UNIVERSITÀ DEGLI STUDI DI MILANO

TO MAGNIFICO RETTORE OF UNIVERSITA' DEGLI STUDI DI MILANO **ID CODE ___4630____**

I the undersigned asks to participate in the public selection, for qualifications and examinations, for the awarding of a type B fellowship at **Dipartimento di __Scienze Biomediche e Cliniche "L. Sacco"____**

Scientist- in – charge: **_____Dr.ssa Sonia Caccia_____**

Djaha Donat EDGAR C. Yoboue

CURRICULUM VITAE

PERSONAL INFORMATION

Surname	YOBOUE
Name	Djaha Donat EDGAR Cassius
Date of birth	07/02/1986

PRESENT (Former) OCCUPATION

Appointment	Structure
Research Fellow	Department of molecular medecine (Pavia University)

EDUCATION AND TRAINING

Degree	Course of studies	University	year of achievement of the degree
Degree **(MASTER 2= Laurea specialistica)**	Sciences, Technology & Health	Bordeaux 2 (Bordeaux, Francia)	2008
Specialization			
PhD	Sciences, Technology & Health, option Biochemistry	Bordeaux 2 (Bordeaux, Francia)	December 2011
Master			
Degree of medical specialization			
Degree of European specialization			
Other			

REGISTRATION IN PROFESSIONAL ASSOCIATIONS

Date of registration	Association	City

Università degli Studi di Milano –Direzione Risorse Umane
Ufficio Contratti di formazione e Ricerca
Via Sant'Antonio 12 - 20122 Milano, Italia
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FOREIGN LANGUAGES

Languages	level of knowledge
English	**C1 level**
Italian	**C1 level**
French	**Mother Tongue**

AWARDS, ACKNOWLEDGEMENTS, SCHOLARSHIPS

Year	Description of award
2016	Assegno di ricerca D.R. 4823 –BIO/11. Biologia molecolare- Univeristà Vita-Salute San Raffaele (1 year)
2013	Marie-Curie fellowship (INVEST-COFUND PROGRAM; see certificate)
2011	Grant for "thesis ending" from the French "Association against mitochondrial diseases" (AMMI)
2011	BBA Bioenergetics travel grant: Participation at the French Bioenergetic Group meeting (GFB) 2011: « Oléron », (France), September 21-25th 2011
2008-2011	PhD fellowship from the French Ministry for higher education and research (After competition: Ranked 5th/66)

TRAINING OR RESEARCH ACTIVITY

description of activity

Throughout my research activity in France and Italy, I have always made the choice to diversify my competencies by tackling new topics, techniques and models while staying productive during these changes. Thus, as you could appreciate in the upcoming lines, I hold a profile with strong and concrete experience with micro-organisms, mammalian models, recombinant proteins construction and characterization, signaling, redox events, enzymatic assay, protein isolation and genomic modifications.

- My first research experiences were internships for my Master degree and were on the yeast *Saccharomyces cerevisiae* mitochondrial proteins. Thus, I had for instance worked on the purification of a fusion protein between the ADP/ATP exchanger (ANT) and the inorganic phosphate transporter. Thus, I performed affinity chromatography purification using a 6His-tag following by gel filtration. I have also performed enzymatic assay in order to monitor *in vitro* the activity of that chimeric protein.

  In addition of that, another internship project was about studying the kinetic regulation of dehydrogenases of the mitochondrial respiratory chain of *S. cerevisiae* through diverse enzymatic quantitative assay of metabolites and **isolated enzyme activities** measurement (by fluorescence and absorbance coupled assays) after purifying mitochondria. My work contributed to the initial observation and further characterisation of the kinetic stimulation of D-lactate dehydrogenases by carboxylic compounds. This phenomenon could have an important role in the cellular detoxification mechanism of methylglyoxal. Indeed, methylglyoxal is a cytotoxic compound formed mainly from glycolysis. In order to avoid the accumulation of this cytotoxic compound, the enzymes Glyoxalase I and II will transform the methylglyoxylate into D-Lactate. Thus the activation of D-Lactate dehydrogenase could increase the activity of this detoxification pathway of methylglyoxal.

- During my PhD, I have studied the regulation of transcription factors involved in the expression of nuclear encoded mitochondrial proteins. In *S. cerevisiae*, a key regulator of that process is the co-activator Hap4p. I have first participated to the demonstration that an increase production of reactive oxygen species (ROS) by defective mitochondria reduces the level of Hap4p and so, the mitochondrial content (reversible by the addition of antioxidants).

  The observation that other oxidative stress elicitors could lead to the same fate, led me to be interested in the glutathione redox state, a key contributor to intracellular defense against oxidative stress. Using different models, I was able to observe a positive correlation between the redox state of glutathione and Hap4p level and thus of mitochondrial biogenesis. We could even tie it up with previous data of the laboratory regarding the positive regulation of mitochondrial biogenesis by cAMP. Indeed, cAMP also modulated the redox potential of glutathione and mitochondrial biogenesis via Hap4p level.

  I have also characterized another regulating actor of Hap4p: the heme molecule. Indeed, heme (which biosynthesis depends on mitochondria), while being an enzymatic co-factor is also a regulatory molecule for some proteins such as some transcription factors. Thus I have shown that the increase of a regulatory pool of heme positively regulates the stability and so the level of Hap4p. By purifying Hap4p and performing *in vitro* spectroscopic analysis, I was able to associate that to a heme-binding property of Hap4p.

  Thus, during that research activity, I have demonstrated and improved my skills for **enzymatic quantization** (e.g.: glutathione, H_2O_2), protein analysis and purification and analysis of signaling **pathways**.

- I then moved to Italy while also making the choice to work on mammalian cells and the endoplasmic reticulum (ER)-associated events. The initial goal of the project was to find new regulators of processes such as protein secretion or calcium signaling. In the course of the project, I have been interested in the Glutathione Peroxidase GPX8, a protein which had been tagged as a scavenger of H_2O_2 produced in the ER. I contributed to showing that GPX8 protein level modulates the calcium concentration in the ER and consequently its transfer to the mitochondria.
  But, I was also intrigued by the topology of GPX8, which is the only transmembrane glutathione peroxidase in mammals. However, no one had been interested in that topological feature at that time. Thus, I have shown that the transmembrane (TM) domain of GPX8 is a key element for the regulation of ER calcium. Thus, deletion or substitution of this TM annihilates all the effects of GPX8 on calcium homeostasis. Moreover, if this TM is attached to another peroxidase, the latter becomes capable of modulating calcium fluxes. Thus, I was able to identify and characterize a new redox actor in ER calcium homeostasis and ER-mitochondrial communication, which is an important process for the regulation of metabolism and cell survival.

  Thus, throughout that working experience, I developed a strong expertise and fondness for **molecular cloning** as I had to build numerous variants and chimeric proteins and also building new tools for the fluorescent staining of organelles, and so developing skills in fluorescence microscopy, the study of **redox** modifications of proteins and additional labeling competencies such as click-chemistry for labeling lipid post-translational modifications such as palmitoylation.

- In my more recent activity, I moved closer to neuroscience-associated proteins, in particular the protein PINK1, a well-known gene associated to autosomal recessive Parkison disease. In that research unit which was starting from scratch after 2 years of “clinical diagnosis only”, I have contributed to the construction of mutants/fragments of PINK1 in order to find interacting regions/residues with some of its putative partners, and also their purification.
  I have also contributed to the characterization of CRISPR-KO PINK1 cells models and also the quantification by bioluminescent assay of metabolites such as the NADH and the NAD+.

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PROJECT ACTIVITY

Year	Project
2013-2015	"Signal Integration at the Endoplasmic reticulum-Golgi interface"
2008-2011	"Regulation of mitochondrial biogenesis by reactive oxygen species"

PATENTS

Patent

CONGRESSES AND SEMINARS

Date	Title	Place
September 26-29, 2019	*Meeting of the French Bioenergetic Group (GFB) 2019* Poster (Bouchez C., Yoboue ED et al.,): Control of mitochondrial biogenesis by heme	(Autrans, France)
January 17, 2017	*Seminar of the Division of Genetics and Cell Biology* Oral presentation ("The endoplasmic reticulum glutathione peroxidases: so identical... and so different")	San Raffaele Hospital Scientific Institute (Milan; Italy)
October 7, 2016	*Monthly Milan ER club meeting (MoMERC) 2016* Oral presentation: (A topological regulation of calcium signaling)	Mario Negri Institute (Milan/Bovisa; Italy)
September 22-24, 2016	*3rd Retreat of the Division of Genetics and Cell Biology (DGCB) of San Raffaele scientific institute (2016):* Poster: (The glutathione peroxidase 8: a new regulator of the ER-mitochondria calcium exchange).	(Cologno al Serio; Italy)
September 15-18, 2016	*EMBO Workshop: Organelle contact sites: Intracellular communication and role in disease* Poster: (The glutathione peroxidase 8: a new regulator of the ER-mitochondria calcium exchange).	("Domus de Maria"; Sardinia; Italy)
May 16-17, 2014	*Meeting of the ABCD (Associazione di Biologia Cellulare e del Differenziamento) ; Mechanisms of Signal Transduction, 2014* Poster: (Finding the key factors in the role of ERp44 in the signal integration at the endoplasmic reticulum-golgi interface).	(Padua; Italy)
September 21-25, 2011	Meeting of the French Bioenergetic Group (GFB) 2011 Oral presentation: Redox control of the mitochondrial biogenesis in the yeast Saccharomyces cerevisiae	(Oléron, France)
July 11-16, 2011	25th International Conference on "Yeast Genetics and Molecular Biology" 2011 Poster: Redox control of the mitochondrial biogenesis in	(Kortowo-Olsztyn, Poland)

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	the yeast Saccharomyces cerevisiae	
July 17-22, 2010.	*16th European Bioenergetic Conference (EBeC) 2010* Poster: Mitochondria quality-control: mechanisms involved in the downregulation of mitochondrial biogenesis by mitochondrial ROS in the yeast *Saccharomyces cerevisiae*.	(Warsaw, Poland)
September 16-19, 2009	*Meeting of the French Bioenergetic Group (GFB) 2009* Poster: Oxidative stress and regulation of mitochondrial biogenesis in the yeast Saccharomyces cerevisiae.	(Parent, France)

PUBLICATIONS

Books

Yoboue ED, *Camougrand N. & Manon S.* (2019). Mitochondria as signaling platforms. In Morio B., Penicaud L., Rigoulet M. (eds): ***Mitochondria in Obesity and Type 2 Diabetes (Comprehensive Review on Mitochondrial Functioning and Involvement in Metabolic Diseases).*** doi: 10.1016/C2016-0-01694-7. Elsevier, 2019 **(Book Chapter Link)**

Articles in reviews

Yoboue ED, *Valente EM.* : PINK1 and Parkin: The Odd Couple. ***Neurosci Res.*** 2020 May 15;S0168-0102(20)30309-6. doi: 10.1016/j.neures.2020.04.007. Online ahead of print.

Bouchez CL, **Yoboue ED***, de la Rosa Vargas LE, Salin B, Cuvellier S, Rigoulet M, Duvezin-Caubet S, Devin A.*: "Labile" heme critically regulates mitochondrial biogenesis through the transcriptional co-activator Hap4p in *Saccharomyces cerevisiae*. ***J Biol Chem***. 2020 Apr 10;295(15):5095-5109. doi: 10.1074/jbc.RA120.012739. Epub 2020 Feb 18.

Yoboue ED, *Sitia R and Simmen T.* (2018). Redox crosstalk at endoplasmic reticulum (ER) membrane contact sites (MCS) uses toxic waste to deliver messages. ***Cell. Death dis.*** doi: 10.1038/s41419-017-0033-4.

*Fra. A, **Yoboue ED**, and Sitia R.* (2017). Cysteines as Redox Molecular Switches and Targets of Disease. ***Front Mol Neurosci.*** 2017 Jun 6;10:167. doi: 10.3389/fnmol.2017.00167. eCollection 2017.

Yoboue ED*, *Rimessi A*., Anelli T., Pinton P., and Sitia R.* Regulation of calcium fluxes by GPX8, a type-II transmembrane peroxidase enriched at the mitochondria-associated endoplasmic reticulum membrane. ***Antioxidants & Redox Signaling***. Antioxid Redox Signal. 2017 Sep 20;27(9):583-595. doi: 10.1089/ars.2016.6866. Epub 2017 Apr 17 *(*Front cover of the printed edition*)*

*Mossuto MF, Sannino S, Mazza D, Fagioli C, Vitale M, **Yoboue ED**, Sitia R, Anelli T*: A dynamic study of protein secretion and aggregation in the secretory pathway. ***PLoS One***. 2014 Oct 3;9(10):e108496. doi: 10.1371/journal.pone.0108496. eCollection 2014.

Yoboue ED, Mougeolle A, Kaiser L, Averet N, Rigoulet M, Devin A.: The role of mitochondrial biogenesis and ROS in the control of energy supply in proliferating cells. ***Biochim Biophys Acta***. *2014 Jul;1837(7):1093-8.doi: 10.1016/j.bbabio.2014.02.023*

Yoboue ED, *Devin A.:* Reactive Oxygen Species-Mediated Control of Mitochondrial Biogenesis. ***International Journal of Cell Biology***. 2012;2012:403870. doi: 10.1155/2012/403870. Epub 2012 May 30.

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Yoboue ED, *Augier E, Galinier A, Blancard C, Pinson B, Casteilla L, Rigoulet M, Devin A.*: cAMP-induced mitochondrial compartment biogenesis: role of the glutathione redox state ***J Biol Chem***. 2012 Apr 27;287(18):14569-78. doi: 10.1074/jbc.M111.302786. Epub 2012 Mar 6.
Rigoulet M, ***Yoboue ED****, Devin A*: Mitochondrial ROS generation and its regulation: mechanisms involved in H(2)O(2) signaling. ***Antioxid Redox Signal***. 2011 Feb 1;14(3):459-68. doi: 10.1089/ars.2010.3363. Epub 2010 Oct 18.
Chevtzoff C, ***Yoboue ED****, Galinier A, Casteilla L, Daignan-Fornier B, Rigoulet M, Devin A*: Reactive oxygen species mediated regulation of mitochondrial biogenesis in the yeast *Saccharomyces cerevisiae*. ***J Biol Chem***. 2010 Jan 15;285(3):1733-42. doi: 10.1074/jbc.M109.019570. Epub 2009 Nov 6.
Mourier A, Vallortigara J*,* ***Yoboue ED****, Rigoulet M, Devin A*: Kinetic activation of yeast mitochondrial D-lactate dehydrogenase by carboxylic acids. ***Biochim Biophys Acta***. 2008 Oct;1777(10):1283-8. doi: 10.1016/j.bbabio.2008.06.007. Epub 2008 Jun 20.

Congress proceedings
[title, structure, place, year]

OTHER INFORMATION

2013-2017: Tutoring and teaching (1st year Medical Students) in the course: "Cell and Molecular Biology" (International MD program, "Università Vita-Salute San Raffaele", Milan, Italy). **Topics covered**: *(**Recombinant proteins**, Ageing Mitochondria/telomere theory, H. pilory toxins, High-throughput CRISPR technology, Mito-nucleus communication, Organelles contact sites, ...)*
2011-2012: Teaching at M.sc.'s students: "Mechanisms involved in the modulation of the mitochondrial energy production" (Bordeaux 2 University, Bordeaux, France).
2010-2012: Active member of the committee of students of the **SFR TRANSBIOMED (TBM Doc's)**: *Organization of meetings with young students and researchers to inform them about the job opportunities in Life Sciences Support for the organization of the scientific seminar of the SFR TRANSBIOMED.*

Declarations given in the present curriculum must be considered released according to art. 46 and 47 of DPR n. 445/2000.

The present curriculum does not contain confidential and legal information according to art. 4, paragraph 1, points d) and e) of D.Lgs. 30.06.2003 n. 196.

Place and date: MILANO, 09/07/2020

SIGNATURE

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