

Autophagy researchers

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Research focus

Autophagy in Parkinson disease (PD). The role of *PARK* genes and pesticides in PD.

Model system

Human fibroblasts from patients with and without mutations in *PARK* genes, and induced pluripotent stem cells from these fibroblasts. Also, human and nonhuman neuronal lines.

Education and career

1988, veterinary degree, University of Extremadura, Cáceres, Spain. 1993, PhD in biochemistry and molecular biology, University of Extremadura; advisor: Germán Soler. 1999–2000, postdoctoral researcher, CEA-Saclay, Gif-sur-Yvette, France; advisor: Marc le Maire. 1989–present, professor of biochemistry and molecular biology, University of Extremadura. 2007–present, group leader of Center for Networked Biomedical Research on Neurodegenerative Diseases (CIBERNED) at the Spanish Carlos III Institute of Health.

You have a veterinary degree, which is not so common for a cell biologist. Can you say anything more about this? Was your original intent to pursue a veterinary career? If so, what made you change your mind?

I really wanted to study medicine. However, due to financial problems in my family (and the fact that there is no school of medicine in Cáceres) I studied the only degree of science available in my city. In my second year, biochemistry fascinated me. My mentor, Germán Soler, introduced me to the world of basic research. Later, I developed an interest towards biomedicine. Currently, my group is composed of nine people, three of whom have studied veterinary medicine.

Why do you study autophagy?

The main topic in my group was the study of the apoptotic mechanism implicated in neurodegeneration caused by pesticides as a model to study Parkinson disease. One member of my group (Rosa A. González-Polo) did her postdoc (2002–2005) in the laboratory of

Dr. Guido Kroemer and introduced the first tools for these studies in my lab. We quickly understood the interest in autophagy in the study of neurodegenerative disorders including PD.

What do you think is a key question(s) in the autophagy field?

Probably (at least for me) to understand the different mechanisms that drive autophagy as a protective pathway or by contrast as a cell death process.

Why is the field of autophagy important to you?

Parkinson disease is characterized by the accumulation of misfolded and altered proteins. Dysfunctions in the systems of protein clearance are clearly implicated in the development of this pathology. I think that autophagy plays a double role in this disease. First, aberrant autophagy induced by genetic mutations can sensitize cells to toxic compounds related with PD (such as MPP⁺ or paraquat). Second, in a normal genetic background, autophagy can constitute a defense mechanism front to protect against the effects of the aforementioned PD-related toxins. Actually in my lab we study the interaction between both factors (genetics and environmental) in relation with the role of autophagy in the development of PD.

Is there a key experiment/finding that stands out in your mind with regard to autophagy?

Really it is very complicated to choose a single finding. The field of autophagy is very hot. Every weeks hundreds of new articles are published. However, I think that the study of regulation of autophagy by acetylation is very promising for the future.

Which paper in your research field represents seminal work on autophagy?

Apoptosis and autophagy in nigral neurons of patients with Parkinson's disease from Anglade et al. (Histol Histopathol 1997). This paper describes characteristics of apoptosis and autophagic degeneration in melanized



neurons of the substantia nigra in PD patients showing an intimate relation between both processes.

Is teaching a substantial part of your current position? If so, what do you teach. Does it benefit your research, or benefit from your research?

I have been a teacher for 25 years. Teaching (and all that comes with the teaching) takes up a substantial amount of my time. However, I can do research because I am a professor. Both activities are closely related. My teaching activities include degree (general biochemistry) and postgraduate (Parkinson disease). I make a great effort to introduce research to degree students. Every year there is time to explain briefly the concept of autophagy. On the other hand, teaching a general biochemistry course provides a global vision of metabolism and cell biology, which are very interesting for the study of autophagy.

Personal comments

Outside of the lab I have two princesses (Andrea and Laura, 16 and 10 years old, respectively), who brighten my life. In my free time (does the free time exist?) I like to read, mostly history books. I particularly like the history of the ancient civilizations, especially the history of Rome. I have more than 100 books concerning this period. A historic person in whom I am very interested is Cayo Julio César. I also enjoy listening to music, especially classical, Renaissance, medieval... (the latter

being ancient music from the XIIIth to the XVIth centuries). However, my favorite activity is working with the Scouts. I have been a Boy

Scout leader over 30 years, and I think that being a Scout is, and has been, fundamental to my way of thinking and acting.

Devrim Gozuacik

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Research focus

Cellular stress and death responses. Mammalian autophagy regulation in health and disease.

Model system

Mammalian cells, mice and rats, and biological materials (cells, tissues, etc.) from patients.

Education and career

1989–1995, student researcher, Medical Biology and Biochemistry Departments, Faculty of Medicine, Hacettepe University, Turkey; advisors: Meral Ozguc, Pervin Dincer and Wayne Criss. 1994, research fellow, Tumor Biology Department, Erasmus University, Netherlands; advisor: Anne Hagemeijer. 1995, medical doctor (MD) degree, Faculty of Medicine, Hacettepe University. 1997, D.E.A. of Biochemistry, Ecole Polytechnique-Paris-XI University, France; advisor: Andrea Parmeggiani. 2001, PhD of molecular and cell biology, Pasteur Institute-Necker IRNEM-Paris-XI University, France; advisor: Christian Brechot. 2001–2006, postdoctoral fellow, Department of Molecular Genetics, Weizmann Institute of Science, Israel; advisor: Adi Kimchi. 2006–2011, assistant professor/lab head, Faculty of Engineering and Natural Sciences (FENS), Sabanci University, Turkey. 2011–present, associate professor/lab head, FENS, Sabanci University.

Why do you study autophagy?

Being an MD with a classical PhD education, I have the strong belief that a molecular understanding of biological events through rigorous basic science is the key for the advancement of medicine. Autophagy deregulation is a very common and usually causative or contributing event in various important human diseases. Therefore, to better understand disease-related changes in autophagy, we focus on the basic mechanisms of autophagy regulation in mammals and on the links and coordination between autophagy and other disease-related cellular pathways including cell death pathways. Doing so, we hope to better understand the molecular biology of autophagy in both health and disease.

Unbiased screens allowed us to discover novel regulators of autophagy. For example, our microRNA screens led to the discovery of several miRNAs targeting autophagy at various steps of the pathway. miRNAs are able to affect the expression of a number of proteins at once. Therefore, miRNA networks seem to integrate cellular stress response pathways including autophagy, and coordinate them to shape cell fate.

We also discovered new proteins involved in autophagy regulation. In fact, some of these proteins were interacting with core autophagy machinery components. Unexpected direct links between autophagy and other cellular pathways were found, allowing us to reveal novel entry points for autophagy regulation and coordination in cells.

Our close collaboration with clinicians gives us privileged access to precious patient materials allowing us to study the relevance of our data about autophagy in diseased tissues and even live cells, and to explore the contribution of autophagy deregulation to pathologies. Moreover, collaborations with engineers help us test biomedical applications of our findings.

What do you think is a key question(s) in the autophagy field?

Important questions in the field include whether we can treat diseases through autophagy modulation and what is the best way to do so with minimal side effects in normal cells and tissues.

Is teaching a substantial part of your current position? If so, what do you teach. Does it benefit your research, or benefit from your research?

I have a heavy teaching load (9 h/week). Undergraduate molecular biology and microbiology courses, graduate courses on cell death, stress and molecular basis of disease. I try to transmit to the students my dedication to science and my enthusiasm about discovery. As a result, some students do their final projects in my lab and later continue as graduate students.

Personal comments

After an 11-year career abroad, it was a critical decision to establish my lab in Turkey. To run a competitive lab here is still a challenge. The collaborative and friendly approach of the autophagy community members was, and still is, a great source of motivation for my students and me. We are proud to be part of this exceptional community and glad to contribute to the field.

When I am not working, I spend time with my two kids and wife. I also like hiking, reading and watching movies. Recently read books: *Winter Journal* by Paul Auster, *Snow* by Orhan Pamuk, *Tesla* by Margaret Cheney. As a sci-fi fan, I have a large collection of sci-fi movies and documentaries. I try to attend live performances (especially concerts, opera, theater and modern dance) and follow art exhibitions in town. In addition to classical music, jazz, especially vocal and ethnic jazz, plays an important role in my life.

Marja Jäättelä

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Research focus

Cancer biology, cell death, lysosomes and sphingolipid metabolism.

Model system

Cell culture, primary human tumor samples and xenograft tumor models in mice.

Education and career

1989, MD, Helsinki University (HU), Finland. 1990, PhD in cancer biology, HU; advisor: Prof. Eero Saksela. 1990, lecturer in pathology, HU. 1991–1992, junior research fellow, Fibiger Institute, Copenhagen, Denmark. 1991, visiting scientist, Memorial Sloan-Kettering Cancer Center, New York, NY USA; advisor: Prof. Gloria Li. 1993–1994, postdoctoral fellow, University of Michigan, Ann Arbor MI USA; advisor: Prof. Vishva Dixit. 1994–2011, head of the Apoptosis Laboratory/Department, Institute of Cancer Biology, Copenhagen, Denmark. 2003–present, professor in cancer biology, Copenhagen University. 2011–present, head of the Cell Death and Metabolism Unit, Danish Cancer Society Research Center, Copenhagen, Denmark

Why do you study autophagy?

My group entered the autophagy field when a talented student, Maria Høyer-Hansen, discovered “funny-looking” vesicles in electron microscopy images of vitamin D-treated breast cancer cells. Her subsequent enthusiasm for the autophagic program was highly contagious and now half of my laboratory is working on different aspects of autophagy with special focus on signaling pathways controlling autophagy and autolysosomal degradation. The utmost aim of our autophagy research is to identify druggable autophagy-regulating enzymes.

What do you hope to achieve in your scientific career?

My early work was mainly driven by pure curiosity and fascination for basic cell biology. In recent years, the focus has, however, shifted to

more translational aspects of research. Thus, my ultimate goal is to apply our expertise on autophagy and lysosomes for the treatment of cancer and degenerative diseases.

Based on our identification of heat shock protein 70 (Hsp70) as a lysosome stabilizing and cytoprotective protein, Thomas Kirkegaard, a gifted former student of mine, founded a company that aims to develop Hsp70-based therapies for lysosomal storage disorders. It would be a dream come true if such therapies could help patients with these devastating diseases. Cancer being my main research area, we naturally continue our search for cancer therapeutics with the opposite effect, i.e., lysosome destabilizing agents displaying cancer-specific cytotoxicity.

Which paper in your research field represents seminal work on autophagy?

The identification of autophagy as a tumorigenesis-controlling program (Liang et al., *Nature* 1999; 402:672) initiated a new active research field focusing on the role of autophagy in cancer initiation and progression. Already now, several autophagy modulators are entering the clinic as anticancer agents and I am convinced that autophagy modulation will prove to be a valuable addition to the current treatment regimens.

If you could meet any scientist, currently living or from the past, who would it be and why?

The Nobel Prize-winning cytologist and biochemist Christian de Duve, “the father of the lysosome” would without a doubt be on the top of my wish list. I have read many of his original papers and interviews, which reveal him as an exceptionally visionary and innovative scientist.



If you could start over and choose a different career, what would it be?

I suppose I would choose medical research once again, provided that I could make it in the tough international competition of today. In addition to my love for science itself, a research career offers fantastic personal freedom, which is essential for the quality of my life. My other dream would be to work as a medical doctor in the Third World.

About teaching

I work in a private research institute without any obligations to teach. However, I consider the supervision of students in the laboratory as one of the most fascinating aspects of my job. There is nothing better than a student that starts challenging your hypotheses and develops into an independent scientist.

Personal comments

I am married to a Danish poet and we have a lovely daughter with whom I have spent most of my free time for the last years. Now that she is growing bigger and I have finally learned to delegate part of my work, I can again spend more time on the tennis courts. Hitting the yellow ball with a good spin is my favorite way to clear the mind. I also have a rather dominant social gene and thus I always enjoy dinners, parties and good company.

Elizete Rizzo

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Research focus

Fish reproduction under natural and stress conditions; a special emphasis has been given on the role of autophagy and apoptosis regulating the development and regression of the ovarian follicles.

Model system

Freshwater fish, especially ovary.

Education and career

1974, graduate in biological science, University of São Paulo, Ribeirão Preto, Brazil; 1980, master in cell biology, University of São Paulo; advisor: Heni Sauaia; 2001, PhD in cell biology, Federal University of Minas Gerais, Belo Horizonte, Brazil; advisor: Hugo P. Godinho; 1979–present, associate professor of cell biology, Department of Morphology, Federal University of Minas Gerais.

Why do you study autophagy?

It is a fascinating field of study in cell biology. In my area of research, some time ago, studying the role of apoptosis in the fish ovary by electron microscopy, we detected large vacuoles with features of autophagy in granulosa cells. This was the first evidence for the participation of autophagy in the follicular regression of the fish ovary. Subsequently, we have analyzed proteins of the autophagy pathway in the regression of postovulatory follicles and atretic follicles.

How is your research funded?

Brazil is rich in natural resources, but its biodiversity is poorly explored, and the research funds are scarce, compromising the development of science and technology. To conduct our research, we have obtained some funding from public institutions, i.e. CNPq (National Council for Scientific and Technological Development) and FAPEMIG (Foundation for Research Support of the State of Minas Gerais). We also have partnerships with institutions that give us support for fieldwork: CODEVASF (Company for the Development of the Sao Francisco Valley) and FURNAS (a power utility company). I offer my sincere thanks to all.

What do you think is a key question(s) in the autophagy field?

An essential issue in this field is the interplay between autophagy and programmed cell death pathways in different cellular types in health and disease conditions of all organisms.

Why is the field of autophagy important to you?

Since the 1980s, our research group has been studying the reproductive biology of freshwater fishes of the main hydrographic basins of South America. For example, why are the fish very sensitive to environmental stress? Their populations have decreased dramatically, and many species of high commercial value are endangered or are considered vulnerable. Our study aims to understand the mechanisms involved in gametogenesis in support of conservation programs for the rich fish fauna in Brazil. In this context, autophagy may clarify many aspects of cell biology in fish gonads under different settings, so we can better understand fish reproduction, and it also has an impact upon germ cell development. As a model study, we have used a species with seasonal reproduction, curimatã-pacu *Prochilodus argenteus*, which has been kept in captivity and is often subjected successfully to induced spawning in hatcheries producing a lot of good quality eggs.

Which paper in your research field represents seminal work on autophagy?

In my research field, autophagy is still a new subject. I could highlight a paper published recently from my lab in *Cell and Tissue Research* (2012) that provides evidence that autophagic and apoptotic proteins may be activated in a coordinated fashion during follicular atresia in fish ovary, and the interplay between autophagy and apoptosis being essential in determining the cell's fate.

If you could meet any scientist, currently living or from the past, who would it be and why?

I could appreciate meeting Robert Hooke surely due to his excellence as a scientist and importance in the area of cell biology.

Is teaching a substantial part of your current position? If so, what do you teach. Does it benefit your research, or benefit from your research?

My teaching activities include mainly a course of cell biology and histology for students of medicine, biology and veterinary. Besides, I am also an advisor in the Graduate Program in Cell Biology and teaching topics on cell biology and biology of reproduction. Obviously, research and teaching complement each other and form a two-way street that brings benefits to both fields. I always try to bring new research findings to the classroom and the results are positive. In recent years, papers with new findings have often been provided to undergraduate students as background to help them search for work on hot topics in cell biology, including autophagy.

Personal comments

In my country, a teacher and researcher works hard and has little free time, which is usually occupied with attention to family and routine housework (I am married, have two beautiful children and a Rottweiler). However, after a day of work, I practice a sport, i.e. walking, swimming, Pilates and more. On weekends, I appreciate a movie, football, listening to music, going to a park, meeting friends, dancing, drinking some wine, a beer... During the holidays, going to the beach (Rio de Janeiro, Brazil) is always very pleasant and restores our energy.