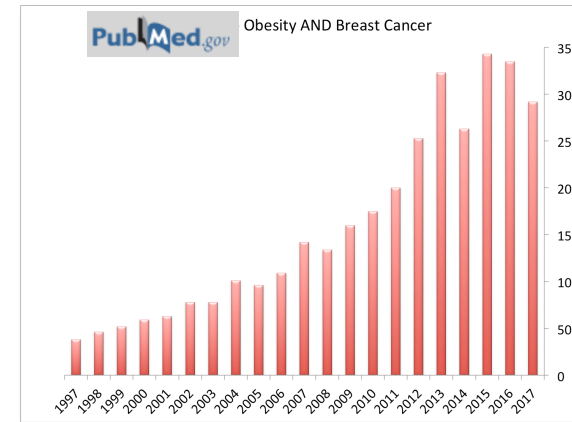
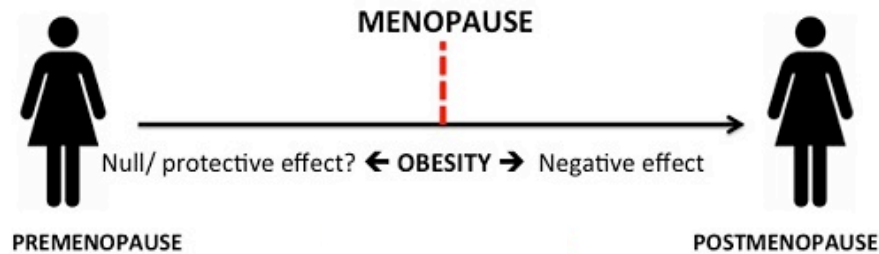


## Exploiting transcriptomic data in genome scale metabolic networks: new insight into obesity

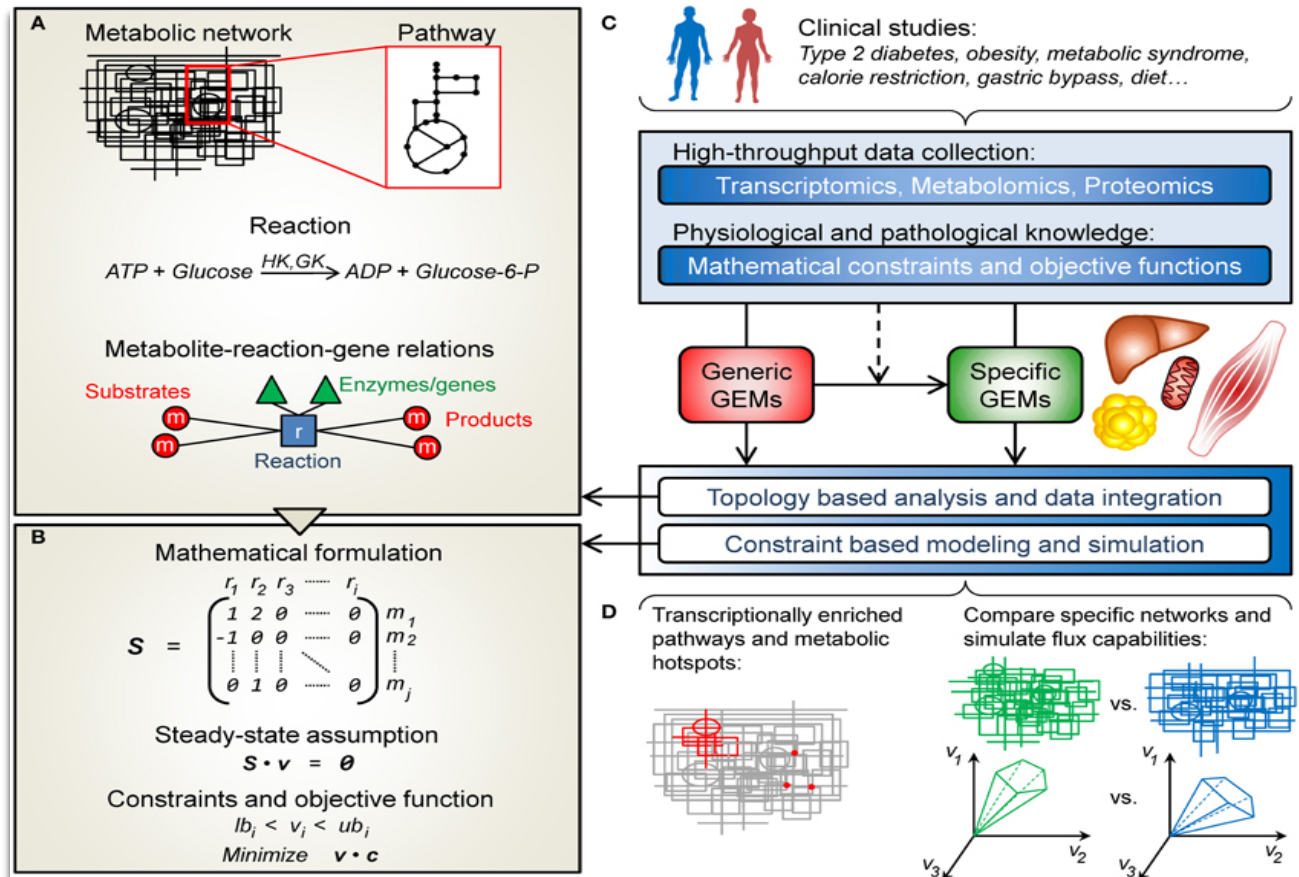
Flash poster presentation  
(Poster P5)



# Obesity & Breast Cancer



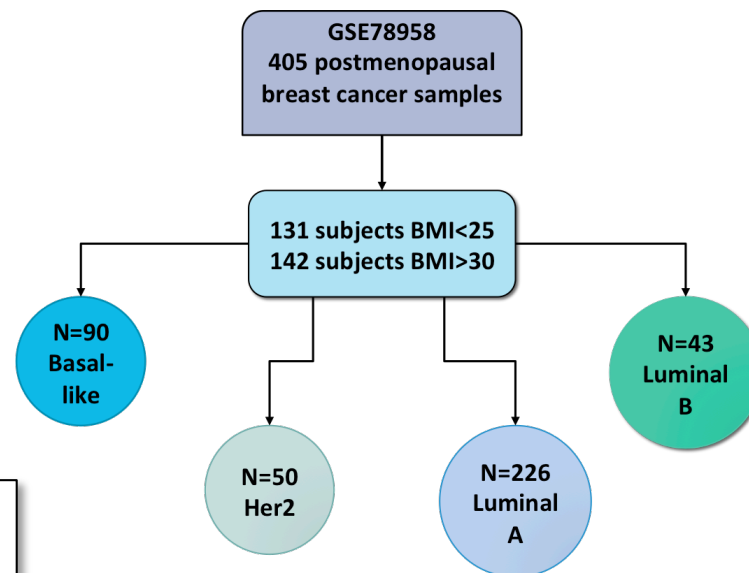
## Genome-scale Metabolic Network



## ➡ Genome Scale Metabolic Model: iAdipocytes 1809 (Mardinoglu et al. 2013)

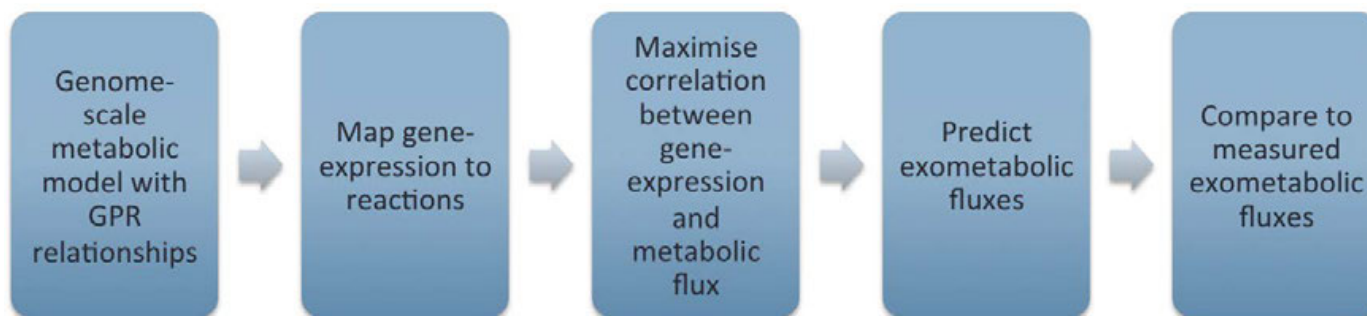
## ➡ Transcriptomic Dataset:

## ➡ Integrative Method:

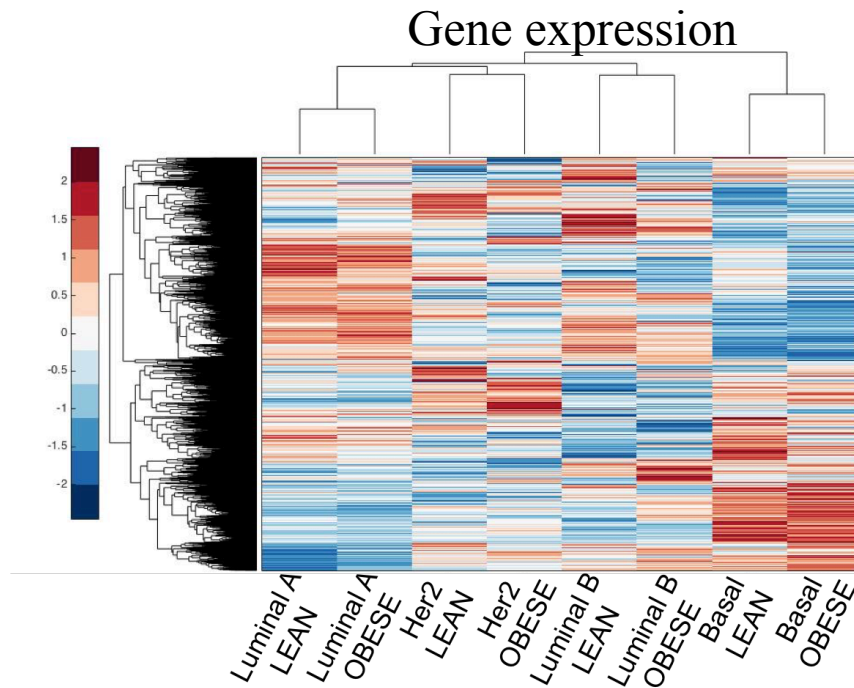


### Improving metabolic flux predictions using absolute gene expression data

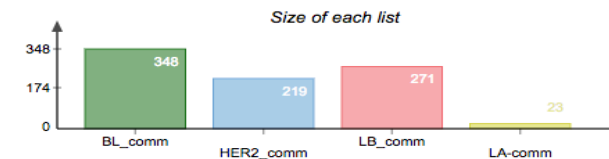
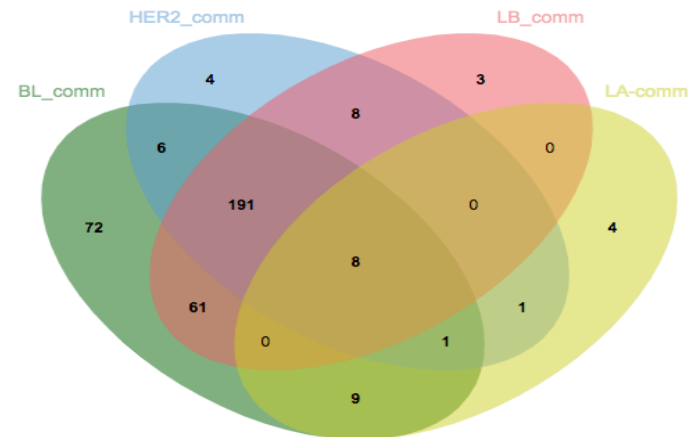
Dave Lee<sup>1†</sup>, Kieran Smallbone<sup>1†</sup>, Warwick B Dunn<sup>1</sup>, Ettore Murabito<sup>1</sup>, Catherine L Winder<sup>1</sup>, Douglas B Kell<sup>1,2</sup>, Pedro Mendes<sup>1,3</sup> and Neil Swainston<sup>1\*</sup>



# RESULTS

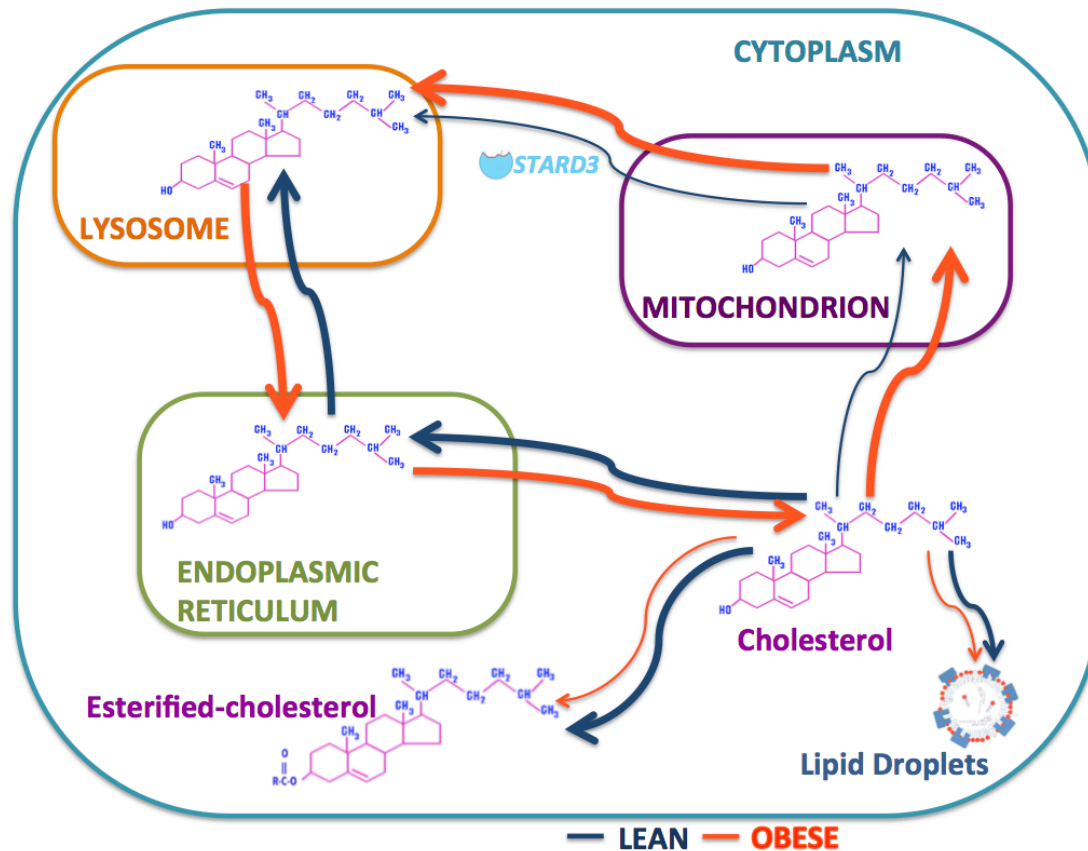


## Reactions with changing fluxes



Subsystem annotation of subtype specific dysregulated reactions	
Basal-like	Her2
Transport, endoplasmic reticular	Fatty acid activation (cytosolic)
Transport, extracellular	Transport, extracellular
Pool reactions	Transport, peroxisomal
Glycerophospholipid metabolism	Transport, endoplasmic reticular
Transport, mitochondrial	<b>LB</b>
Terpenoid backbone biosynthesis	Glycerophospholipid metabolism
Carnitine shuttle (cytosolic)	Transport, extracellular
Carnitine shuttle (endoplasmic reticular)	Transport, mitochondrial
Beta oxidation of even-chain fatty acids (peroxisomal)	<b>LA</b>
Formation and hydrolysis of cholesterol esters	Transport, extracellular
Tryptophan metabolism	Transport, extracellular
Tricarboxylic acid cycle and glyoxylate/dicarboxylate metabolism	Transport, mitochondrial
Glycolysis / Gluconeogenesis	Transport, mitochondrial
Inositol phosphate metabolism	
Nucleotide metabolism	

# RESULTS



In Luminal A subtype the reactions associated to cholesterol transport and esterification showed different rates between lean and obese subjects



# RESULTS

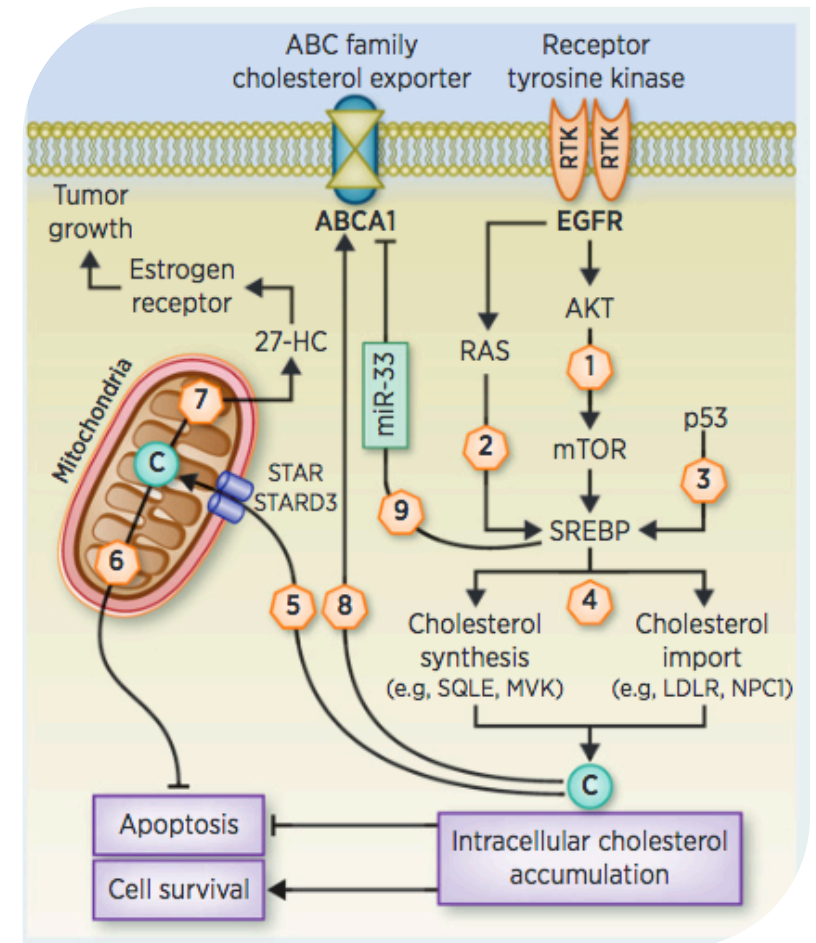
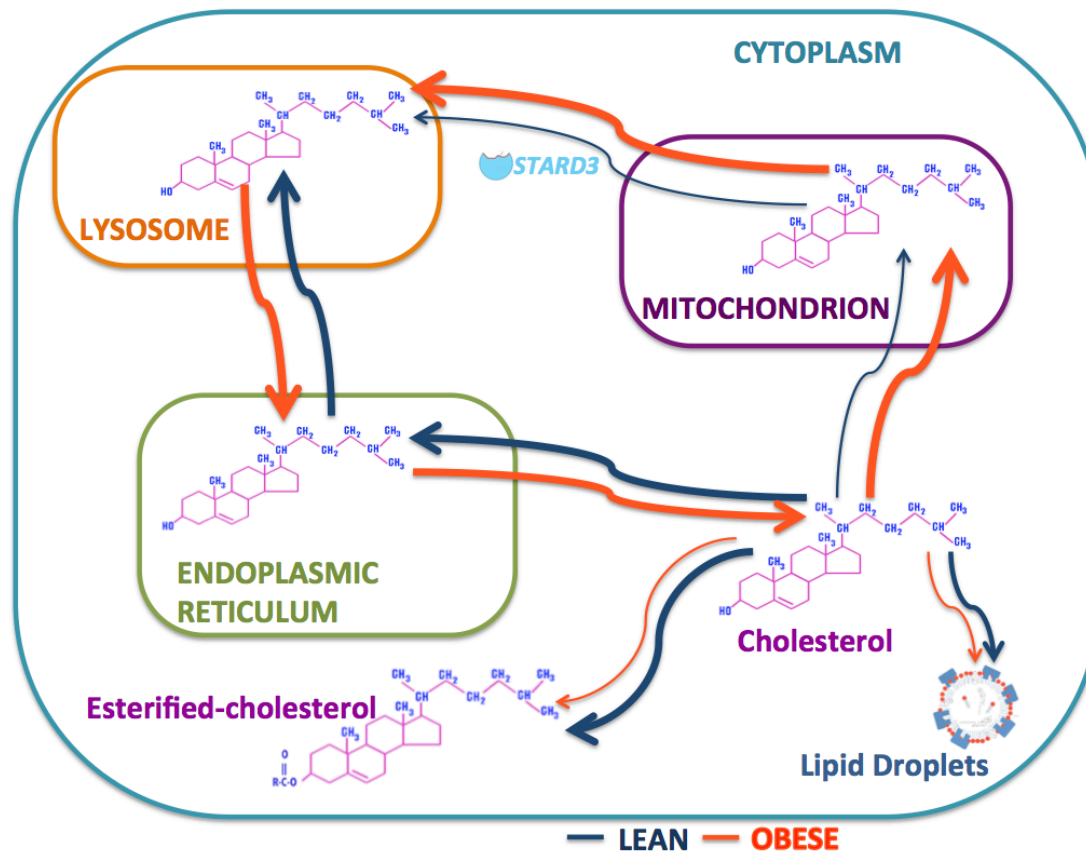
Published OnlineFirst April 5, 2016; DOI: 10.1158/0008-5472.CAN-15-2613

Review

Cancer  
Research

## The Role of Cholesterol in Cancer

Omer F. Kuzu<sup>1</sup>, Mohammad A. Noory<sup>1</sup>, and Gavin P. Robertson<sup>1,2,3,4,5,6,7,8</sup>



# Acknowledgements



*Consiglio Nazionale delle Ricerche*  
Istituto di Calcolo e Reti ad Alte Prestazioni

Mario Rosario Guarracino

Mara Sangiovanni

Enrico Troiano

**THANK  
YOU!**



# Conclusions

- The integration of gene expression data into the adipocyte GEM allowed the identification of reactions and associated genes dysregulated in obese cancer patients.
- The knowledge at metabolic level overcomes the limit of looking at the gene expression alone without investigating the effect on cellular mechanisms.
- Intracellular cholesterol accumulation, inferred by flux rates in LumA obese women, is suggested to play an important role in development and progression of breast cancer.
- Further investigations are needed to unravel the differences in terms of mechanisms and outcomes of the obesity-BC subtypes association.