XXVI WORLD CONGRESS

EXPRESSION OF VISCERAL ADIPOSE TISSUE EXTRACELLULAR MATRIX RELATED GENES CORRELATES WITH INSULIN RESISTANCE AND PREDICTS METABOLIC IMPROVEMENT FOLLOWING BARIATRIC SURGERY

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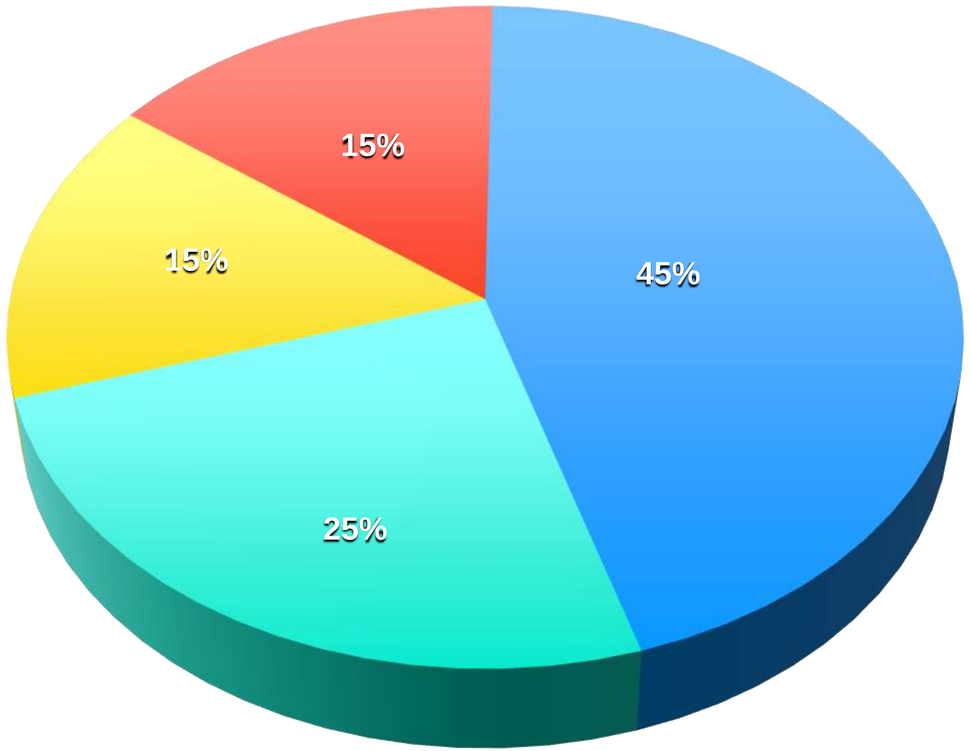
CONFLICT OF INTEREST DISCLOSURE

In accordance with «EACCME criteria for the Accreditation of Live Educational Events»:

I have the following potential conflict(s) of interest to report:

- Speaker/ Consultant for Abex® SPAIN, Smith & Nephew, Johnson & Johnson (Ethicon) SPAIN, BBraun Spain
- Director of the iVascular Surgical Research Chair
- The present work has been funded by a state grant for Health Research Projects of the Acción Estratégica en Salud 2013-2016 (Instituto de Salud Carlos III, Spain), awarded in the 2017 call (FIS PI17-01879)

CASE MIX DISCLOSURE



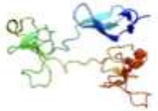
- RYGB
- SG
- OAGB
- DS/SADI-S
- REVISIONAL
- ENDOSCOPIC

SINCE 2018:
25% FULLY ROBOTIC
30% ROBOTIC ASSISTED
45% LAPAROSCOPIC

BACKGROUND

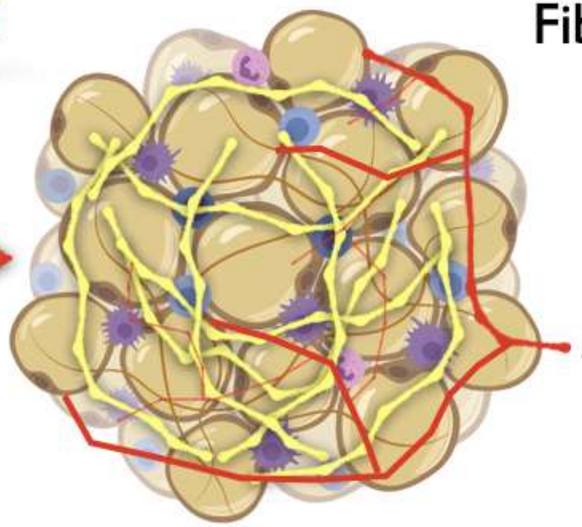
POSITIVE ENERGY BALANCE

MMP-14



Fibronectin

Colagen VI



Fibrosis?

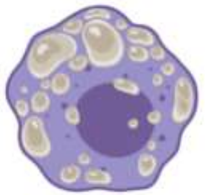
Angiogenesis

Adipose tissue hypertrophy

WEIGHT AND VOLUME GAIN

HYPOXIA → ADIPOSOPATHY → METABOLIC SYNDROME

M2 macrophages



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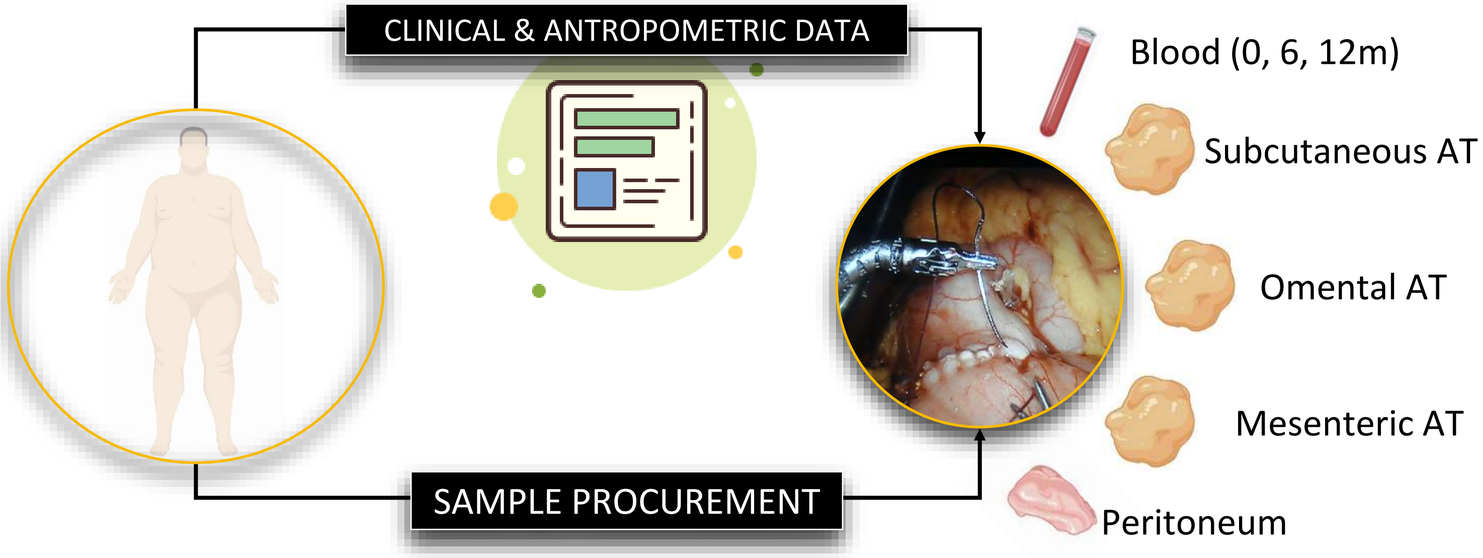
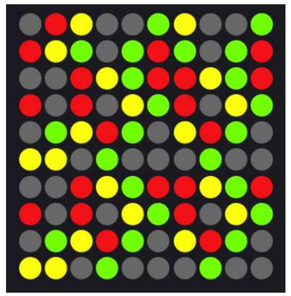
METHODS

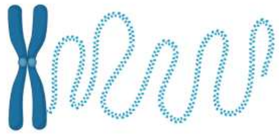

CLINICAL & ANTROPOMETRIC DATA
SAMPLE PROCUREMENT
Blood (0, 6, 12m)
Subcutaneous AT
Omental AT
Mesenteric AT
Peritoneum

MOLECULAR CHARACTERISATION OF TISSUE SAMPLES

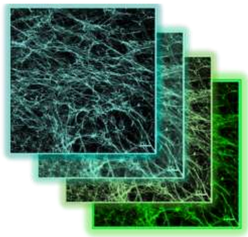


- Scanning
- Quantification
- Normalization

PrimePCR Assays/ Pannels



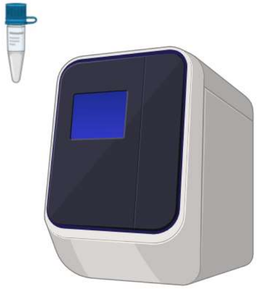
DEGs



The Matrisome Project

KOCH INSTITUTE for Integrative Cancer Research at MIT

ECM related genes



qPRC

VALIDATION

CLUSTER IDENTIFICATION

BARIATRIC SURGERY OUTCOME

CORRELATIONS

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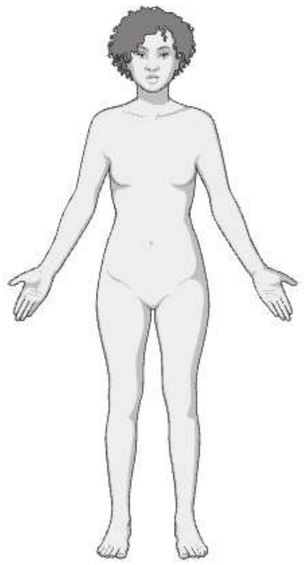
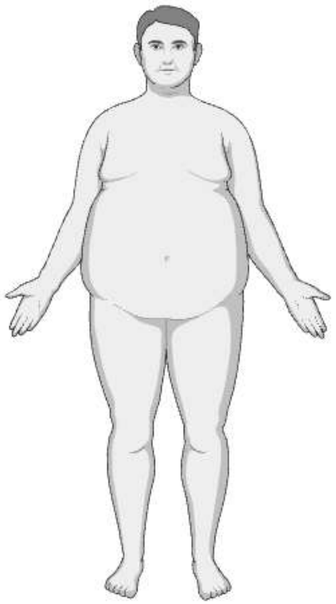
RESULTS



CLINICAL AND DEMOGRAPHIC DATA			
	People with obesity (n=30)	**Controls (n=13)**	**p-value**
Age(years)	45,7 (±8,5)	45,5 (±8,9)	0,7
Sex (female)	22 (73,3%)	9 (69,2%)	0,8
Tobacco	3 (10%)	0 (0%)	0,2
ASA I/II	26 (86,7%)	13 (100%)	0,2
BMI $_{t0}$ (kg/m^2)	42,2 (±3,9)	26,7 (±1,4)	<0,001*
HbA1c $_{t0}$	5,6 (±0,3)	5,4 (±0,2)	0,03*
Glucose $_{t0}$ (mg/dl)	96 (±10,6)	88,6 (±7,3)	0,03*
Insulin $_{t0}$ (mU/l)	22,3 (±10,4)	7,4 (±2)	<0,001*
HOMA-IR $_{t0}$	5,4 (±2,9)	1,6 (±0,5)	<0,001*
HOMA-IR $_{t0}$ >3,8	20 (66,7%)	0 (0%)	<0,001*
HTA $_{t0}$	11 (36,7%)	1 (7,7%)	0,052
DLP $_{t0}$	9 (30%)	1 (7,7%)	0,1
SAHS $_{t0}$	20 (66,7%)	0 (0%)	<0,001*

Qualitative variables are expressed as n (percentage); quantitative variables as mean (± standard deviation).
* Statistically significant differences.
ASA: American Society of Anesthesiology Score; BMI: Body Mass Index; HOMA-IR Homeostatic Model Assessment for Insulin Resistance; HbA1c: glycosylated hemoglobin; HTA: arterial hypertension; DLP: dyslipidemia; SAHS: sleep apnea-hypopnea syndrome.



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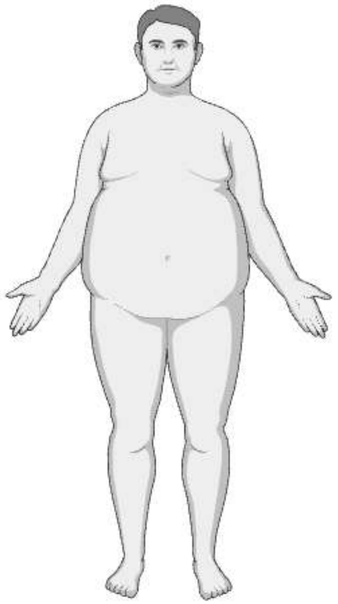
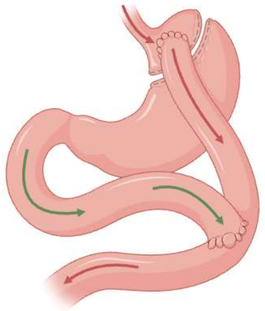
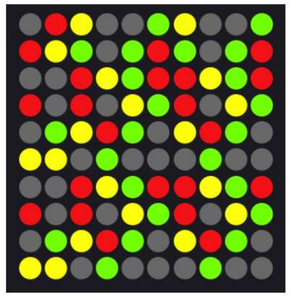


12m CLINICAL OUTCOME			
	t0 (n=30)	**t12 (n=30)**	**p-value**
BMI (kg/m²)	42,2 (±3,9)	27,6 (±3)	<0,001*
HbA1c (%)	5,6 (±0,3)	5,2 (±0,3)	<0,001*
Glucose (mg/dl)	96 (±10,6)	82,1 (±6,7)	<0,001*
Insulin (mU/l)	22,3 (±10,4)	5,8 (±2,2)	<0,001*
HOMA-IR	5,4 (±2,9)	1,2 (±0,5)	<0,001*
HOMA-IR $_{t0}$ >3,8	20 (66,7%)	0 (0%)	<0,001*
C-peptide (ng/mL)	2,7 (±1,1)	1,4 (±0,6)	<0,001*
HTA	11 (36,7%)	6 (20%)	0,063
DLP	9 (30%)	2 (6,7%)	0,039*
TG (mg/dl)	133 (±47)	87,4 (±23)	<0,001*
Total cholesterol (mg/dl)	208 (±31)	186 (±29)	<0,001*
LDL (mg/dl)	133 (±25)	111 (±25)	0.001*
HDL (mg/dl)	49,2 (±10)	57 (±12)	<0,001*

Qualitative variables are expressed as n (percentage); quantitative variables as mean (±standard deviation).
* Statistically significant differences.
BMI: Body Mass Index; HbA1c: glycosylated hemoglobin; HOMA-IR Homeostatic Model Assessment for Insulin Resistance; HTA: arterial hypertension; DLP: dyslipidemia; TG: triglycerides; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein.



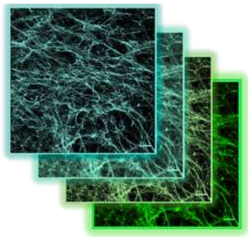
MOLECULAR CHARACTERISATION OF TISSUE SAMPLES



- Scanning
- Quantification
- Normalization

PrimePCR Assays/ Pannels

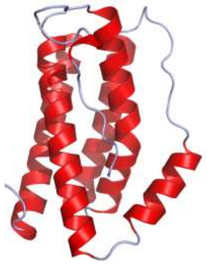
6485 DEGs



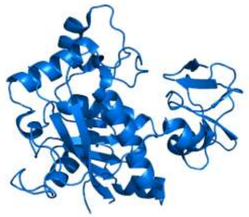
The Matrisome Project

KOCH INSTITUTE for Integrative Cancer Research at MIT

380 ECM related genes



IL-6



ADAMST4

- 90 Genes in mesentery
- 78 genes in omentum
- 75 genes in peritoneum
- 51 genes in SCT

✓Fibrosis
✓Adipogenesis
✓Inflammation

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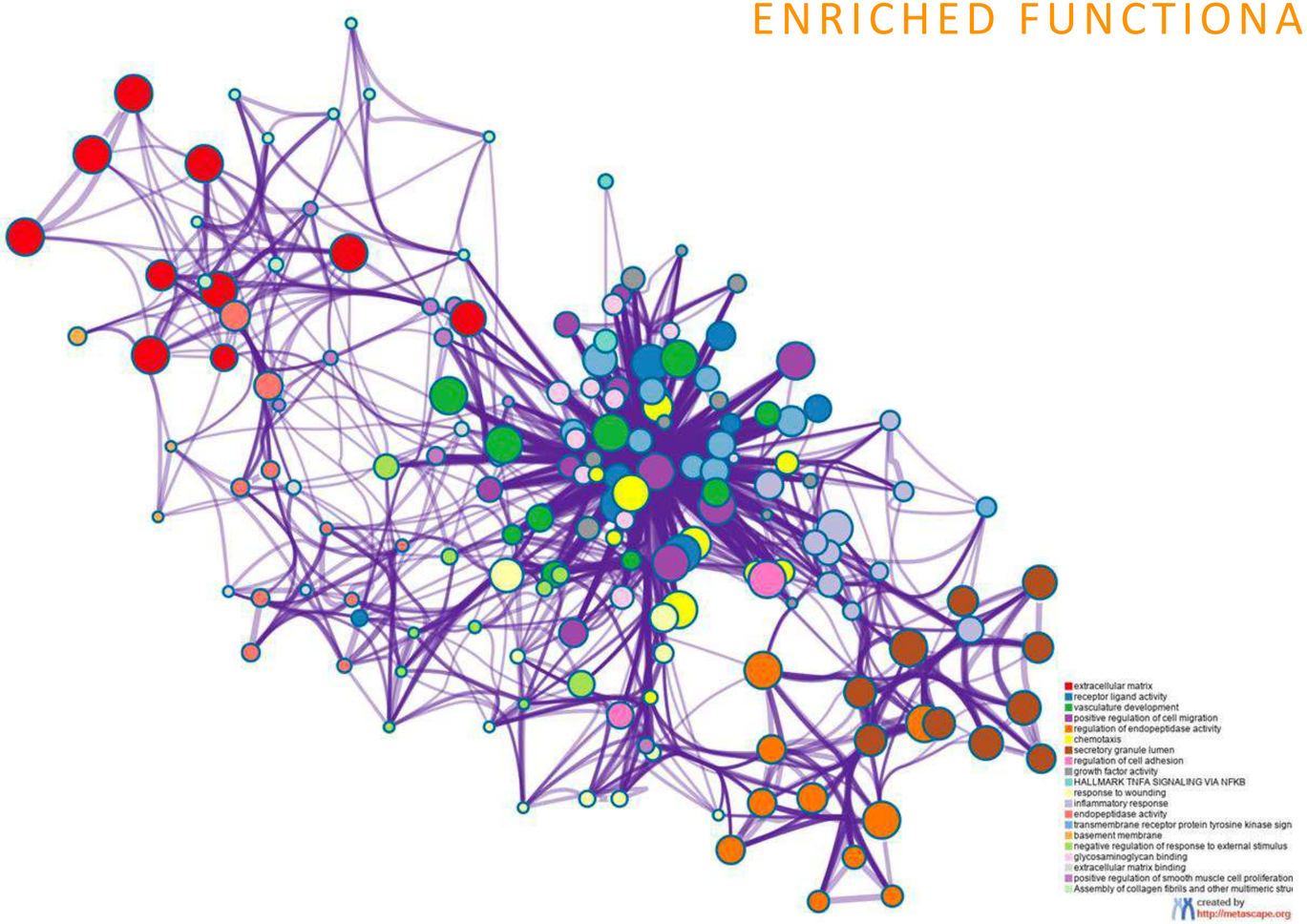
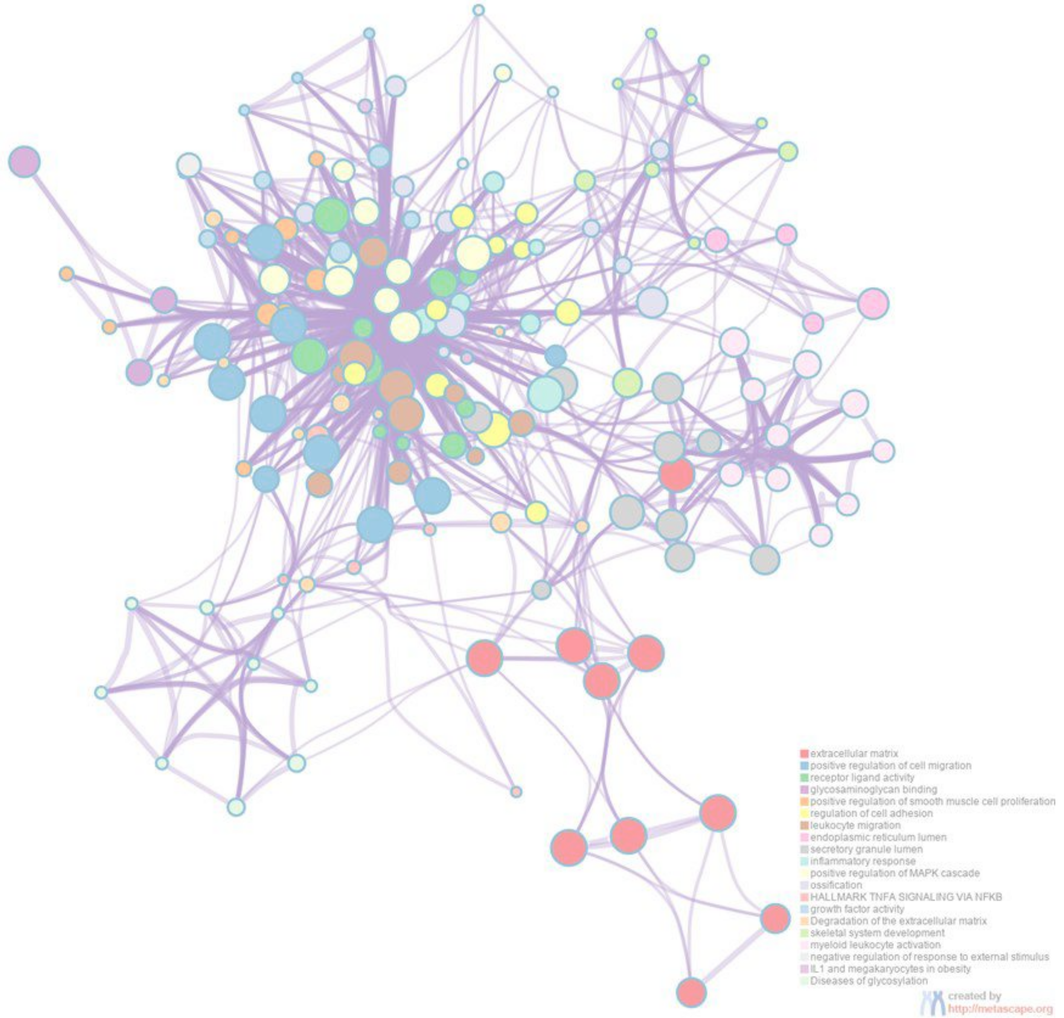
ENRICHED FUNCTIONAL CATEGORIES



MESENTERY



OMENTUM

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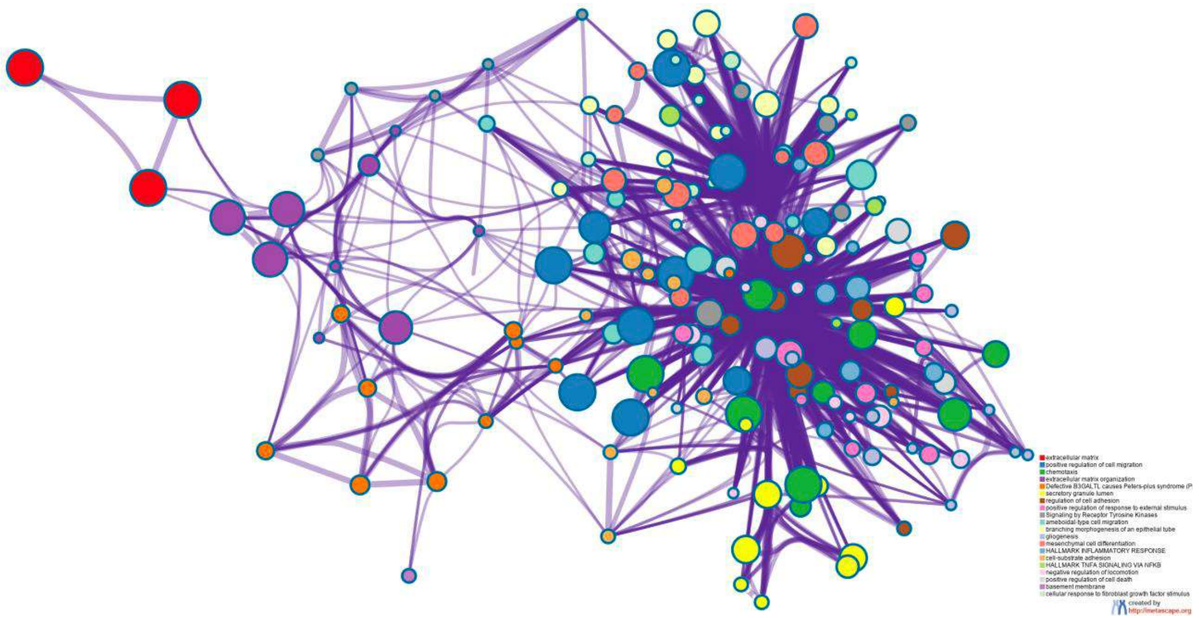
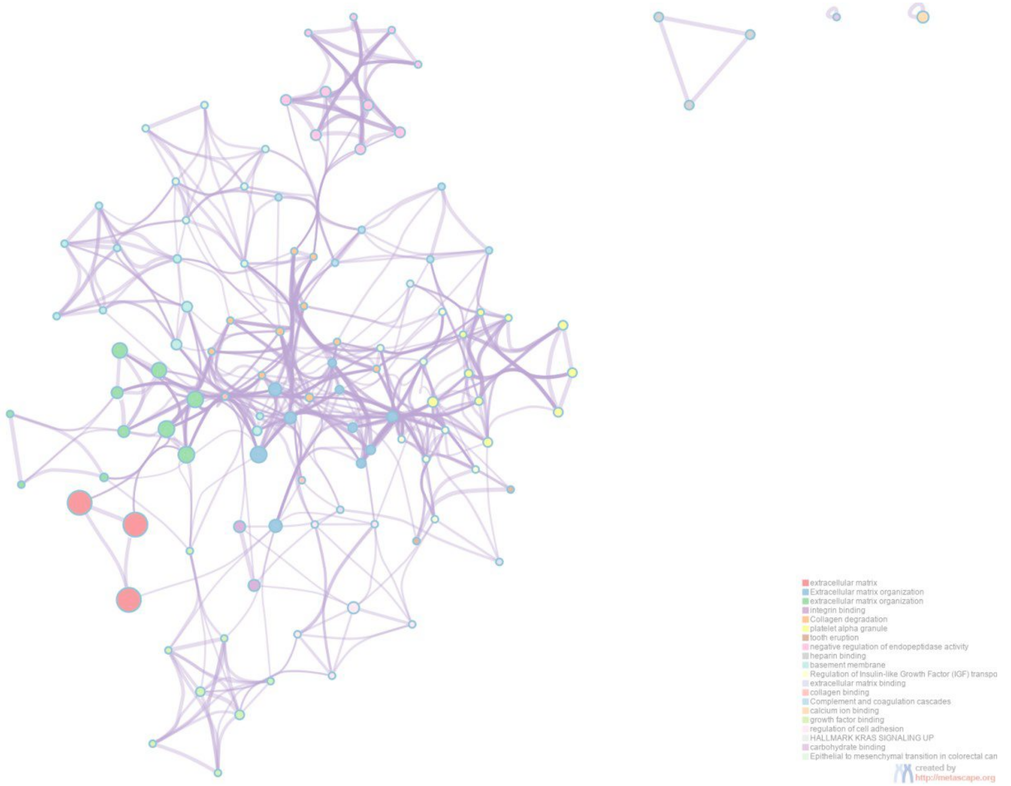
ENRICHED FUNCTIONAL CATEGORIES



PERITONEUM



SUBCUTANEOUS TISSUE

GENES VALIDATING DIFFERENTIAL EXPRESSION BY qPCR					
Gene	***Type***	**Subcutaneous**	**Omentum**	**Mesentery**	**Peritoneum**
VCAN	Proteoglycan	♦	*		**
PRG4	Proteoglycan				**
SRGN	Proteoglycan			*	**
S100A8	Secreted factor		**	**	**
CRISPLD2	ECM Glycoprotein				**
THBS1	ECM Glycoprotein		*		**
ADAMTS1	ECM Regulator		*		**
ADAMTS4	ECM Regulator		*	*	**
ADAMTS9	ECM Regulator				*
MMP19***	ECM Regulator	-	-	-	-
HAS1	ECM Constituent / Cell Migration		*	*	**

♦: under-expression in the obese group ($p < 0.05$); *: over-expression in the obese group (*: $p < 0.05$; **: $p < 0.01$).
******MMP19***: expression data not assessable.

CLUSTER IDENTIFICATION

CORRELATIONS

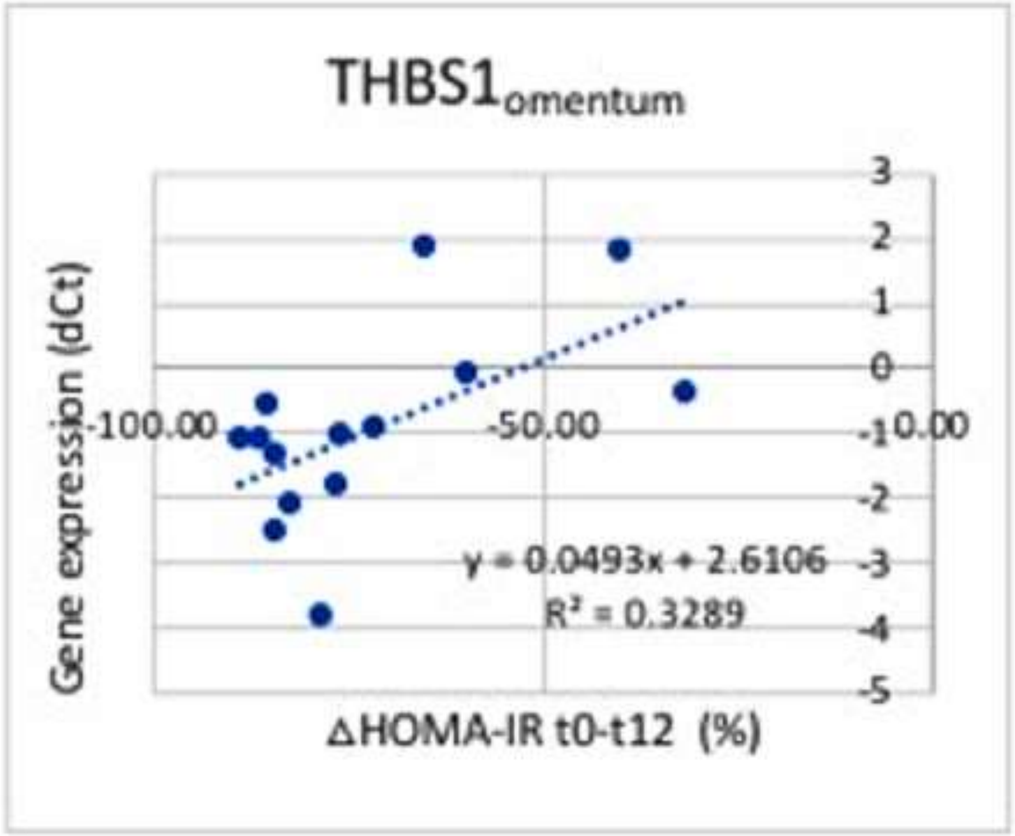
INSULIN RESISTANCE
(HOMA-IR)

Omental AT: HAS1, ADAMST4, THBS1, S100A8, VCAN

Mesenteric AT: HAS1, ADAMST4,1,9, THBS1, S100A8

Peritoneum: ADAMST4

RELATIONSHIP BETWEEN GENE EXPRESSION AND 12m METABOLIC OUTCOME



CONCLUSIONS

- Overall, our findings show a relationship between the overexpression of some ECM-related genes in visceral tissues of obese patients and altered glucose metabolism.

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CMCiB Centre de Medicina Comparativa i Bioimatge de Catalunya

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