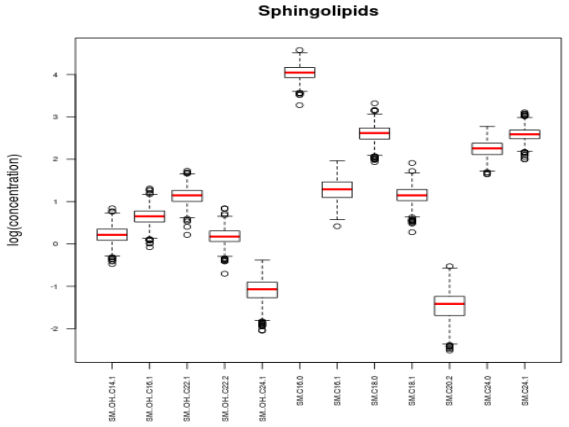




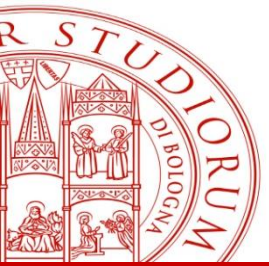




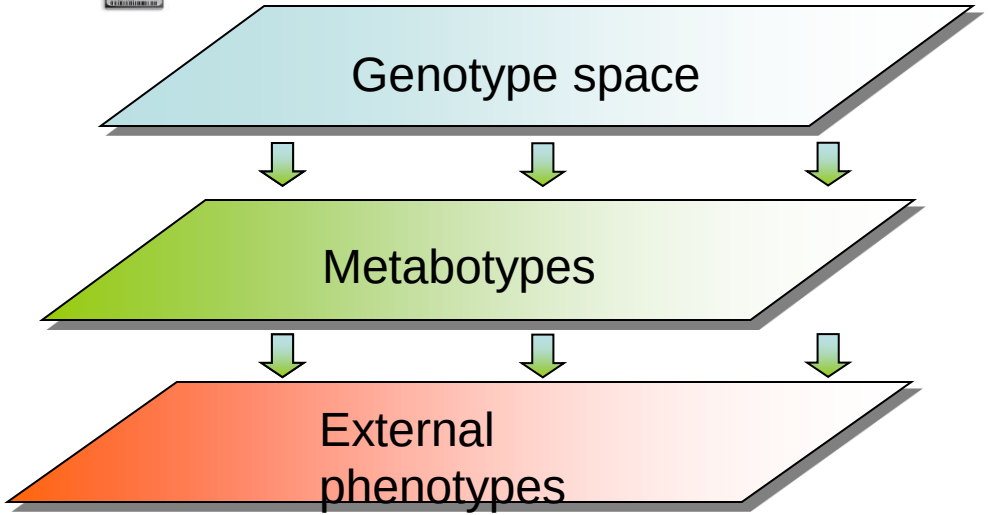




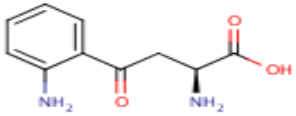
Genomics
+
Metabolomics

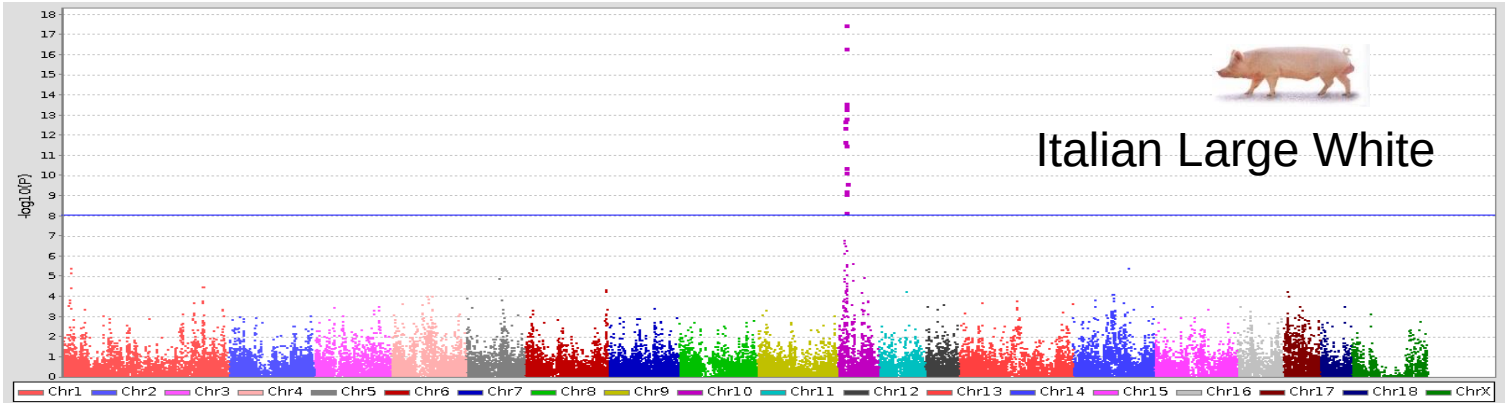


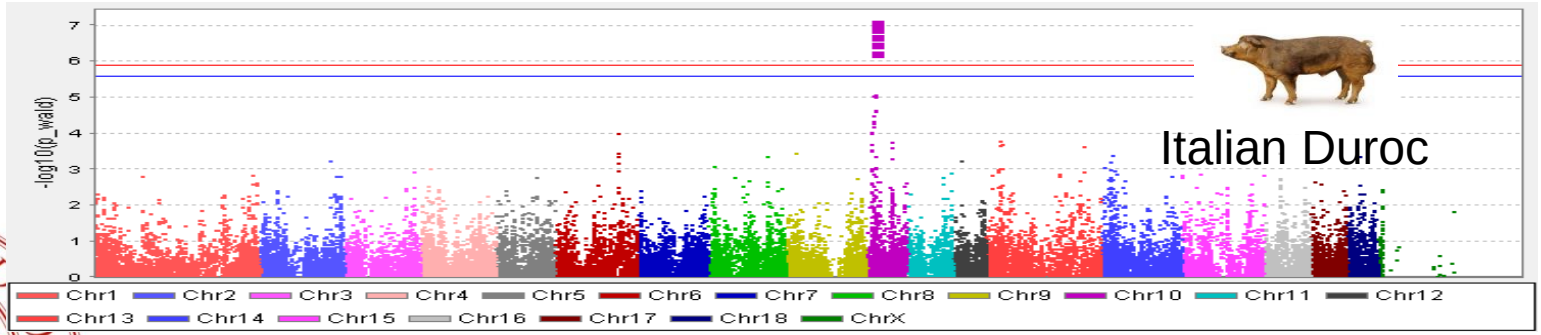
PorcineSNP60 BeadChip



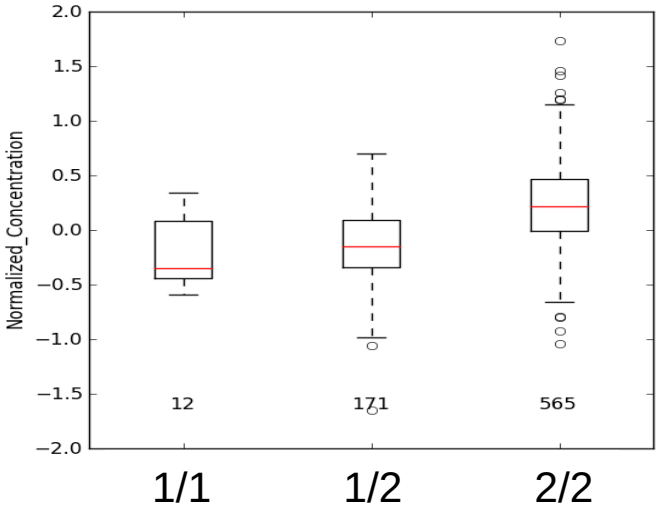
Kynurenine







Kynurenine level
Box plot with the three genotypes



SNP1 Genotypes

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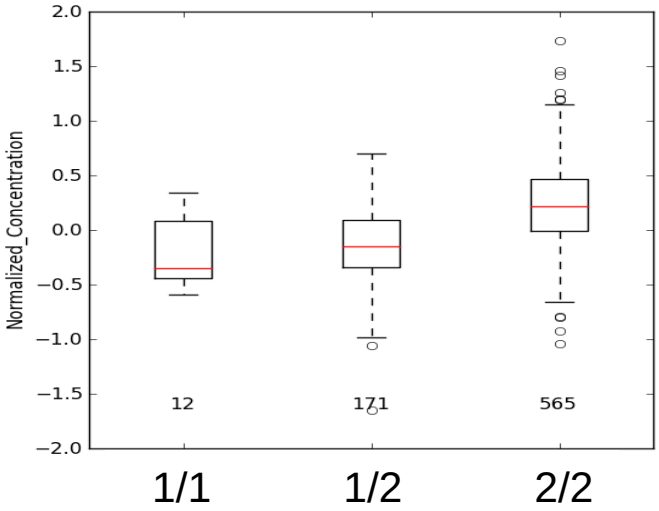
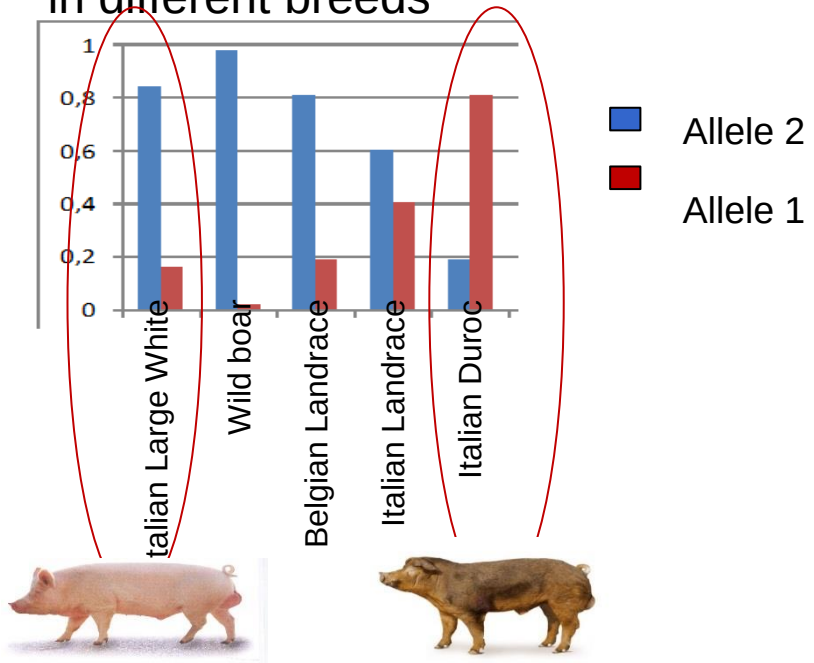


Allele frequencies of SNP1 in different breeds



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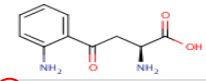
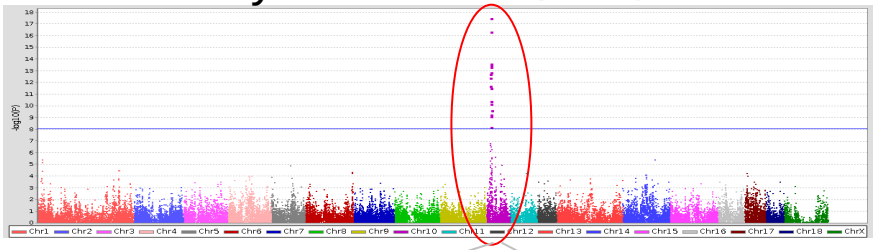
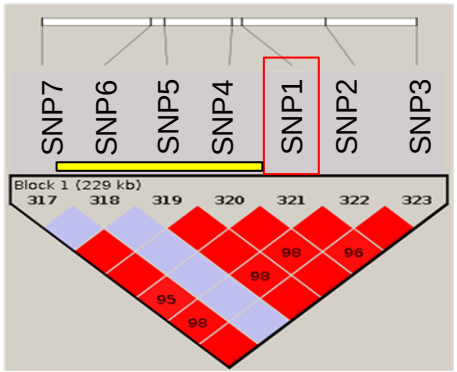
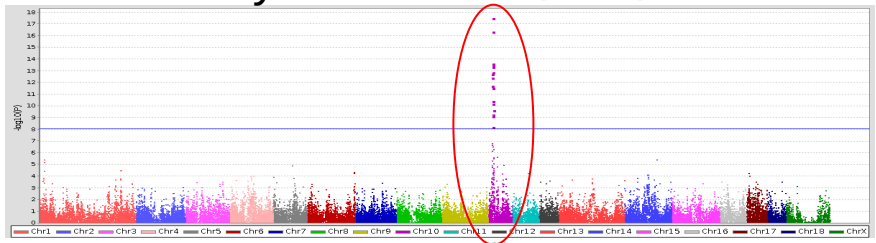


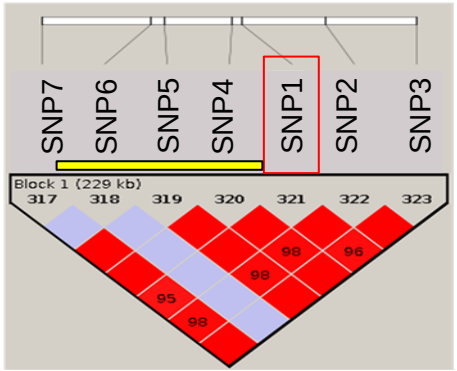




Kynurenine 3-monooxygenase (KMO)

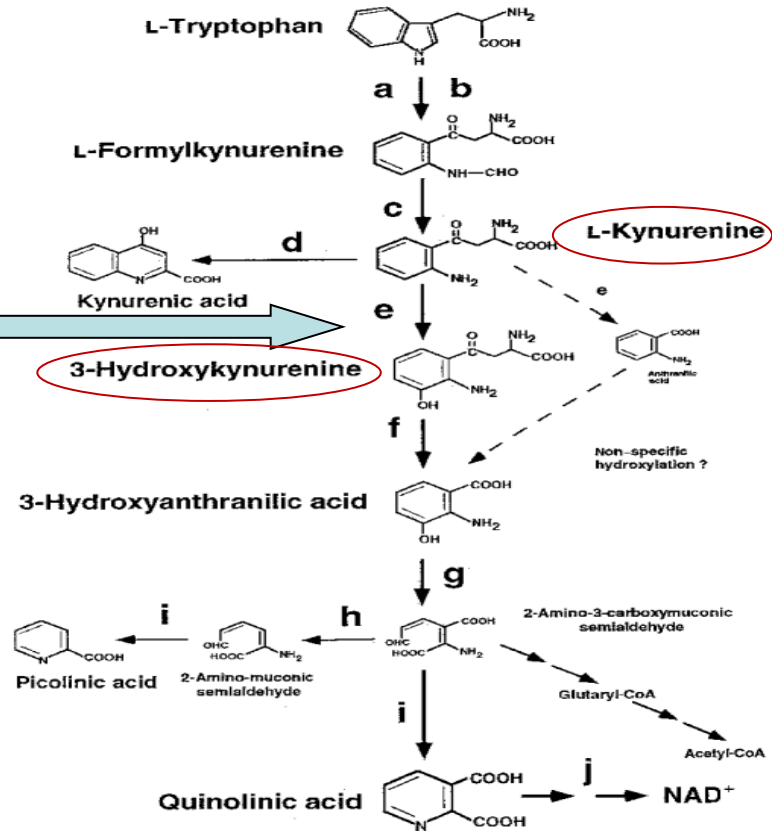
Kynurenine



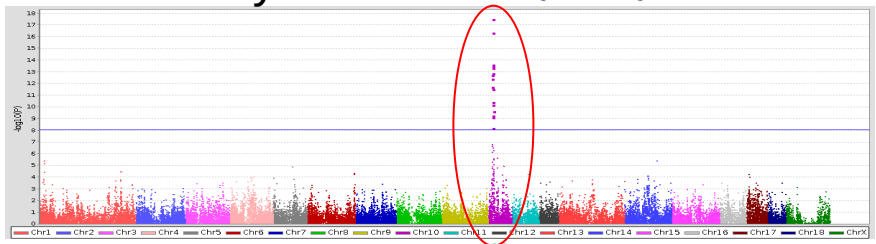


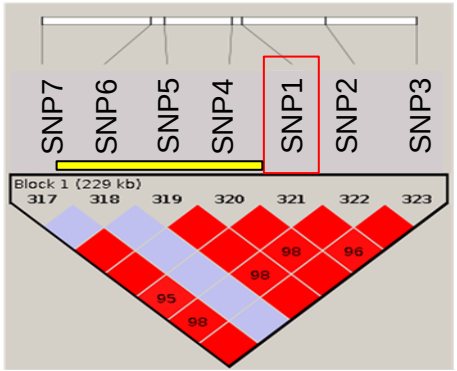
Kynurenine 3-monooxygenase (KMO)

Tryptophan catabolism



Kynurenine





Kynurenine 3-monooxygenase (KMO)

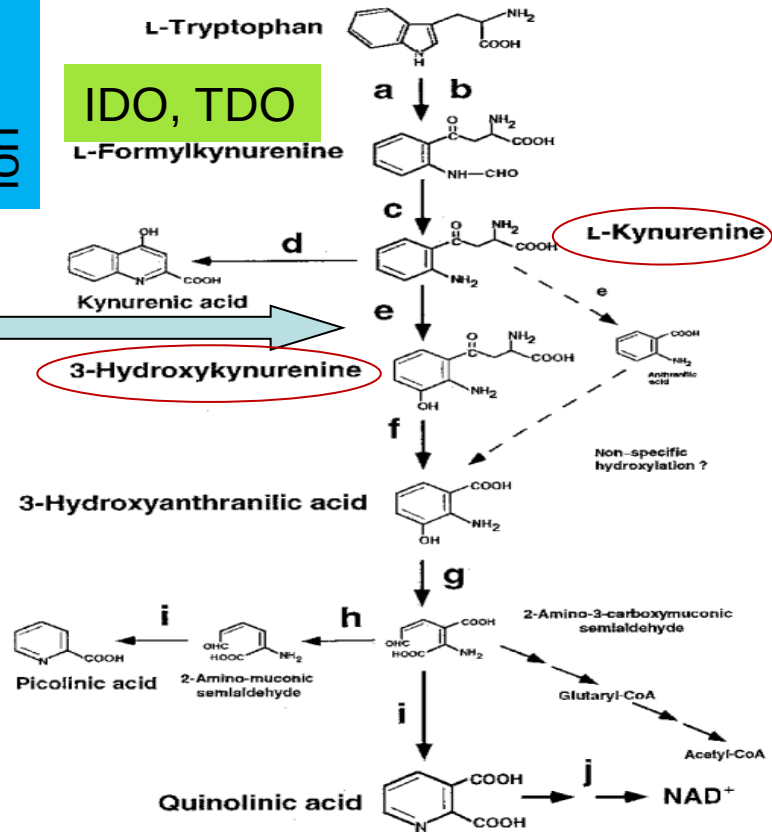
Tryptophan catabolism

Immunity/ inflammation

IDO, TDO

KMO

Behaviour



Can these results on KMO be useful for practical applications?

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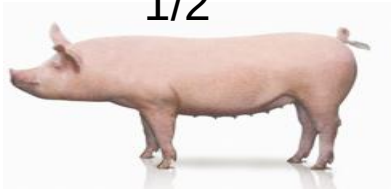
1/2

x

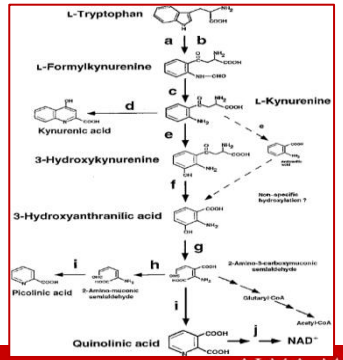
1/2



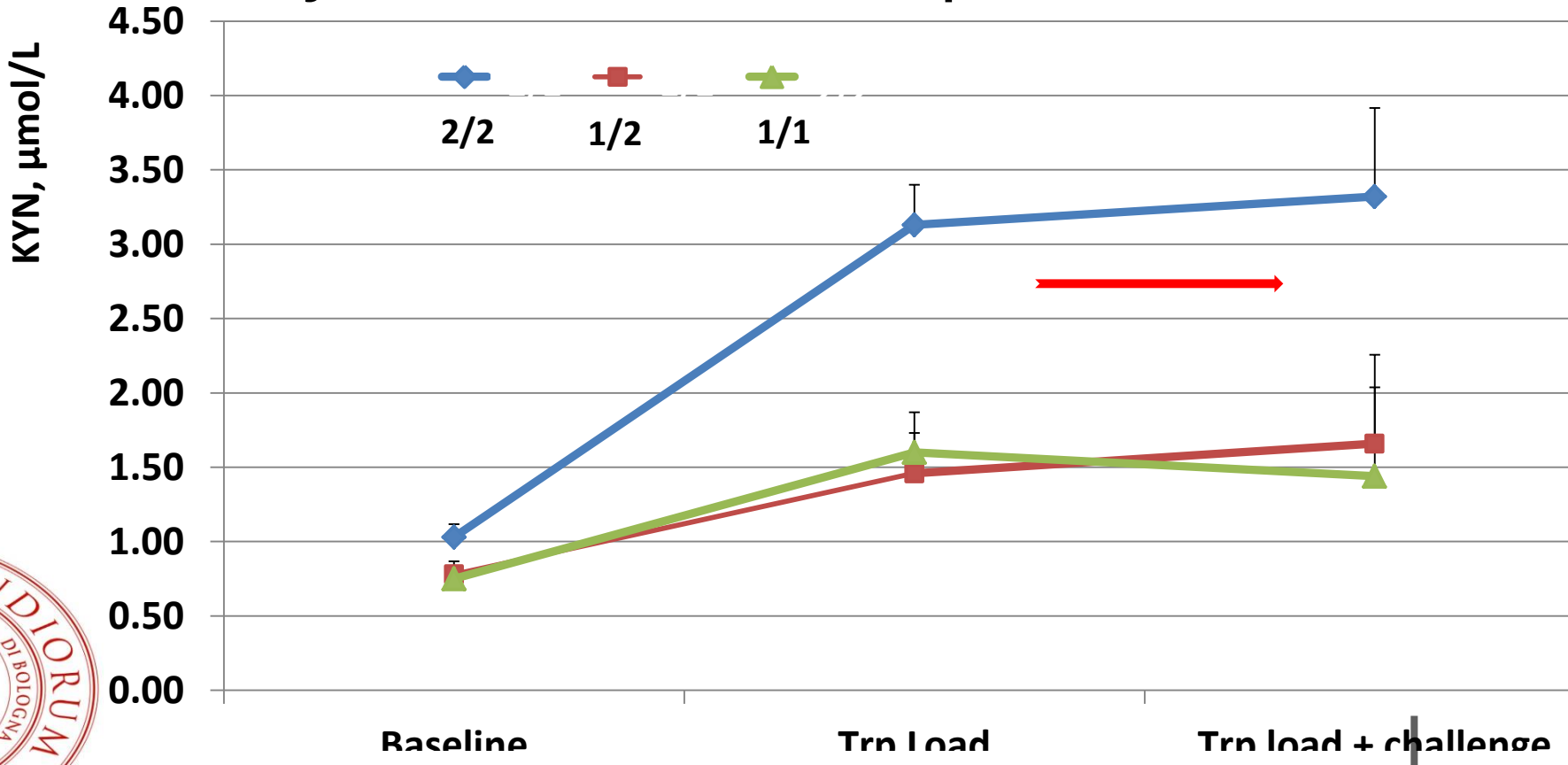
1/1 1/2 2/2

- **baseline conditions**
- **TRP dietary load**
- **TRP dietary load and challenge with enterotoxigenic E. coli K88**

Partition of the different metabolites



Kynurenine in blood plasma



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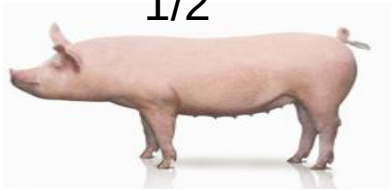


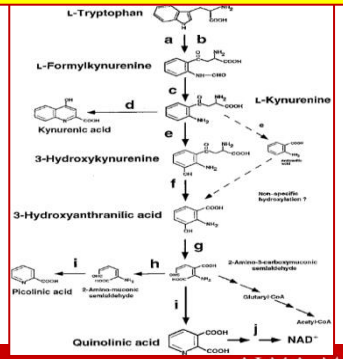
Patent pending

We are developing the first nutrigenomics approaches in pigs

baseline conditions
TRP dietary load
TRP dietary load and challenge with enterotoxigenic E.

Definition of amino acid requirement based on animal genotype and environmental interactions

Partition of the different metabolites



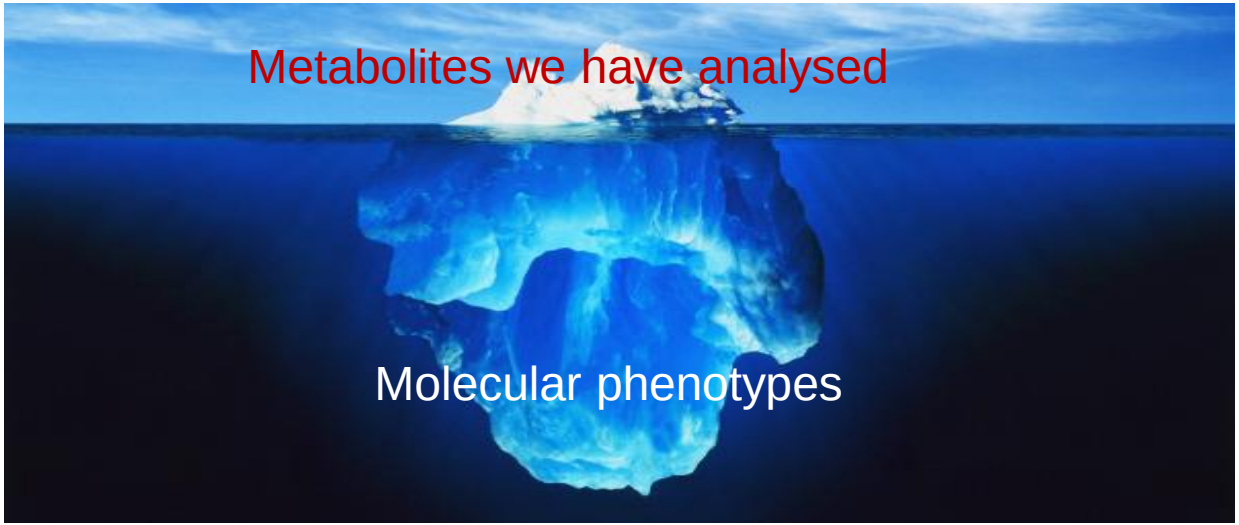
Conclusions

a) Metabotypes + genomics = fine biological mechanisms

b) Applications that merge metabolomics and genomics information are possibile

c) Many other questions and opportunities can be opened by integrating genomics and metabolomics using non-conventional approaches (not presented here)

We are just at the beginning of a very interesting story……..



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Diana Luise
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Giuliano Galimberti

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