

## ALLEGATO B

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## [Nome e cognome] CURRICULUM VITAE

### INFORMAZIONI PERSONALI (NON INSERIRE INDIRIZZO PRIVATO E TELEFONO FISSO O CELLULARE)

COGNOME	RAGNI
NOME	MAURIZIO
DATA DI NASCITA	7/8/1968

### INSERIRE IL PROPRIO CURRICULUM (non eccedente le 30 pagine)

#### PERSONAL INFORMATION

Maurizio Ragni

**Institutional Address:** Department of Medical Biotechnology and Translational Medicine

University of Milan

Via Vanvitelli 32, 20129 Milan (Italy)

**Phone:** +390250317116

**E-mail:** [maurizio.ragni@guest.unimi.it](mailto:maurizio.ragni@guest.unimi.it)

**Nationality**

Italian

#### WORK EXPERIENCE

June 2006 – present

University of Milan, Department of Medical Biotechnology and Translational Medicine, Medical Pharmacology Unit (Supervisor: Prof. Enzo Nisoli).

*Development of the projects:*

*“Nutritional and pharmacological approaches to promote mitochondrial biogenesis in age-related metabolic disorders in vitro and in vivo”*

*“Multicomponent analysis of physical frailty biomarkers: focus on mitochondrial health”*

*“The manipulation of macronutrient in diet as a therapeutic approach to ameliorate metabolic responses in obese mice model”*

*"Caloric restriction and neuroprotection: role of nitric oxide in mitochondriogenesis and neuronal bioenergetics"*

*"Neuroprotective role of Leptin in in vitro models of cerebral stroke"*

*"Nutritional approaches to study statin toxicity"*

January 2009 – August 2010

Research Fellow at University of Milan, Department of Medical Biotechnology and Translational Medicine, Medical Pharmacology Unit

January 2008-December 2008

Research Fellow at University of Milan, Department of Medical Biotechnology and Translational Medicine, Medical Pharmacology Unit

September 2006- December 2007

Research Fellow at University of Milan, Department of Medical Biotechnology and Translational Medicine, Medical Pharmacology Unit

*Research Project: Neuroprotective role of Leptin in in vitro models of cerebral stroke*

May 2005 – June 2006

DTI (Dulbecco Telethon Institute) at Department of Endocrinology and Metabolism of Ospedale Cisanello - Pisa (Italy).

*Research project: "Static and dynamic localization of Cathepsin K in adipocytes". Tutor: Dr. Margherita Maffei*

March 2001 – October 2004

Department of Life Sciences of 2nd University of Naples

*Research Project: Molecular aspects of cellular bioenergetics: the uncoupling proteins"*

February 1999 – September 2000

"Tecnogen ScpA" research center in Piana di Monteverna (Caserta - Italy)

*Research Project: Genetic transformation of african violet (Saintpaulia ionantha)*

## EDUCATION AND TRAINING

October 2004

### **PhD in Molecules of biotechnological interest**

Department of Life Sciences of 2nd University of Naples (Italy).

▪ Thesis : *"Molecular aspects of cellular bioenergetics: the uncoupling proteins"*

October 2000

### **Biology degree**

2nd University of Naples (Italy)

Thesis: *"Genetic transformation of african violet (Saintpaulia ionantha) for pathogen resistance with a wound-inducible RIP gene"*

Grade: 110/110 cum laude

## PERSONAL SKILLS

Native Language Italian

Other language

English

UNDERSTANDING		SPEAKING		WRITING
Listening	Reading	Spoken interaction	Listening	Reading
Good	Excellent	Good	Good	Excellent

Competences and Research  
Topic

**ANIMAL HANDLING.** Handling of small laboratory animals (rats and mice). Pharmacological and cellular treatments *in vivo* by intraperitoneal, intravenous, subcutaneous, intramuscular injections and oral administration (gavage). Surgery in small laboratory animals: muscular biopsy, ovariectomy. Oral glucose tolerance test (OGTT), intraperitoneal glucose tolerance test (IPGTT) and insulin tolerance test (ITT). Exercise training of mice with tread mill apparatus. Blood samples collection by submandibular puncture of the facial vein in mice. Mouse xenografts models set up and measurement Tissues and organs collection.

**CELL BIOLOGY.** Mammalian cell culture: white and brown adipose tissue and skeletal muscle primary cell lines isolation, transient and stable transfection of mammalian cells. Maintenance of primary and immortalized cell lines (i.e., C2C12 myoblast, HL-1 cardiomyocytes, 3T3L1 adipocytes). Mitochondrial extraction and oxygen consumption measurement with both Clark electrode and Seahorse analyzer XF24

**MOLECULAR BIOLOGY.** Genomic and plasmid DNA extraction, RNA and DNA extraction from tissues, cells and whole blood, Real Time qPCR, standard cloning techniques in *Escherichia coli*, Western blotting, siRNA gene silencing.

My research interest has been mainly focused on the regulation of metabolism. During my PhD at University of Naples, I first investigated the mechanisms underlying the well-known role of thyroid hormones in this process; together with my research group, I showed that mitochondrial uncoupling protein 3 (UCP3), by regulating mitochondrial oxygen consumption, is one major target of triiodothyronine action. Afterwards, I was involved in the discovery of diiodothyronine, a previously underappreciated thyroid hormone, as a powerful drug able to decrease body weight by increasing the burning of fat. On these basis, with the aim to extend my knowledge of adipose tissue biology, I moved to Pisa for my post-doc; my work in the Dulbecco Telethon Institute lab of Dr Margherita Maffei has then helped to shed light on the role of the cathepsin K protease in the regulation of fat stores. After that, I won a research fellow in Prof. Enzo Nisoli lab in Milan where, by studying the function of nitric oxide (NO) in the process of mitochondrial biogenesis, I further investigated the mitochondrial mechanisms which control energy metabolism; during this period, I contributed to several findings revealing the many cellular functions of this molecule, all of which stem from its ability to powerful boost mitochondrial activity, thus greatly broadening the knowledge of NO biology. After that, I was intrigued by a different approach, that is, the role of nutrients as a pharmacological tool for the stimulation of mitochondriogenesis. In particular, I am currently studying how manipulation of amino acids supply can modulate energy metabolism. In support of our experimental approach are our recent data, which point towards a pivotal role of amino acids as being able to counteract the harmful effects of aging and other morbidities such as liver and muscle diseases.

Computer skills Excellent knowledge of Microsoft Office (Word, Excel, Power Point); and statistic program (GraphPad Prism). Good knowledge of MacOS

Driving license Driving license B

## TEACHING

**2008 - Present** Lectures for the medical pharmacology course (Prof. Enzo Nisoli) at the school of nursing, department of medicine and surgery, University of Milan.

**November 2004 – February 2005** Teacher of “Methods in Physiology” six-month course at school of Mathematics, Physics and Natural sciences (2<sup>nd</sup> University of Naples).

## THESIS COSUPERVISOR

September 2008 -present: Coordination of students for the period of training and thesis. Cotutor for the graduation thesis students in Biology.

## PEER REVIEWED ARTICLES

Barazzoni R, Gortan Cappellari G, **Ragni M**, Nisoli E. Insulin resistance in obesity: an overview of fundamental alterations. *Eat Weight Disord.* 2018 Apr;23(2):149-157. Epub 2018 Feb 3. Review

Tedesco L, Corsetti G, Ruocco C, **Ragni M**, Rossi F, Carruba MO, Valerio A, Nisoli E. A specific amino acid formula prevents alcoholic liver disease in rodents. *Am J Physiol Gastrointest Liver Physiol.* 2018 May 1;314(5): G566-G582

D'Antona G, Tedesco L, Ruocco C, Corsetti G, **Ragni M**, Fossati A, Saba E, Fenaroli F, Montinaro M, Carruba MO, Valerio A, Nisoli E. A Peculiar Formula of Essential Amino Acids Prevents Rosuvastatin Myopathy in Mice. *Antioxid Redox Signal.* 2016 Oct 10;25(11):595-608

Vettor, R., Valerio, A., **Ragni, M.**, Trevellin, E., Granzotto, M., Olivieri, M., Tedesco, L., Ruocco, C., Fossati, A., Fabris, R., Serra, R., Carruba, M.O., Nisoli, E. Exercise training boosts eNOS-dependent mitochondrial biogenesis in mouse heart: Role in adaptation of glucose metabolism (2014) *American Journal of Physiology - Endocrinology and Metabolism*, 306 (5), pp. E519-E528.

Cattaneo, M.G., Cappellini, E., **Ragni, M.**, Tacchini, L., Scaccabarozzi, D., Nisoli, E., Vicentini, L.M. Chronic nitric oxide deprivation induces an adaptive antioxidant status in human endothelial cells (2013) *Cellular Signalling*, 25 (11), pp. 2290-2297. doi: 10.1016/j.cellsig.2013.07.026

Cattaneo, M.G., Cappellini, E., Benfante, R., **Ragni, M.**, Omodeo-Salè, F., Nisoli, E., Borgese, N., Vicentini, L.M. Chronic deficiency of nitric oxide affects hypoxia inducible factor-1 $\alpha$  (HIF-1 $\alpha$ ) stability and migration in human endothelial cells (2011) *PLoS ONE*, 6 (12)

Valerio, A., Bertolotti, P., Delbarba, A., Perego, C., Dossena, M., **Ragni, M.**, Spano, P., Carruba, M.O., De Simoni, M.G., Nisoli, E. Glycogen synthase kinase-3 inhibition reduces ischemic cerebral damage, restores impaired mitochondrial biogenesis and prevents ROS production (2011) *Journal of Neurochemistry*, 116 (6), pp. 1148-1159.

Tedesco, L., Valerio, A., Dossena, M., Cardile, A., **Ragni, M.**, Pagano, C., Pagotto, U., Carruba, M.O., Vettor, R., Nisoli, E. Cannabinoid receptor stimulation impairs mitochondrial biogenesis in mouse white adipose tissue, muscle, and liver: The role of eNOS, p38 MAPK, and AMPK pathways (2010) *Diabetes*, 59 (11), pp. 2826-2836.

D'Antona, G., **Ragni, M.**, Cardile, A., Tedesco, L., Dossena, M., Bruttini, F., Caliaro, F., Corsetti, G., Bottinelli, R., Carruba, M.O., Valerio, A., Nisoli, E. Branched-chain amino acid supplementation promotes survival and supports cardiac and skeletal muscle mitochondrial biogenesis in middle-aged mice (2010) *Cell Metabolism*, 12 (4), pp. 362-372.

De Lange, P., Feola, A., **Ragni, M.**, Senese, R., Moreno, M., Lombardi, A., Silvestri, E., Amat, R., Villarroja, F., Goglia, F., Lanni, A. Differential 3,5,3'-triiodothyronine-mediated regulation of uncoupling protein 3 transcription: Role of fatty acids (2007) *Endocrinology*, 148 (8), pp. 4064-4072. DOI:

Funicello, M., Novelli, M., **Ragni, M.**, Vottari, T., Cocuzza, C., Soriano-Lopez, J., Chiellini, C., Boschi, F., Marzola, P., Masiello, P., Saftig, P., Santini, F., St-Jacques, R., Desmarais, S., Morin, N., Mancini, J., Percival, M.D., Pinchera, A., Maffei, M. Cathepsin K null mice show reduced adiposity during the rapid accumulation of fat stores (2007) *PLoS ONE*, 2 (8) e683

De Lange, P., Farina, P., Moreno, M., **Ragni, M.**, Lombardi, A., Silvestri, E., Burrone, L., Lanni, A., Goglia, F. Sequential changes in the signal transduction responses of skeletal muscle following food deprivation (2006) *FASEB Journal*, 20 (14), pp. E2015-E2025.

Silvestri, E., de Lange, P., Moreno, M., Lombardi, A., **Ragni, M.**, Feola, A., Schiavo, L., Goglia, F., Lanni, A. Fenofibrate activates the biochemical pathways and the de novo expression of genes related to lipid handling and uncoupling protein-3 functions in liver of normal rats (2006) *Biochimica et Biophysica Acta - Bioenergetics*, 1757 (5-6), pp. 486-495.

Lanni, A., Moreno, M., Lombardi, A., De Lange, P., Silvestri, E., **Ragni, M.**, Farina, P., Baccari, G.C., Fallahi, P., Antonelli, A., Goglia, F. 3,5-Diiodo-L-thyronine powerfully reduces adiposity in rats by increasing the burning of fats (2005) *FASEB Journal*, 19 (11), pp. 1552-1574.

Silvestri, E., Moreno, M., Lombardi, A., **Ragni, M.**, De Lange, P., Alexson, S.E.H., Lanni, A., Goglia, F. Thyroid-hormone effects on putative biochemical pathways involved in UCP3 activation in rat skeletal muscle mitochondria (2005) *FEBS Letters*, 579 (7), pp. 1639-1645.

de Lange, P., **Ragni, M.\***, Silvestri, E., Moreno, M., Schiavo, L., Lombardi, A., Farina, P., Feola, A., Goglia, F., Lanni, A. Combined cDNA array/RT-PCR analysis of gene expression profile in rat gastrocnemius muscle: relation to its adaptive function in energy metabolism during fasting. (2004) *FASEB journal* 18 (2), pp. 350-372

**\*first co-author**

Moreno, M., Lombardi, A., De Lange, P., Silvestri, E., **Ragni, M.**, Lanni, A., Goglia, F. Fasting, lipid metabolism, and triiodothyronine in rat gastrocnemius muscle: interrelated roles of uncoupling protein 3, mitochondrial thioesterase, and coenzyme Q. (2003) *FASEB journal* 17 (9), pp. 1112-1132

## BIBLIOMETRIC INDICES

TOTAL H INDEX (ISI)	14
TOTAL CITATIONS (ISI)	748
TOTAL H INDEX (SCOPUS)	13
TOTAL CITATIONS (SCOPUS)	761
Number of Papers over 5 years*(ISI)	5
Citation numbers over 10 years** (ISI)	450
H-index over 10 years (ISI)	7
Number of Papers over 5 years* (SCOPUS)	5
Citation numbers over 10 years** (SCOPUS)	689
H-index over 10 years (SCOPUS)	7

\*(2014-2019)

\*\* (2009-2019)

## CONFERENCES

Speaker

**Ragni M.**, Funicello M., Costa M., Santini F., Pinchera A. Maffei M. L'espressione del gene spata-6, aumentata nell'obesità, mostra un andamento opposto a quella del suo antisense 7H in diversi modelli di obesità nel topo XXVI Giornate Endocrinologiche Pisane, Pisa giugno 2006

**Ragni M**, Fossati A, Tedesco L, Ruocco C, Carruba MO, Valerio A, Nisoli E A branched-chain amino acid enriched mixture selectively induces endoplasmic reticulum stress-mediated apoptosis and blocks cancer cell proliferation VII congresso nazionale S.I.O., Milano luglio 2014

#### Abstracts and Posters

Chieffi Baccari G, **Ragni M**, Farina P, Monteforte R, Raucci F, Lanni A. Espressione delle proteine disaccoppianti nella ghiandola di Harder di ratti eu e ipertiroidei LXIII Congresso Nazionale Unione Zoologica Italiana, Rende (Cs) settembre 2002

Moreno M, Lombardi A, De Lange P, **Ragni M**, Silvestri E, Goglia F, Lanni A. T3 administration to fasted rats stimulates uncoupling protein 3 activity 28th Annual meeting of European Thyroid Association, Goteborg (Svezia) Settembre 2002

**Ragni M**, De Lange P, Moreno M., Silvestri E, Farina P., Schiavo L, Feola A., Goglia F, Combined cDNA array/ RT-PCR analysis of the gene expression profile in rat gastrocnemius muscle in relation to its adaptive function in energy metabolism during fasting LIV congresso della Società Italiana di Fisiologia, Chieti Settembre-Ottobre 2003

Farina P, Lombardi A., **Ragni M**., Feola A., Grasso P., Lanni A. Involvement of adenine nucleotide translocase and Uncoupling Protein 3 in the effect of 3,5-diiodo-L-thyronine on skeletal muscle mitochondria efficiency 54° congresso della Società Italiana di Fisiologia, Chieti Settembre-Ottobre 2003

Chieffi Baccari G., Santillo A., Raucci F., **Ragni M.**, Farina P., Feola A., Lanni A. Sex differences in the uncoupling protein 3 expression in the harderian gland of syrian hamster 50th Meeting of the Italian Embryological group – Pavia Giugno 2004

Lanni A , Moreno M , Lombardi A , de Lange P , Silvestri E , **Ragni M** , Farina P , Chieffi G, Fallahi P, Antonelli A, Goglia F. 3,5-diiodo-L-thyronine (T2) reduces adiposity and body weight gain in rats by increasing fatty acid oxidation 30th Annual Meeting of the European Thyroid Association, 18-22 Settembre, 2004, Istanbul

Lanni A, Moreno M, Lombardi A, de Lange P, Silvestri E, **Ragni M**, Farina P, Chieffi G, Fallahi P, Antonelli A, Goglia F La 3,5-diiodo-L-tironina (T2) riduce l'adiposità e l'aumento di peso corporeo nei ratti incrementando l'ossidazione degli acidi grassi LV congresso della Società Italiana di Fisiologia, Pisa -Ottobre 2004

**Ragni M**, Funicello M, Costa M, Maffei M. The obesity induced gene SPATA-6 and its 5' UTR natural antisense show an opposite expression pattern in several models of murine obesity. Keystone symposia on "Diabetes Mellitus and the Control of Cellular Energy Metabolism"- Gennaio 2006 Vancouver, Canada

**Ragni M.**, Funicello M., Costa M., Santini F., Pinchera A. and Maffei M. L'espressione del gene SPATA-6, aumentata nell'obesità, mostra un andamento opposto a quella del suo antisense 7H in diversi modelli di obesità nel topo XXVI Giornate Endocrinologiche Pisane, Pisa Giugno 2006

**Ragni M.**, Funicello M., Costa M., Santini F., Pinchera A. and Maffei M. The obesity induced gene SPATA-6 and its 5'UTR natural antisense show an opposite expression pattern in several models of murine obesity III Congresso Nazionale S.I.O., Milano Giugno 2006

Trevellin E, Granzotto M., Calcagno A, **Ragni M**, Valerio A, Federspil G, Nisoli E, Vettor R Effetto dell'ossido nitrico sulla captazione di glucosio nell'adipocita in vitro V Congresso Nazionale S.I.O., Roma aprile 2010

Cardile A, Dossena M, **Ragni M**, Tedesco L, Bertolotti P, Delbarba A, Valerio A, Carruba MO, Nisoli E Gli amminoacidi come nuova terapia preventiva nell'insorgenza delle complicanze metaboliche legate all'obesità? V Congresso Nazionale S.I.O., Roma aprile 2010

Tedesco L, Dossena M, Cardile A, **Ragni M**, Bertolotti P, Delbarba A, Valerio A, Carruba MO, Nisoli E Effetti della modulazione del recettore dei cannabinoidi di tipo 1 sul metabolismo

energetico nel tessuto adiposo bianco di topo e uomo V Congresso Nazionale S.I.O., Roma aprile 2010

Bracale R, Cardile A, Dossena M, Tedesco L, **Ragni M**, Bertolotti P, Delbarba A, Valerio A, Carruba MO, Nisoli E Studio dell' effetto mitocondriogenetico di diverse molecole in adipociti bianchi e bruni V Congresso Nazionale S.I.O., Roma aprile 2010

Dossena M, **Ragni M**, Granzotto M, Cardile A, Trevellin E, Tedesco L, Delbarba A, Bertolotti P, Valerio A, Carruba MO, Vettor R, Nisoli E Il ruolo della mitocondriogenesi dipendente dall'ossido nitrico nell'uptake del glucosio in cardiomiociti in vitro V Congresso Nazionale S.I.O., Roma aprile 2010

Fossati A, Cardile A, **Ragni M**, Tedesco L, Ruocco C, Bracale R, Fenaroli F, Valerio A, Carruba MO, Nisoli E Studio degli effetti mitocondriogenetici di composti attivatori di sirt1 in cellule adipose e muscolari VI congresso nazionale S.I.O. Abano terme (PD) aprile 2012

Tedesco L, **Ragni M**, Ruocco C, Fossati A, Corsetti G, Bracale R; Fenaroli F, Carruba MO, Valerio A, Nisoli E Branched-chain amino acid enriched mixture prevents mitochondrial damage in liver of rats consuming ethanol and in cultured Hepg2 cells VII congresso nazionale S.I.O., Milano luglio 2014

Bracale R, Milani L, Ferrara E, Tedesco L, Balzaretto C, Ruocco C, Fossati A, **Ragni M**, Valerio A, Fenaroli F, Russo V, Nisoli E, Carruba MO childhood obesity, overweight and underweight: a study in primary schools in Milan VII congresso nazionale S.I.O., Milano luglio 2014

Bracale R, Milani L, Zavarrone E, Ferrara E, Tedesco L, Balzaretto C, Ruocco C, Fossati A, **Ragni M**, Valerio A, Fenaroli F, Russo V, Pasanisi F, Nisoli E Carruba MO Family's vegetables consumption and children lifestyle and obesity in a cosmopolitan city of northern Italy VII congresso nazionale S.I.O., Milano luglio 2014

Fossati A **Ragni M**, Ruocco C Tedesco L Carruba MO, Valerio A, Nisoli E Resveratrol and its "friends": a comparative study VII congresso nazionale S.I.O., Milano luglio 2014

Fenaroli F, Montinaro M, Bicelli M, Tedesco L, Ruocco C, **Ragni M**, Fossati A, D'antona G, Carruba MO, Nisoli E, Valerio A A BCAA-enriched amino acid formula promotes neuronal mitochondrial biogenesis and mimics the effects of exercise training in middle-aged mice brain VII congresso nazionale S.I.O., Milano luglio 2014

**Ragni M**, Greco C, Carullo P, Ruocco C, Chen M, Kunderfranco PL, Rossi F, Tedesco L, Carruba MO, Gao C, Valerio A, Condorelli G, Nisoli E Dietary induction of mitochondrial branched-chain amino acid oxidation both prevents and ameliorates heart failure in mice. IX Congresso Nazionale S.I.O. Milano ottobre 2018

Data 26/7/2019

Luogo Milano