



Lipedema and inflammation

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CIRC annual meeting, Bologna (ITA)

Oct 25-26, 2019

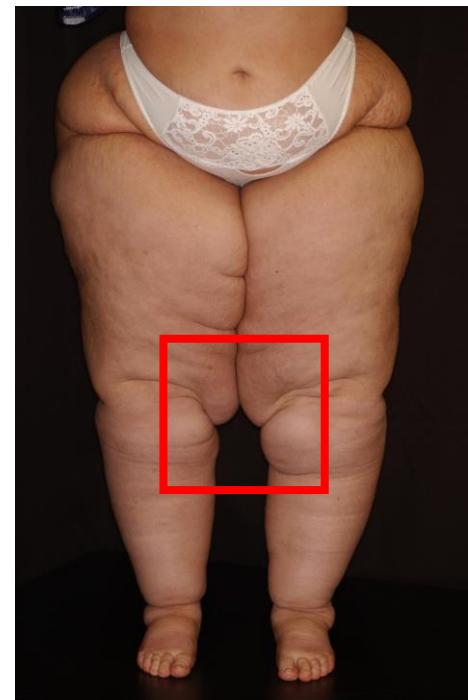
Conflict of Interest

- Travel expenses (flight and accommodation) have been fully covered by CIRC

Hallmarks of lipedema



cuffing sign



bilateral fat pads

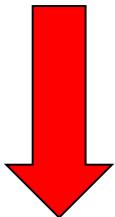


retromalleolar fat pads

General clinical features of lipedema

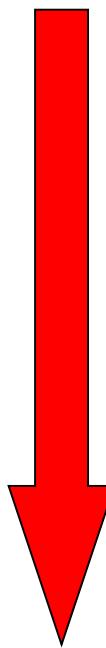
- #1 Low risk of diabetes despite higher body mass index (BMI)**
- #2 Normal blood pressure despite obese BMI**
- #3 Gynoid shape and relatively low risk of cardiovascular morbidity**
- #4 Relative resistance of lipedematous fat loss to lifestyle changes**
- #5 Relatively normal lipid panel**
- #6 Soft skin**
- #7 Lower resting energy expenditure**
- #8 Hypermobility and gait abnormality**
- #9 Pain and easy bruising**

Inflammation in lipedema



Lymphatic insufficiency?
Micro- and macrovascular
changes?

Adipogenic
inflammation?



Inflammatory cells
and their cytokines?

MRI lymphography in lipedema

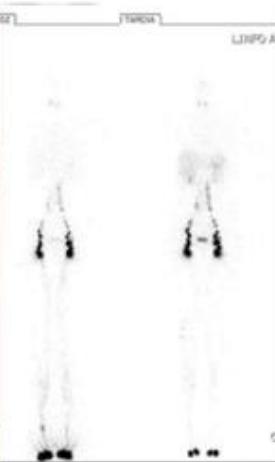
B



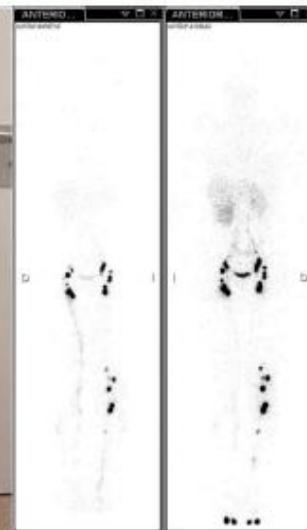
Lymph flow alterations in lipedema

Tabla 4. Alteraciones linfogammagráficas.

Pacientes	83
Pacientes con algún grado de afectación	39 (47%)
Grado de alteración:	
1- Bajo	14 (35,9%)
2- Bajo-moderado	19 (48,7%)
3- Moderado	6 (15,4%)
4- Moderado-severo	0%
5- Severo	0%



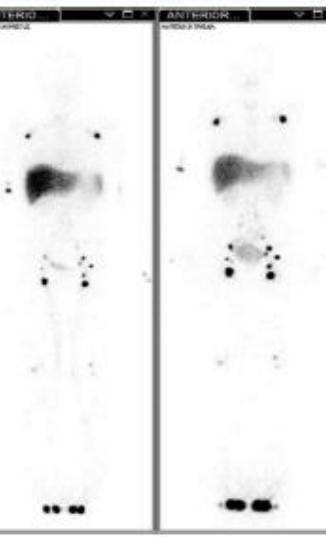
Figuras 1a y 1b. Lipedema estadio 3 con linfogammagrafía normal.



Figuras 2a y 2b. Lipedema estadio 1 con alteraciones linfogammagráficas grado bajo-moderado.



Figuras 3a y 3b. Lipedema estadio 2 con alteraciones linfogammagráficas bajo-moderado

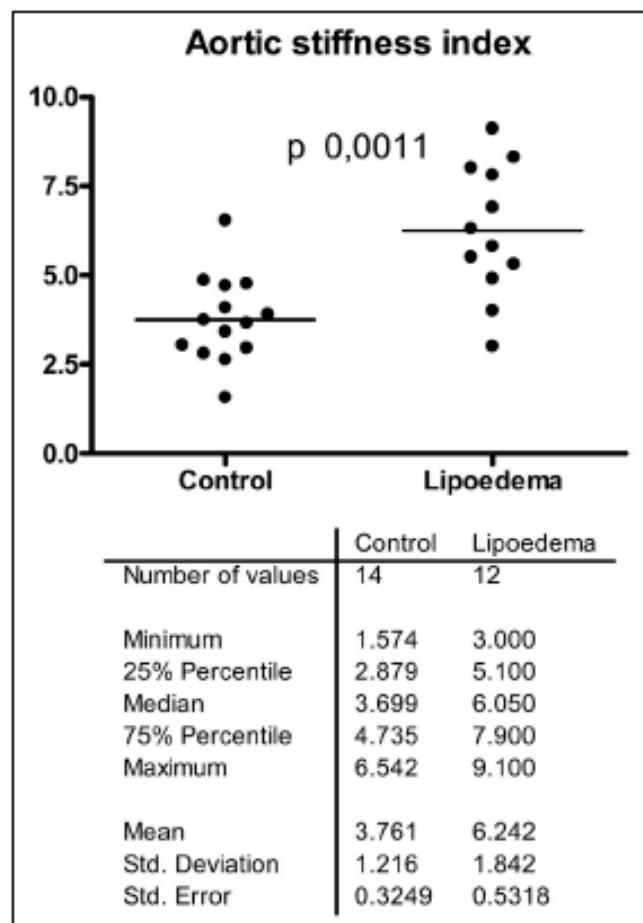


Figuras 4a y 4b. Hallazgos moderados en niña de 18 años con lipedema estadio 2.

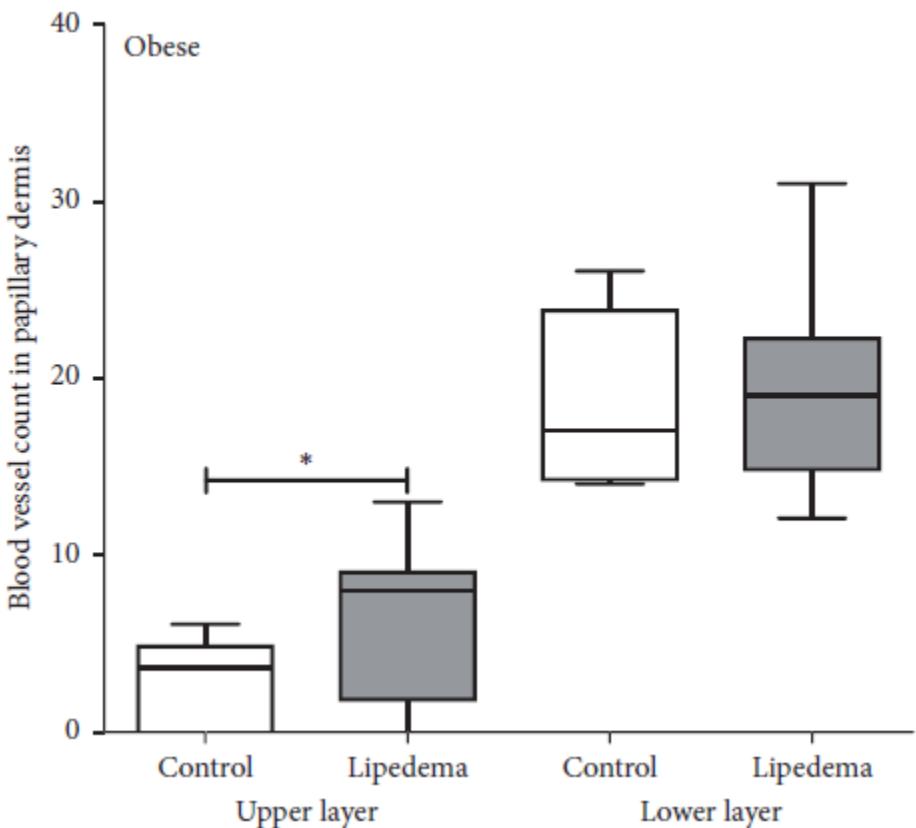
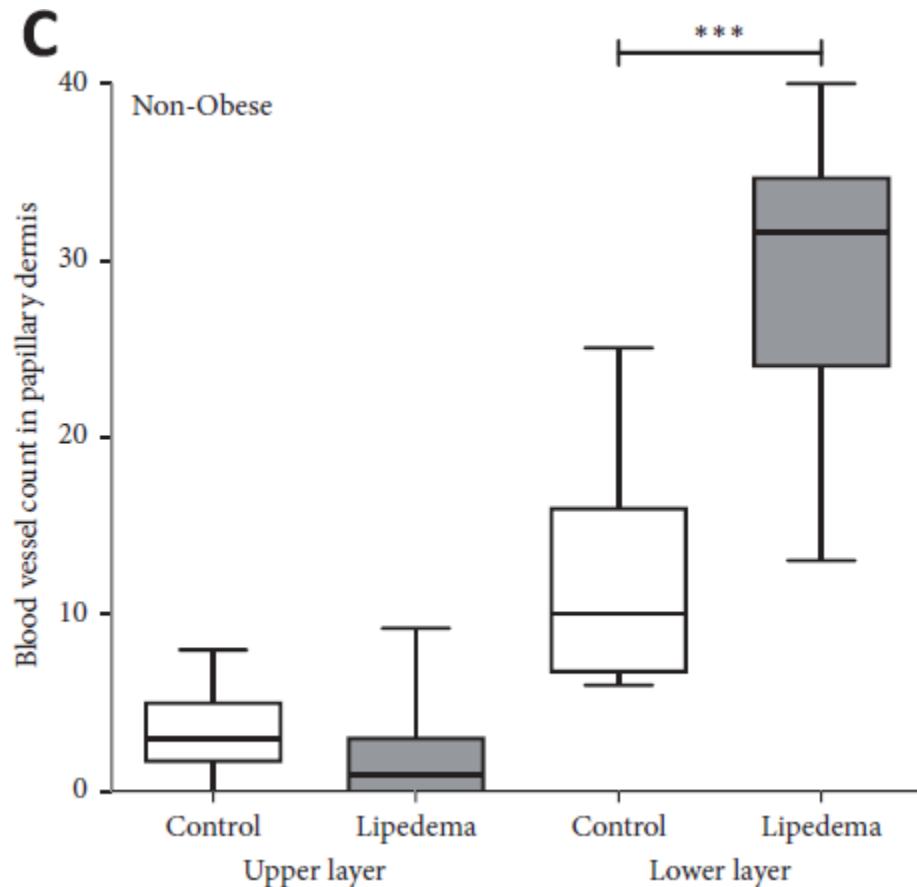
LIPEDEMA IS ASSOCIATED WITH INCREASED AORTIC STIFFNESS

G. Szolnoky, A. Nemes, H. Gavallér, T. Forster, L. Kemény

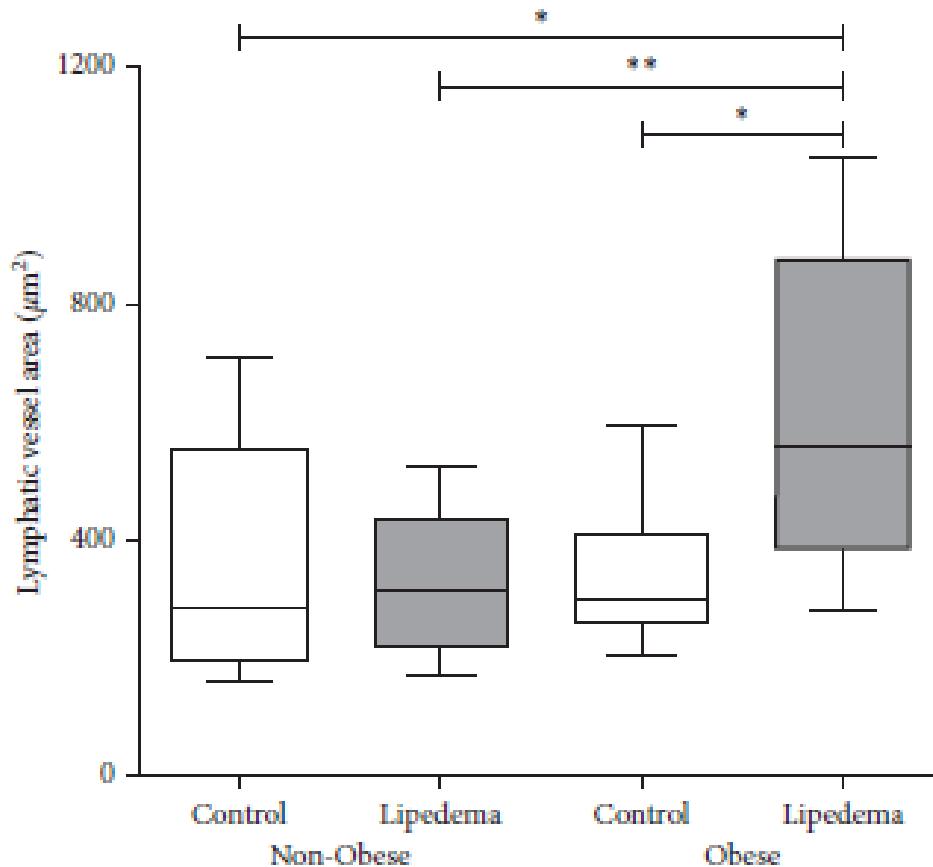
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Histological findings in lipedema: capillaries



Histological findings in lipedema: lymphatic vessels

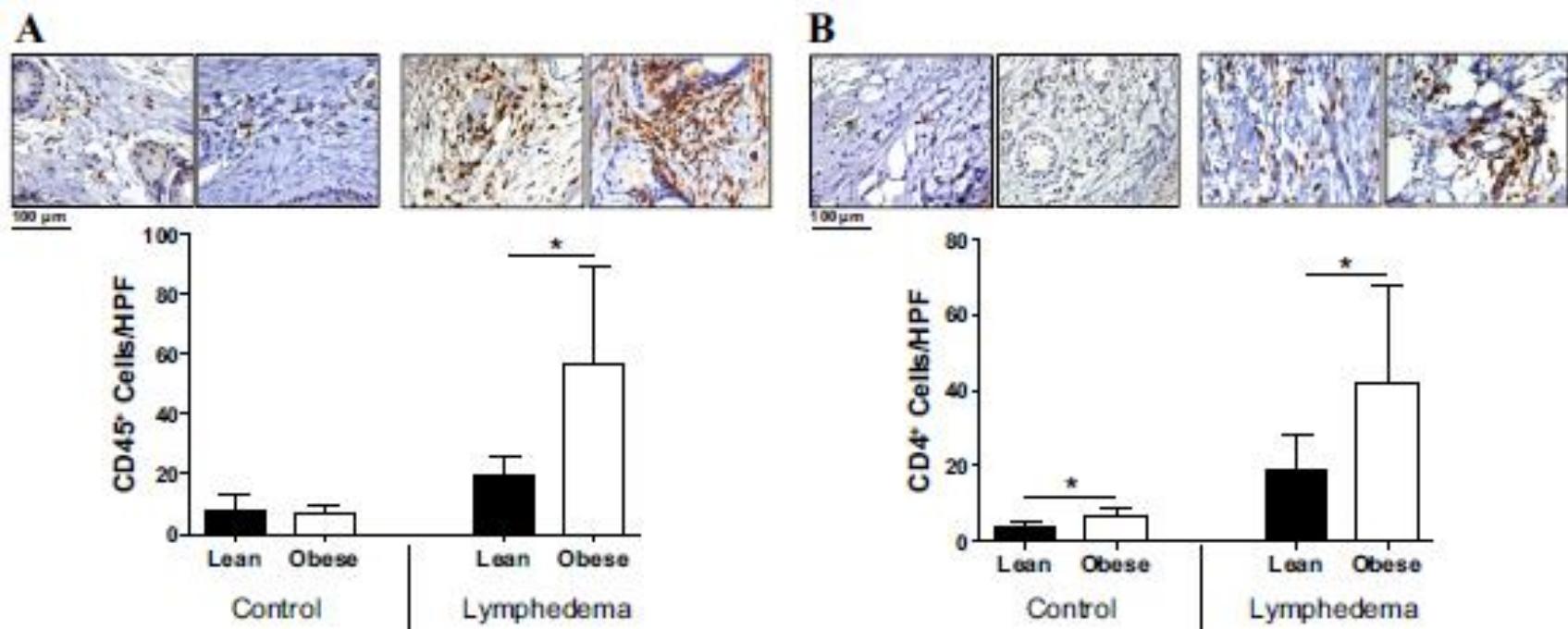


Local pathognomic features

- Capillary constriction in obese lipedema patients
- Increased capillary leakage and increased amount of interstitial fluid
- Hypoxia leads to adipocyte cell death and macrophage recruitment
- Lymph stagnation and concomitant inflammation stimulate adipogenesis and fibrosis

Indirect proofs of inflammation related to lymphatic insufficiency

Inflammation in lymphedema



Inflammation in lymphedema

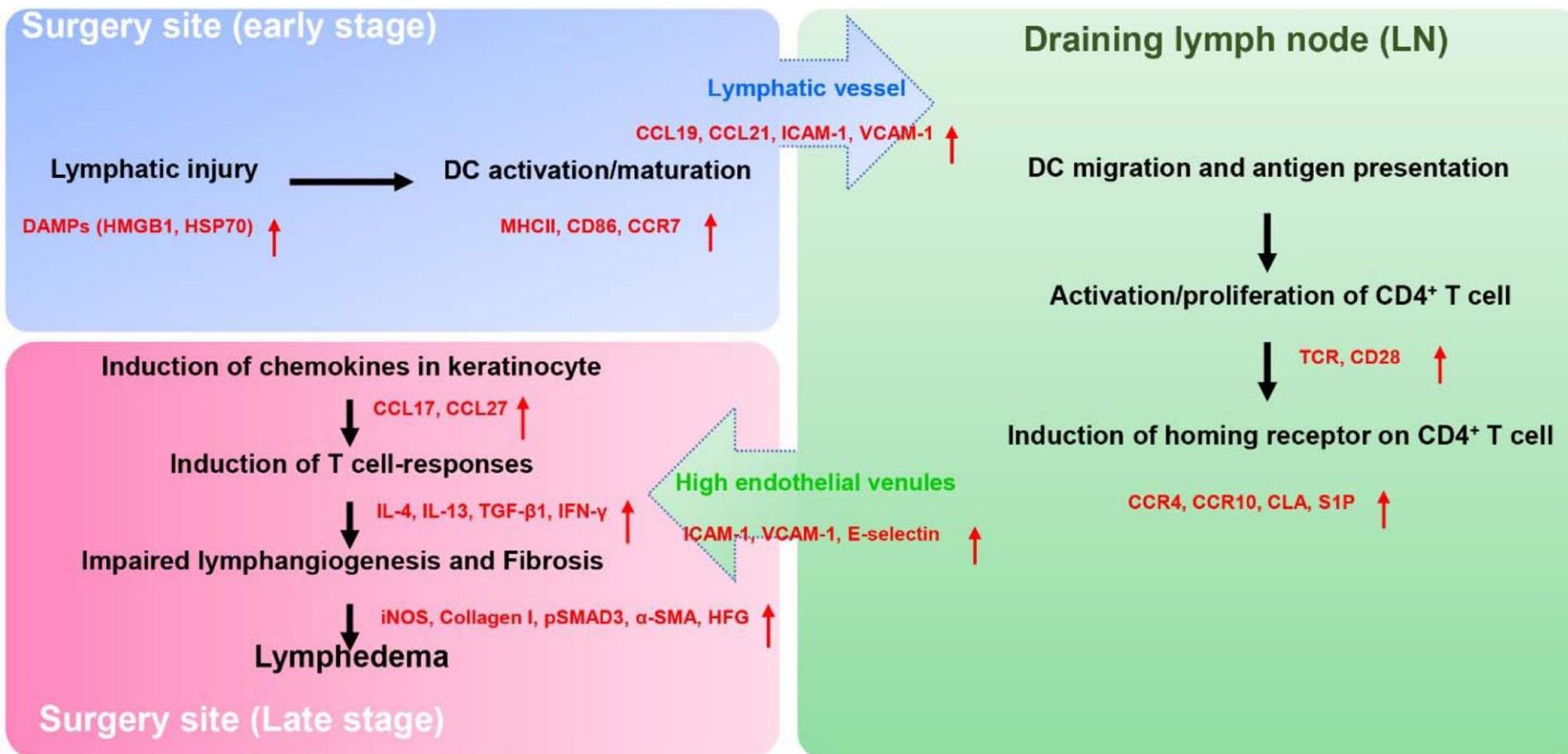
Comparative microarray results:

- Lymphangiogenesis (FGFb)
- Inflammation (IL-4, IL-10, TNF beta)
- Fibrosis (TGF β)

Role of Leukotriene B₄ in lymphedema

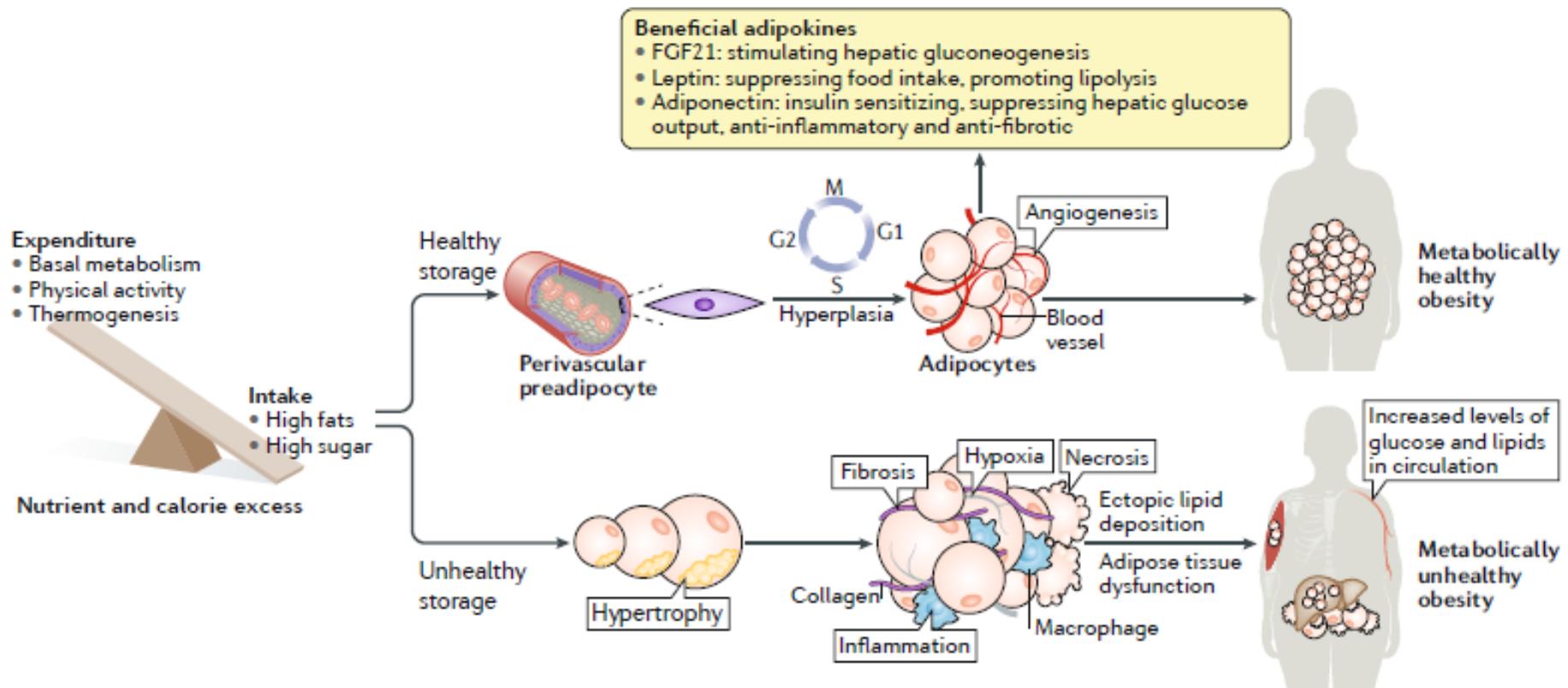
- Lymphangiogenesis
- Inflammation (eg. macrophage, PMNL and T lymphocyte recruitment; Th₁₇ differentiation)
- Fibroblast and adipocyte stimulation
- Edema formation

Inflammation in lymphedema: proposed pathophysiology of secondary lymphedema

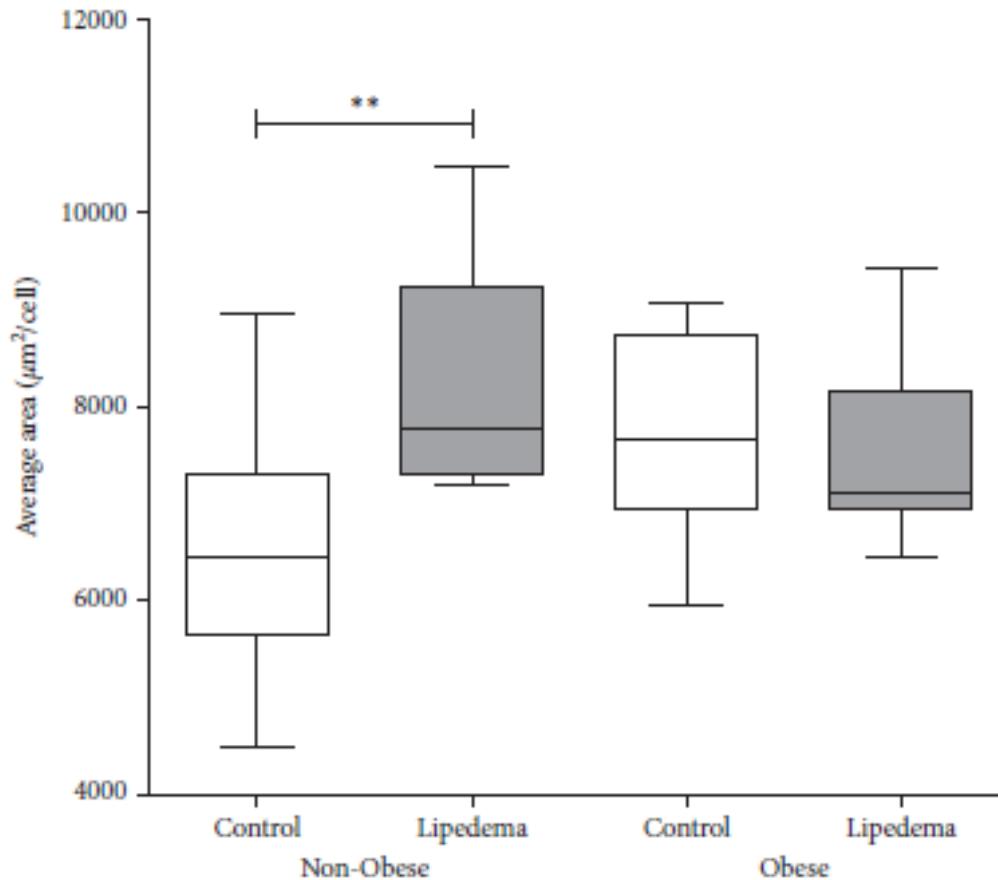


Adipogenic inflammation

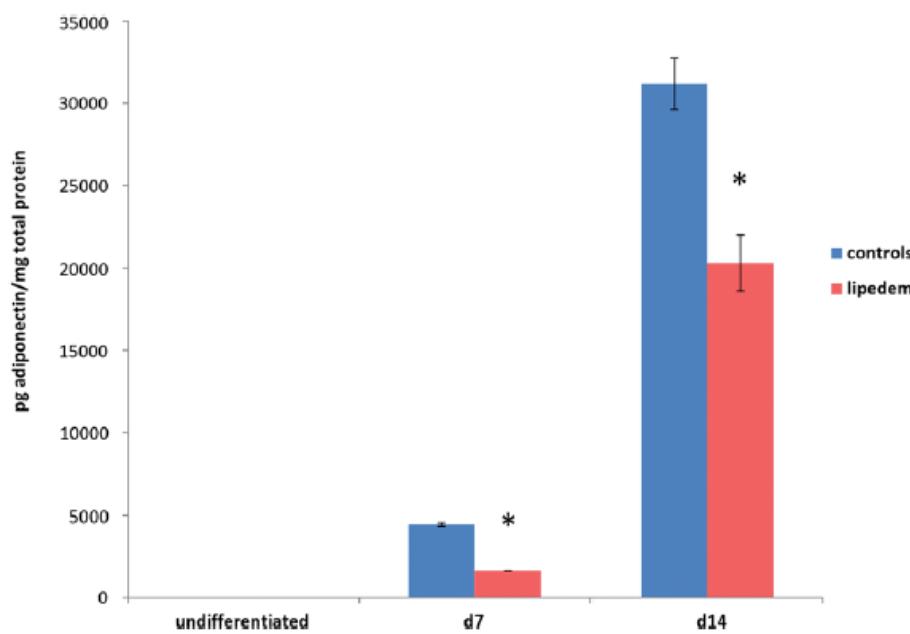
Adipogenesis



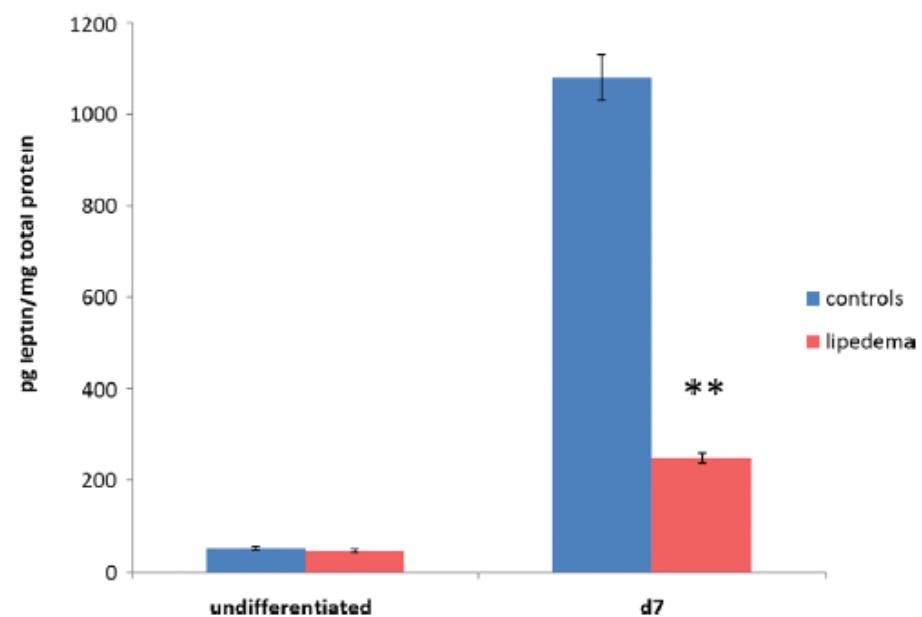
Histological findings in lipedema: sizes of adipocytes



Lipedema vs Control: adipokine expression

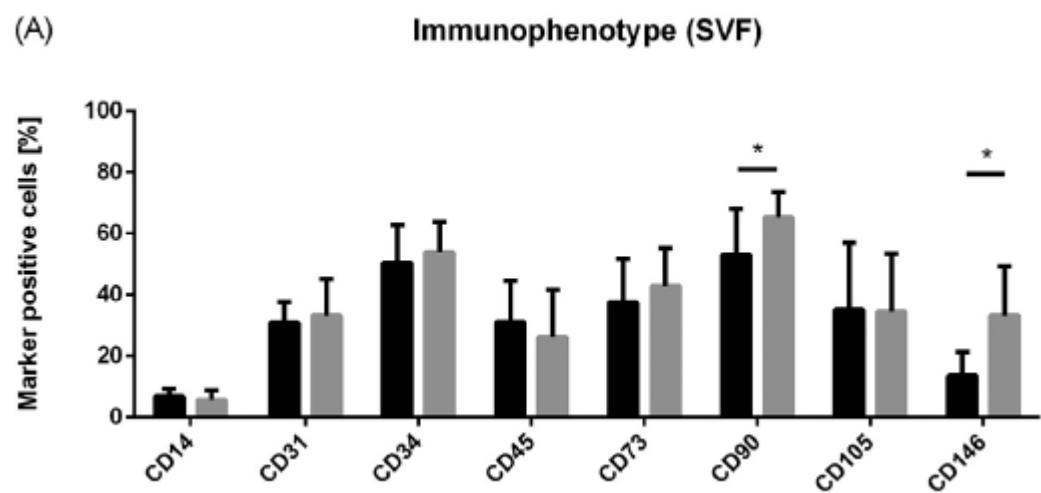
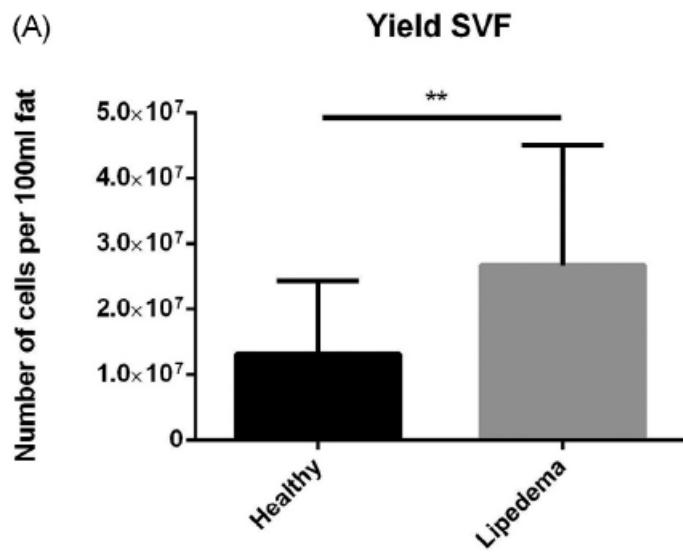


Adiponectin



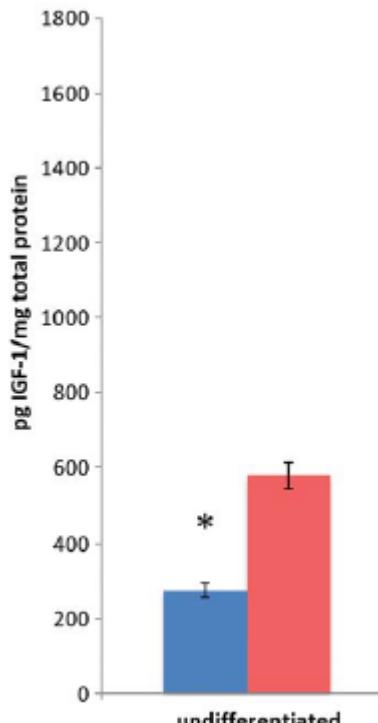
Leptin

Stromal vascular cells of lipedema

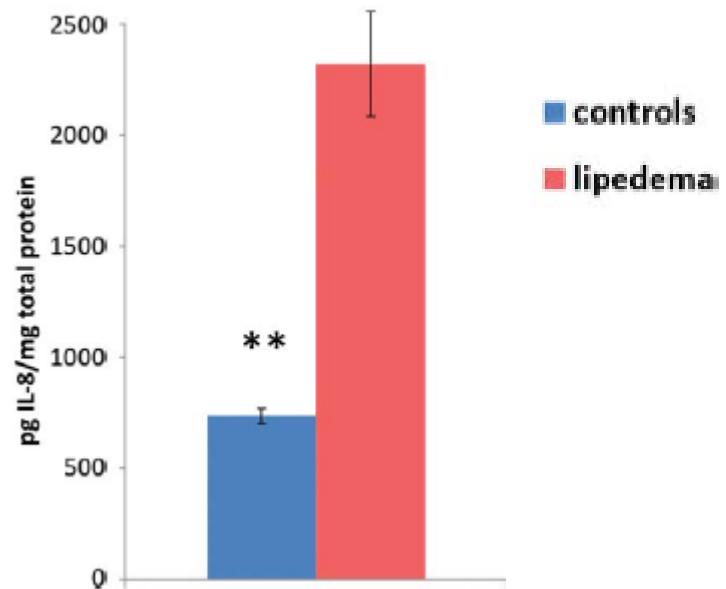


Inflammatory cells and their cytokines in lipedema

Lipedema vs Control: IGF-1 and IL-8 protein expressions



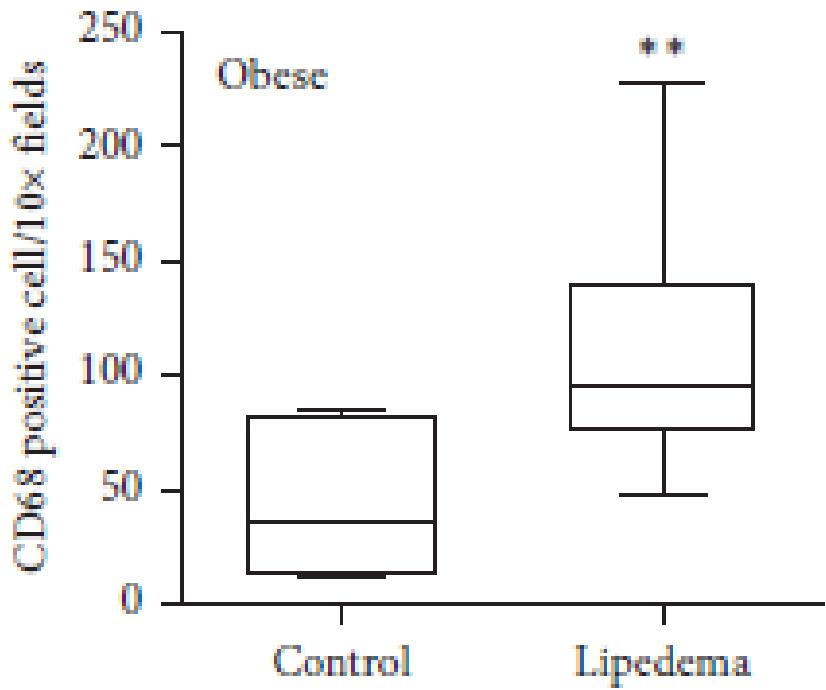
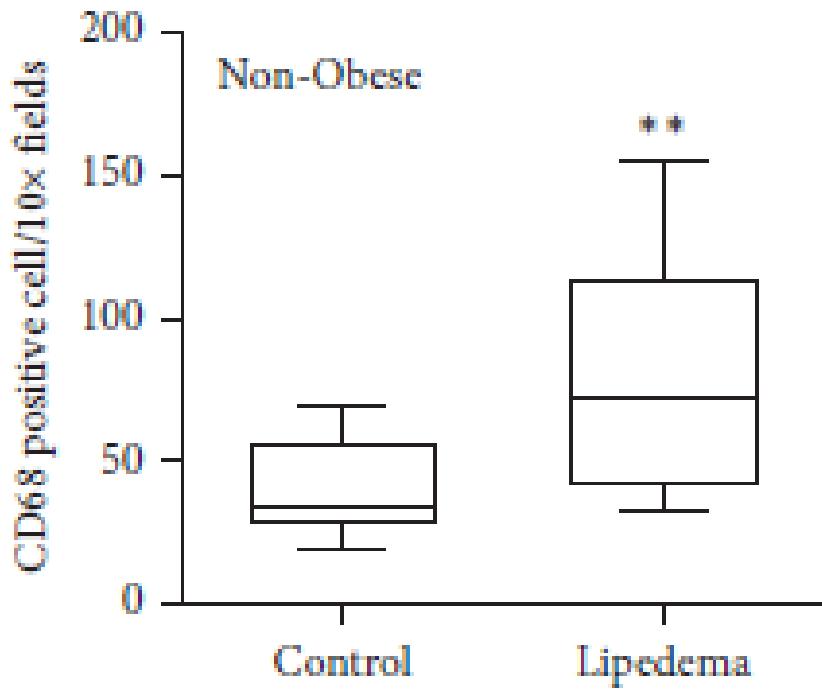
IGF-1



IL-8

Bauer AT et al, Plast Reconstr Surg 2019

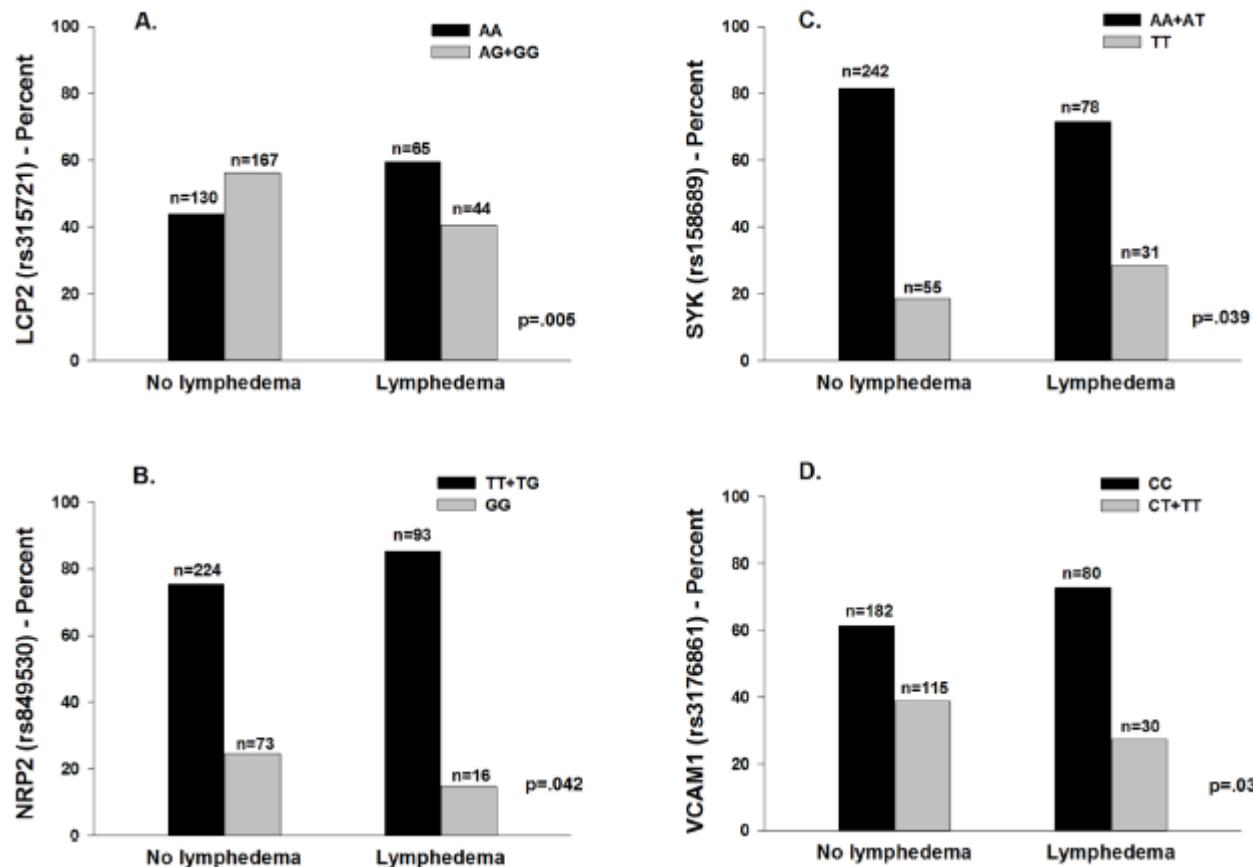
Histological findings in lipedema: macrophages



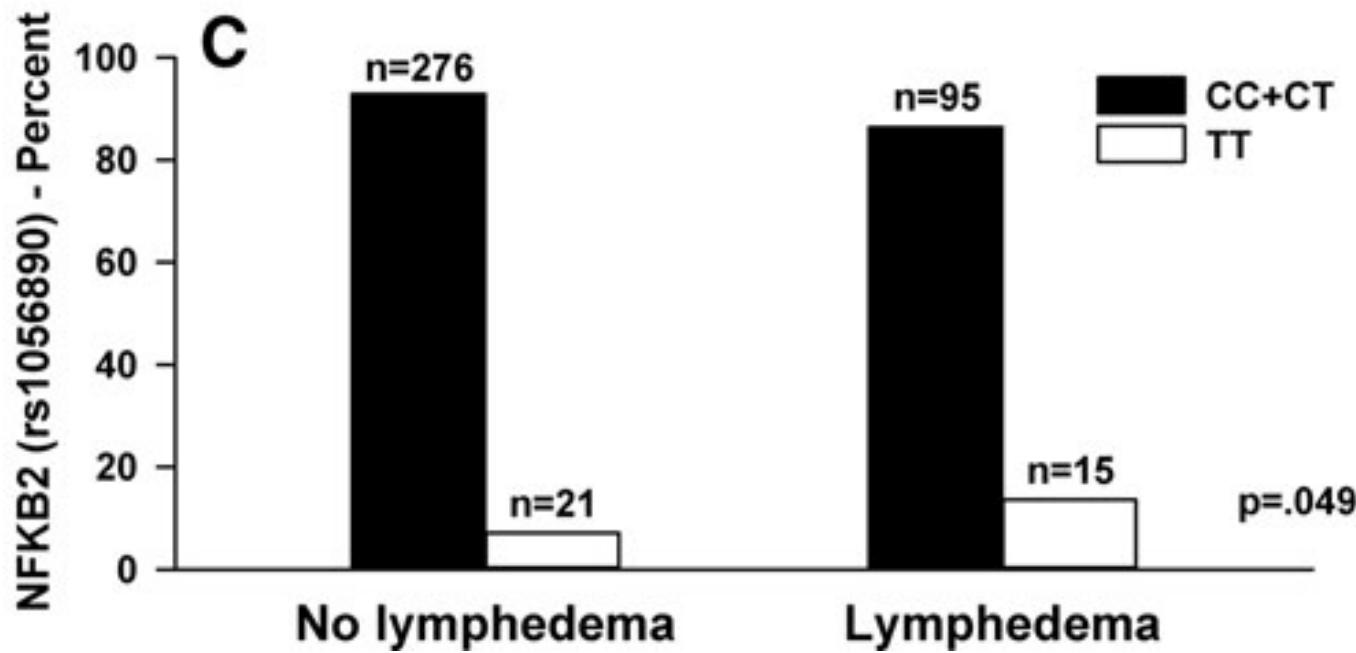
Grazie mille per l'attenzione!



Breast cancer treatment-related secondary lymphedema-associated genetic predispositions



Breast cancer treatment-related secondary lymphedema-associated genetic predisposition



Inflammation in lymphedema

Table 1 Top 10 of the highest priority genes according to the criterion 6 calculated as the average value of five criteria

Gene Symbol	Protein name	Gene Id	1	2	3	4 A	4 B	5	6
			ToppGene	Endeavour	GO BP	Gene CTC	Protein CTC	Comorbid	Average
KDR ^a	Vascular Endothelial Growth Factor Receptor 2	3791	1	1	2	1	4	11	1
TNF	Tumor Necrosis Factor alpha	7124	20	7	32	2	1	1	2
TEK	TEK Receptor Tyrosine Kinase	7010	2	5	4	19,5	11,5	27,5	3
BMPR2	Bone Morphogenetic Protein Receptor Type 2	659	15	12	25	9	10	18,5	4
SERPINE1	Serpin Family E Member 1	5054	10	27	36,5	9	11,5	3	5
IL10	Interleukin 10	3586	19	26	44	5,5	3	3	6
CD40LG	CD40 Ligand	959	29	31	20	7	5	11	7
CCL2	C-C Motif Chemokine Ligand 2	6347	6	43	46	5,5	6	3	8
FASLG	Fas Ligand	356	7	9	40	19,5	27,5	11	9
ABL1	ABL Proto-Oncogene 1, Non-Receptor Tyrosine Kinase	25	4	4	42	9	7,5	49	10

^aControl gene with known associations with lymphedema