Andrea Frontini

Biographical sketch

BORN: 26 September 1972, Reggio Emilia, Italy.

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GOOGLE SCHOLAR PAGE:
https://scholar.google.it/citations?hl=it&user=oA1QTHkAAAAJ&view_op=list_works

RESEARCH FIELD: Molecular mechanisms that control energy balance. This include central mechanisms of action in the hypothalamus but also peripheral signaling pathways in adipose tissue. I have analyzed the biology of adipose tissue in physiological conditions as well as in pathologies such as obesity and diabetes.

RESEARCH ACTIVITY: I have focused my research mainly on central mechanisms that control food intake and energy expenditure. I have investigated hypothalamic and extra hypothalamic sites of leptin action in several independent works and in collaboration with other laboratories. In the last years, I have participated in a FP7 European Project for the recruitment and activation of brown adipose tissue in humans with the intention to curb obesity and metabolic diseases.

The results of his research work have been published in 46 publications in journal indexed in PUB MED and with impact factor; total impact factor 330, mean 7; H index 25 (ISI), 27 (Scopus; from 2003), 28 (Google Scholar); citations: 3518; 3055 from 2012.

The most important works were published in Nature Review Drug Discovery (2016), Cell (2014); Cell Metabolism (2012; 2010), Journal of Clinical Investigation (2011).

EDITORIAL ACTIVITY: Ad Hoc Reviewer for: Nature Communication; Journal of Lipid research; Journal of Clinical Endocrinology and Metabolism; Plos One.

MEMBERSHIPS
Italian Society of Anatomy and Histology
Italian Society for the Study of Obesity

Current position

Associate Professor of Morphology and Human Anatomy, University of Pavia, Italy.

Educational background

Università Politecnica delle Marche, Ph.D. 2006
University of Windsor (ON, Canada) M.Sc. 2002
University of Ancona, Ancona, Italy, B.Sc. 1998

Previous employment

2006-2010	Post Doc at the Università Politecnica delle Marche, Italy.
2010-2015	Assistant Professor at the Università Politecnica delle Marche, School of Medicine, Italy
2015-	Assistant Professor of Human Anatomy, University of Pavia, School of Medicine, Italy

Experience:

Teaching:

I have been teaching Functional Anatomy to the Students enrolled in Obstetrics at the Università Politecnica delle Marche from 2013 to 2015.

I currently teach Morphology ad Human Anatomy to med students enrolled in the Golgi Course (Italian) and Cytology, Histology and Microscopic Anatomy to the students Harvey Course (English). Both courses are provided by the University of Pavia, Italy.

Research:

I have been involved in several International networks (European and US) of research laboratories. The focus of my research in the last ten years is mainly devoted to adipose tissue biology especially in the characterization of morphological and physiological aspects of brown adipose tissue in humans. The morphological approach is the main to try to solve the biological issues in my hands. I have participated to several National and European projects dealing with obesity and diabetes. I have also acted as Reviewer for several Grants proposed at National level or to international foundation in the same field of research.

Experimental:

My main expertise, in the experimental settings, is related to all types of microscopies (light, TEM, SEM and confocal) but also to molecular biology. In the last few years I used Laser microdissection and PALM. I am now approaching FISH (Fluorescent in-situ hybridization) in order to link the expertise in the morphological examination with gene expression analysis**.** I have participated as tutors and as supervisor to several (at least 15) autopsies for research purposes.

Publications:

1. Giordano A, Perugini J, Kristensen DM, Sartini L, **Frontini A**, Kajimura S, Kristiansen K and Cinti S. (2017). Mammary Alveolar Epithelial Cells Convert to Brown Adipocytes in Post-lactating
   Mice. J Cell Physiol. Epub ahead of print
2. Reis FC, Branquinho JL, Brandão BB, Guerra BA, Silva ID, **Frontini A**, Thomou T, Sartini L, Cinti S, Kahn CR, Festuccia WT, Kowaltowski AJ, Mori MA (2016). Fat-specific Dicer deficiency accelerates aging and mitigates several effects of dietary restriction in mice. Aging (Albany NY) 8(6):1201-22
3. Giordano A, **Frontini A**, Cinti S (2016). Convertible visceral fat as a therapeutic target to curb obesity. Nat Rev Drug Discov. 15(6):405-24.
4. Razzoli M, **Frontini A,** Gurney A, Mondini E, Cubuk C, Katz LS, Cero C, Bolan PJ, Dopazo J, Vidal-Puig A, Cinti S, Bartolomucci A (2015) Stress-induced activation of brown adipose tissue prevents obesity in conditions of low adaptive thermogenesis. Mol Metab. 11;5(1):19-33.
5. Pisani DF, Beranger GE, Corinus A, Giroud M, Ghandour RA, Altirriba J, Chambard JC, Mazure NM, Bendahhou S), Duranton C, Michiels JF, **Frontini A**, Rohner-Jeanrenaud F, Cinti S, Christian M, Barhanin J, Amri EZ (2015). The K+ channel TASK1 modulates β-adrenergic response in brown adipose tissue through the mineralocorticoid receptor pathway. FASEB J. 2015 Nov 2. pii: fj.15-277475.
6. Sartini L and **Frontini A** (2015). Potential novel therapeutic strategies from understanding adipocyte transdifferentiation mechanisms. Expert Rev Endocrinol Metab. 10 (2): 143-152.

7. Rosell M, Kaforou M, **Frontini A**, Okolo A, Chan YW, Nikolopoulou E, Millership S, Fenech ME, MacIntyre D, Turner JO, Moore JD, Blackburn E, Gullick WJ, Cinti S, Montana G, Parker MG, Christian M (2014). Brown and white adipose tissues: intrinsic differences in gene expression and response to cold exposure in mice. Am J Physiol Endocrinol Metab. 15;306(8):E945-64
8. Kiskinis E, Chatzeli L, Curry E, Kaforou M, **Frontini A**, Cinti S, Montana G, Parker MG, Christian M (2014). RIP140 represses the "brown-in-white" adipocyte program including a futile cycle of triacyclglycerol breakdown and synthesis. Mol Endocrinol. 28(3):344-56.
9. Giordano A, Smorlesi A, **Frontini A**, Barbatelli G, Cinti S (2014). White, brown and pink adipocytes: the extraordinary plasticity of the adipose organ. Eur J Endocrinol. 10;170(5):R159-71.
10. Giannulis I, Mondini E, Cinti F, **Frontini A**, Murano I, Barazzoni R, Barbatelli G, Accili D, Cinti S (2013). Increased density of inhibitory noradrenergic parenchymal nerve fibers in hypertrophic islets of Langerhans of obese mice. Nutr Metab Cardiovasc Dis 24(4):384-92.
11. Cohen P, Levy JD, Zhang Y, **Frontini A**, Kolodin DP, Svensson KJ, Lo JC, Zeng X, Ye L, Khandekar MJ, Wu J, Gunawardana SC, Banks AS, Camporez JP, Jurczak MJ, Kajimura S, Piston DW, Mathis D, Cinti S, Shulman GI, Seale P, Spiegelman BM (2014). Ablation of PRDM16 and Beige Adipose Causes Metabolic Dysfunction and a Subcutaneous to Visceral Fat Switch. Cell. 156(1-2):304-16.
12. Karbiener M, Pisani DF, **Frontini A**, Oberreiter LM, Lang E, Vegiopoulos A, Mössenböck K, Bernhardt GA, Mayr T, Hildner F, Grillari J, Ailhaud G, Herzig S, Cinti S, Amri EZ, Scheideler M (2014). MicroRNA-26 family is required for human adipogenesis and drives characteristics of brown adipocytes. Stem Cells. 32(6):1578-90.
13. Hondares E, Gallego-Escuredo JM, Flachs P, **Frontini A**, Cereijo R, Goday A, Perugini J, Kopecky P, Giralt M, Cinti S, Kopecky J, Villarroya F (2014). Fibroblast growth factor-21 is expressed in neonatal and pheochromocytoma-induced adult human brown adipose tissue. Metabolism. 63(3):312-7.
14. Crucianelli E, Bruni P, **Frontini A**, Massaccesi M, Pisani M, Smorlesi A and Mobbili G (2014) Liposomes containing mannose-6-phosphate-cholesteryl conjugates for lysosome-specific delivery. RSC Advances 4 (102), 58204-58207
15. Sacks HS, Fain JN, Bahouth SW, Ojha S, **Frontini A**, Budge H, Cinti S, Symonds ME (2013). Adult Epicardial Fat Exhibits Beige Features. J Clin Endocrinol Metab. 98(9):E1448-55.
16. **Frontini A**, Vitali A, Perugini J, Murano I, Romiti C, Ricquier D, Guerrieri M, Cinti S (2013). White-to-brown transdifferentiation of omental adipocytes in patients affected by pheochromocytoma. Biochim Biophys Acta. 1831(5):950-9.
17. Poloni A, Maurizi G, Serrani F, Mancini S, Zingaretti MC, **Frontini A**, Cinti S, Olivieri A, Leoni P (2013). Molecular and functional characterization of human bone marrow adipocytes. Exp Hematol. 41(6):558-566.e2.
18. Barneda D, **Frontini A**, Cinti S, Christian M (2013). Dynamic changes in lipid droplet-associated proteins in the "browning" of white adipose tissues. Biochim Biophys Acta. 1831(5):924-33.
19. Severi I, Perugini J, Mondini E, Smorlesi A, **Frontini A**, Cinti S, Giordano A (2013). Opposite effects of a high-fat diet and calorie restriction on ciliary neurotrophic factor signaling in the mouse hypothalamus. Front Neurosci. 27;7:263.

20. Smorlesi A, **Frontini A**, Giordano A, Cinti S (2012). The adipose organ: white-brown adipocyte plasticity and metabolic inflammation. Obes Rev. 13 Suppl 2:83-96.
21. **Frontini A**, Giordano A, Cinti S (2012) Endothelial cells of adipose tissues: A niche of adipogenesis. Cell Cycle 11(15): 2765-2766
22. Jung KM, Clapper JR, Fu J, D'Agostino G, Guijarro A, Thongkham D, Avanesian A, Astarita G, Dipatrizio NV, **Frontini A**, Cinti S, Diano S, Piomelli D (2012). 2-arachidonoylglycerol signaling in forebrain regulates systemic energy metabolism. Cell Metab. 15(3):299-310
23. Poloni A, Maurizi G, Leoni P, Serrani F, Mancini S, **Frontini A**, Zingaretti C, Siquini W, Sarzani R and Cinti S. (2012) Human de-differentiated adipocytes show similar properties to bone marrow derived mesenchymal stem cells. Stem Cells 30(5):965-7
24. Gupta RK, Mepani RJ, Kleiner S, Lo JC, Khandekar MJ, Cohen P, **Frontini A**, Bhowmick DC, Ye L, Cinti S, Spiegelman BM (2012). Zfp423 expression identifies committed preadipocytes and localizes to adipose
endothelial and perivascular cells. Cell Metab. 15(2):230-9
25. Tran KV*, Gealekman O*, **Frontini A***, Zingaretti MC, Morroni M, Giordano A, Smorlesi A, Perugini J, De Matteis R, Sbarbati A, Corvera S, Cinti S (2012). The vascular endothelium of the adipose tissue gives rise to both white and brown fat cells. Cell Metab. 15(2):222-9
equal contribution as first author
26. Vitali A, Murano I, Zingaretti MC, **Frontini A**, Ricquier D, Cinti S (2012) The adipose organ of obesity-prone C57BL/6J mice is composed of mixed white and brown adipocytes. J Lipid Research 53(4):619-29
27. Possenti R, Muccioli G, Petrocchi P, Cero C, Cabassi A, Vulchanova L, Riedl M, Manieri M, **Frontini A**, Giordano A, Cinti S, Govoni P, Graiani G, Quaini F, Ghe C, Bresciani E, Bulgarelli I, Torsello A, Locatelli V, Sanghez V, Larsen B, Petersen J, Palanza P, Parmigiani S, Moles A, Levi A, Bartolomucci A (2012). Characterization of a novel peripheral pro-lipolytic mechanism in mice: role of VGF-derived peptide TLQP-21. Biochem J. 441(1):511-22
28. Gaidhu MP, **Frontini A**, Hung S, Pistor K, Cinti S, Ceddia RB (2011). Chronic AMP-kinase activation with AICAR reduces adiposity by remodeling adipocyte metabolism and increasing leptin sensitivity. J Lipid Res. 52(9):1702-11
29. Seale P, Conrow HM, Estall J, Kajimura S, **Frontini A**, Ishibashi J, Cohen P, Cinti S and Spiegelman B (2011). Prdm16 determines the thermogenic program of subcutaneous white adipose tissue in mice. *JCI* 121 (1):96-105
30. Betti M, Ambrogini P, Minelli A, Floridi A, Lattanzi D, Ciuffoli S, Bucherelli C, Prospero E, **Frontini A**, Santarelli L, Baldi E, Benetti F, Galli F, Cuppini R (2011). Maternal dietary loads of alpha-tocopherol depress protein kinase C signaling and synaptic plasticity in rat postnatal developing hippocampus and promote permanent deficits in adult offspring. *J Nutr Biochem*. 2*2(1):60-70*
31. **Frontini A**, Cinti S (2010). Distribution and development of brown adipocytes in the murine and human adipose organ. *Cell Metabolism* 11(4):253-6
32. **Frontini A** and Giordano A (2010). Leptin-sensitive neurons in mouse preoptic area express alpha(1A)- and alpha(2A)-adrenergic receptor isoforms. *Neuroscience Letters* 471(2):83-8
33. De Matteis R, Zingaretti MC, Murano I, Vitali A, **Frontini A**, Giannulis I, Barbatelli G, Marcucci F, Bordicchia M, Sarzani R, Raviola E, Cinti S (2009). In vivo Physiologic Transdifferentiation of Adult Adipose Cells. *Stem Cells* 27(11):2761-8

34. Ambrogini P, Cuppini R, Lattanzi D, Ciuffoli S, **Frontini A**, Fanelli M (2009). Synaptogenesis in adult-generated hippocampal granule cells is affected by behavioral experiences. *Hippocampus* 20(7):799-810
35. Zingaretti MC, Crosta F, Vitali A, Guerrieri M, **Frontini A**, Cannon B, Nedergaard J, Cinti S (2009). The presence of UCP1 demonstrates that metabolically active adipose tissue in the neck of adult humans truly represents brown adipose tissue. *FASEB* J. 23(9):3113-20
36. Valerio A, Dossena M, Bertolotti P, Boroni P, Sarnico I, Delbarba A, Faraco G, Chiarugi A, Giordano A, **Frontini A**, Tonello C, Liou HC, De Simoni MG, Spano P, Carruba M, Pizzi M (2009) Leptin protects against cerebral ischemia through inhibition of glycogen synthase kinase-3beta and activation of NF-kappaB/c-Rel-dependent transcription. *Stroke 40(2):610-7*
37. Latini C, **Frontini A***, Morroni M, Marzioni D, Castellucci M and Smith P. G. (2008). Remodeling of uterine innervation. *Cell and Tissue Research 334(1):1-6.*

equal contribution as first author
38. Giordano A, **Frontini A** and Cinti S (2008). Adipose organ nerves revealed by immunohistochemistry. *Methods in Molecular Biology, Humana Press 456:83-95.*
39. **Frontini A,** Tonello C, Nisoli E, Cinti S and Giordano A (2008). Leptin-dependent STAT3 phosphorylation in postnatal mouse hypothalamus. *Brain research 1215:105-115*
40. **Frontini A**, Rousset S, Cassard-Doulcier AM, Zingaretti C, Ricquier D and Cinti S (2007). Thymus Uncoupling protein 1 is exclusively localized in surrounding typical brown adipocytes and is absent in thymocytes. *The Journal of Histochemistry and Cytochemistry* 55(2):183-9
41. Giordano A, Song CK, Bowers RR, Ehlen JC, Frontini A, Cinti S, Bartness TJ (2007). Reply to Kreier and Buijs: No sympathy for the claim of parasympathetic innervation of white adipose tissue. *American Journal of Physiology-Regul. Integr. Comp. Physiol* 293(1):R550-R552.
42. Giordano A, Song CK, Bowers R, Ehlen JC, **Frontini A**, Cinti S and Bartness T (2006). White adipose tissue lacks significant vagal innervation and immunohistochemical evidence of parasympathetic innervation. *American Journal of Physiology-Regul. Integr. Comp. Physiol. 291(5)R1243-55*
43. Valerio A, Ghisi V, Dossena M, Tonello C, Giordano A, **Frontini A**, Ferrario M, Pizzi M, Spano P, Carruba M, Nisoli E (2006). Leptin increases growth cone size in developing mouse cortical axons by convergent signals inactivating glycogen synthase kinase-3β. *Journal of Biological Chemistry* 281(18):12950-12958
44. Giordano A, **Frontini A**, Murano I, Tonello C, Marino MA, Carruba MO, Nisoli E and Cinti S Regional-Dependent Increase of Sympathetic Innervation in Rat White Adipose Tissue during Prolonged Fasting (2005). *The Journal of Histochemistry and Cytochemistry* 53(6):679-87.
45. Giordano A, **Frontini A**, Castellucci M and Cinti S (2004) Presence and distribution of Cholinergic Nerves in Rat Mediastinal Brown Adipose Tissue. *The Journal of Histochemistry and Cytochemistry* 52(7):923-30
46. **Frontini A**, Zaidi AU, Hua H, Wolak TP, Greer CA, Kafitz KW, Li W and Zielinski B (2003). Olfactory bulb organization in the larval stage of the sea lamprey Petromyzon marinus: discrete subsetsof olfactory glomeruli with Golf localization and with serotonin innervation. *The Journal of Comparative Neurology* 465:27-37
47. Salvolini E, Nanetti L, Moretti N, Vignini A, Martarelli D, **Frontini A**, Santroni AM, Falcioni G and L. Mazzanti (2002) Relationship between Na^+, K^+- ATP ase, sialic acid content and fluidity in

rainbow trout density-separated erythocytes. *Journal of Fish Biology* 61, 489-491.

Chapters in books:

- M.A. Shiffman et al. (Eds.), Stem Cells in Aesthetic Procedures, © Springer-Verlag Berlin Heidelberg 2014. The Adipose Organ: Morphological Perspectives of Adipose Tissues. Arianna Smorlesi, Andrea Frontini and Saverio Cinti
- Leptin: Biosynthesis, Functions and Clinical Significance © Nova Science Publishers, Inc., 2014. Leptin: From energy balance to inflammatory process in obesity. Corgosinho, F.C., Frontini, A, Giordano, A, Cinti, S, Dâmaso, A.R
- Yihai Cao Ed. Angiogenesis in Adipose Tissue, © Springer Science-Business Media New York 2013. Origin of Adipocyte Precursors from Adipose Vascular Endothelium. Andrea Frontini, Silvia Corvera, and Saverio Cinti

Acts of Congress

- ***Invited Speaker:*** VII Congresso Nazionale Società Italiana dell'Obesità, 29 Settembre - 1° Ottobre, Rome, Italy. Title: Uomini e Topi: Studio comparativo sullo sviluppo e sulla distribuzione del tessuto adiposo bruno.

- ***Invited Speaker:*** **"**Symposium on Brown adipose tissue and euthermia" Wenner-Gren Center, Stockholm (Sweden) May 25-28, 2016. Title: Ultrastructure of human brown adipocytes.
- ***Poster presentation:*** Keystone Symposia Beige and brown fat: Basic Biology and Novel Therapeutics. April 17-22, 2015 Snowbird, Utah, USA. Title of the poster: From fetus to adult human: developmental cues to unravel different shades of fat". Andrea Frontini, Loris Sartini, Monica Banita, Catalina Pisoschi, Marina Fusaru, Cristina Zingaretti and Saverio Cinti.
- ***Invited speaker*** for: BHF Centre of Research Excellence Workshop and 40th UK Adipose Tissue Discussion Group. Title: *Browning of the Adipose Organ in Humans.* 12- 13 December 2013. THE QUEEN'S MEDICAL RESEARCH INSTITUTE, Edinburgh, Scotland.
- ***Attender***: 11th Stock Conference - Brown Adipose Tissue - a human anti-obesity tissue? November 2-4, 2012; Montreal, Canada.
- BENZON SYMPOSIUM- Adipose Tissue in Health and Disease - Copenhagen, August 27-30, 2012. ***Poster***: Origin of white and brown adipose cells from vascular endothelium
  Andrea Frontini*, Khanh-Van Tran, Olga Gealekman, Maria Cristina Zingaretti, Silvia Corvera and Saverio Cinti.*
- ECO2011 18th European Congress on Obesity; Istanbul, Turkey, 25-28 May 2011.
  Poster presentation: WAT to BAT transdifferentiation in omental fat of patients with pheochromocytoma.
  A. Frontini*, A. Vitali, J. Perugini, M.C. Zingaretti, C. Romiti, M. Guerrieri and S. Cinti*
- ECO2009 17thEuropean Congress on Obesity; Amsterdam, The Netherlands, 6-9 May 2009.
  Poster presentation: The presence of UCP1 demonstrates that metabolically active adipose tissue in the neck of adult humans truly represents brown adipose tissue.
  M.C. Zingaretti, F. Crosta, A. Vitali, M. Guerrieri , ***A. Frontini****, B. Cannon , J. Nedergaard, and S. Cinti.*
- SINS 2007 Società Nazionale di Neuroscienze. Verona (Italia) 27-30 Settembre 2007.
  Poster presentation: Leptin action in the hypothalamus of postnatal developing mice.

***Frontini A**, Cinti S and Giordano A*

- XXXV^{eme} Symposium National de Morphologie Normale et Pathologique. Craiova (Romania) 27-29 Maggio 2004. ***Poster***: Neuronal Plasticity in Uterus and Placenta.
  ***Frontini A**, Capparuccia L, Giovannelli A, Banita M, Marzioni D and Castellucci M.*
- ECO2004 13th European Congress on Obesity. Prague, 26-29 Maggio 2004.
  - Cholinergic nerves in mediastinic brown adipose tissue.
    *Giordano A, **Frontini A**, Castellucci M and Cinti S*
  - Sema3A-sensitive nerves in rat white adipose tissue.
    *Giordano A, Cesari P, Capparuccia L, **Frontini A**, Castellucci M and Cinti S.*
- 5th International Weber Symposium on innovative Fluorescence Methodologies in Biochemistry and Medicine, Kauai, Hawaii (USA), 2002, 25-29 June "A preparation for in situ spatial and temporal analysis of olfactory sensory neuron activity in the primary olfactory pathway". *Zielinski B and **Frontini A.***
- XXIV Annual Meeting of AChemS 24-28 April 2002, Sarasota, Florida. "G-protein coupled receptors in the olfactory system: a strongly conserved mechanism of signal transduction". ***Speaker***: ***Frontini A**, Zielinski B, Li W, Dakhil C, Yun S.*
- Work shop of Great Lake Fishery Commission, 15th February 2002 Detroit, Michigan.
- XXIII Annual Meeting of AChemS (Association for Chemoreception Sciences). 20-24 April 2001, Sarasota, Florida. "A preparation of the primary olfactory pathway in larval sea lamprey for dinamic optical images". ***Speaker***: ***Frontini A** and Zielinski B.*
- Meeting of Marine Biochemistry (Ozzano Emilia, 9 Luglio 1999). "Seasonal variations of physical and biochemical membrane properties in trout erythrocytes". *Breccia T, **Frontini A**, Salvolini E, Moretti N, Falcioni G, Mazzanti L*.

In faith

Signature: Prof. Andrea Frontini