Autophagy 10:9, 1483–1486; September 2014; © 2014 Landes Bioscience

Autophagy researchers

Patrizia Agostinis

Email: Patrizia.agostinis@med.kuleuven.be

Research focus

Role of autophagy in tumor cell-stromal cell interactions

Model system

Cancer cells lines (mostly melanoma cells), mice

Education and career

1983, master in biology, University of Padova, Italy; advisor: Prof LA Pinna. 1988, PhD, biomedical science, University of Leuven, Belgium; advisor: Prof W Merlevede. 1988–1993, postdoc, FWO (Research Foundation Flanders), University of Leuven; cosupervisors: Prof LA Pinna, Prof W Merlevede. 1993–2000, research director, FWO. 2000–2008, associate professor, University of Leuven. 2008–present, full professor, Faculty of Medicine, Department of Cellular & Molecular Medicine, University of Leuven

Why do you study autophagy? Why is the field of autophagy important to you?

I am fascinated by this self-eating process and all the emerging implications it has in physiopathology. As a scientist coming from the field of cell death in cancer therapy, the discovery of autophagy as a major mechanism of cancer cells' protection against various stresses was probably a natural one. We started to investigate the role of autophagy pathways and their capacity to modulate and shape reactive oxygen species (ROS) signaling, as a major mechanism of cancer cell killing by anticancer treatments. We are now expanding our knowledge on the role of autophagy in cancer cell-stromal cell interaction, during carcinogenesis and after treatment. How this catabolic process with profound implications in cancer cell metabolism, adaptation, and secretion affects the tumor microenvironment and the crosstalk between cancer cells and other stromal cells, is now our major focus. We recently found that the widely used autophagy-inhibitor chloroquine has autophagy-independent actions in vivo and targets the tumor vasculature, by enhancing NOTCH1 signaling in endothelial cells and normalizing the tumor vessels. This is just an example and I think in the future we will need to further our knowledge of the many emerging functions autophagy has in different stromal compartments. Understanding this interface will allow us to design new therapeutic strategies based on autophagy modulation of the cancer microenvironment.

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

I think that what we currently know about autophagy mechanisms and pathways intersecting key cell autonomous and non-autonomous processes such as endocytic trafficking, cell death/phagocytosis, secretion, immunity, and inflammation is just the tip of the iceberg. I am sure that exciting times are ahead of us. The major future challenges, will be to contextualize all these possible intersections and understand how, when, and why autophagy modulates these cell biological processes and their pathological impact.

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

There are many outstanding scientists working in this field whom have contributed with seminal works to the understanding of the molecular machinery of autophagy and its implications in a variety of physiological and pathological instances. However, since my main research interest focuses on deciphering the role of autophagy in tumor progression and as a response to anticancer therapy, I really admire the outstanding contributions of Eileen White and her group. I think she is a great scientist who has contributed and continues to do so, with cutting-edge research to decipher the dynamic role of autophagy in cancer.

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

There are many scientists, of course, who I would have liked to meet, and many who I wish to meet in the future. However, I really regret I didn't have the possibility to meet Christian de Duve before he decided to leave us, even if

we were both living in the same small country (Belgium). I feel I missed a unique opportunity to know this great scientist and to discuss with him his vision on modern autophagy research.

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

After high school, I debated for a few months if I wanted to become a cell biologist or take philosophy or social science as my main studies. It turned out to be the first one, and I am very glad, but I think, if I would have the chance to choose a different career, I would do anything to become an inspirational politician and do something that might directly affect people's lives, and help in making them better.

Personal comments

I always had and have to find a good balance between lab/scientific work (a passion, the main hobby) and family (I have two wonderful girls). I always thought, though, that in spite of the demanding task to combine and balance these activities, it is so worth doing it! I try to transmit this enthusiasm to my own girls. I love my job as it puts me in contact with the new generation of scientists, who are a constant source of inspirations, both scientific and nonscientific. To see how my students evolve, and I co-evolve with them, how we address new questions, and how I can help them growing in their career as independent scientists, is one aspect of this 'hobby' I really love. In my

spare time, I love listening to jazz music—but good music of any kind in general, going to the cinema, traveling and spending time with my family, visiting my beautiful (ex) town Venice, and of course reading novels (my favorite novelists; Ian McEwan, Sandor Marai, Haruki Murakami, Alice Munro, Margaret Mazzantini) I keep on telling myself I should also do more sports…but I am rather lazy.

Angelo De Milito

Email: angelo.de-milito@ki.se

Research focus

Role of acidosis in tumor progression and therapy

Model system

Human cancer cells lines cultured at different pH conditions, human cancer xenografts

Education and career

1993, BS, biology, University of Siena, Italy; advisor: Pier Egisto Valensin. 1997, residency degree, microbiology and virology, University of Siena; advisor: Maurizio Zazzi. 2002, PhD, immunobiology, Microbiology and Tumor Biology Center, Karolinska Institute, Sweden; advisor: Francesca Chiodi. 2004–2009, postdoctoral fellow, Istituto Superiore di Sanita, Rome; advisor: Stefano Fais. 2009–2012, researcher, Department of Oncology-Pathology, CCK, Karolinska Institute, Sweden; advisor: Stig Linder. 2012–present, researcher and associate professor, experimental oncology, Karolinska Institute

Why do you study autophagy?

My interest in autophagy started during my postdoc after I met Patrice Codogno. I was fascinated by the simplicity of recycling cellular components and, working with pH-modulating agents, it sounded attractive to study autophagy in the context of cancer therapy. Since then I have been puzzled by the actual complexity of autophagy, its regulation, its contribution to cancer biology, and its importance in tumor response to therapy. While working on the idea of targeting tumor acidosis I came across 2 observations related to the role of autophagy in sustaining cancer cell adaptation to acidic stress and the role of acidosis in conferring resistance to autophagy inhibition by chloroquine. I think it is very challenging to study what role autophagy has in tumor biology and I think that modulation of autophagy may be a useful therapeutic tool once we understand more about the contribution of autophagy to tumor development and progression.

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

An important issue is the understanding of the complex relationship between autophagy and metabolism, and how these processes interact in pathological conditions like cancer.

Why is the field of autophagy important to you?

There is great interest in the role of autophagy in cancer, in terms of its biological role in tumor development and progression, and as a therapeutic target.

What do you hope to achieve in your scientific career?

I hope to contribute to scientific and medical knowledge and to provide useful information to translate laboratory findings into clinically meaningful applications. Education and professional growth of students is a major motivation. I am very curious and passionate about research and I try to transfer this driving force to my students. Research feeds my wish to know more about human diseases. I also hope to get a more stable academic position.

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

The paper by Liang et al. (Nature 1999; 402:672) described the tumor suppressive function of BECN1, paving the way to important research on the role of autophagy in oncology.

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

I would have liked to meet Otto Warburg since he was a controversial personality and performed crucial experiments with simple tools.

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

I come from a nonacademic family and my mother was very sad when I chose an ordinary course like biology instead of medicine. My dream was to become a surgeon and I would have liked to be a medical doctor.

What one scientific discovery do you wish you had made?

I graduated with a thesis in clinical virology when the new herpesvirus HHV-8 was discovered. The way it was identified was very interesting since the authors used representational difference analysis and since then I wished I could make a similar discovery.

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?

Teaching is part of my activities. I am co-organizer of a post-graduate course on cancer cell metabolism at KI and I am engaged in lectures and seminars for graduate and post-graduate education, teaching subjects related to cancer biology. I also act as a supervisor for students running projects and experimental theses at the undergraduate level. I think that both students and I benefit from these activities because they are exposed to updated concepts and research and I take the opportunity to widen and refresh my knowledge in cancer biology.

Personal comments

I was a promising soccer player but my mother decided for a different career after

I got a brain concussion during a match when I was 16. My biology teacher at high school thought I had a "forma mentis" not suited to become a researcher. The combination of these 2 events convinced me to become a researcher and I started by testing Mendelian inheritance in generations of fruit flies cultivated at home! Besides my working life, I dedicate my time and energies to my children, Emma (7) and Leonardo (3), and my wife, Susanne. At the stage of career and family life I am now, free time does not exist in reality. I like to read books (Swedish crime fiction and Italian novels), follow my favorite soccer team Juventus, and I enjoy cooking (Italian) and eating sea food. I like to travel with my family and I cannot spend a summer without visiting my parents and enjoying the magic atmosphere of my home-region, Salento in the South of Italy.

Audrey Esclatine

Email: audrey.esclatine@u-psud.fr

Research focus

I want to understand how and why human herpesviruses manipulate autophagy during their replication cycle

Model system

We use mammalian cells, mainly human cells, and we infect them with different herpesviruses that represent major threats to human health and patient care, such as human cytomegalovirus (HCMV), herpes simplex virus type 1 (HSV-1), and Epstein-Barr virus

Education and career

2001, PharmD, School of Pharmacy, Université Paris Sud, France. 2001, PhD, virology, Université Paris Sud; advisors: Anne-Marie Quéro and Monique Géniteau-Legendre. 2002–2004, postdoctoral researcher, University of Chicago, Chicago, IL, USA; advisor: Bernard Roizman. 2005–2010, associate professor, INSERM Université Paris Sud (UPSud) joint research lab; advisor: Patrice Codogno. 2010–present, associate professor, INSERM UPSud lab; advisor: Isabelle Beau.

Why do you study autophagy?

Virus is my first passion, especially herpesviruses, and for a long time, HCMV. I have been fortunate enough to work 3 years in Chicago, in the laboratory of Bernard Roizman, internationally recognized as the "godfather of herpes." Upon my return to France in 2005, it was my encounter with Patrice Codogno, a pioneer in the field of autophagy regulation, which is at the origin of my second passion: autophagy. When I joined his laboratory, he offered me the opportunity to develop a new research axis, based on my skills on herpesviruses. Patrice was kind enough to share and transmit his passion for autophagy, to channel my boundless enthusiasm and to believe in my projects.

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

Regarding relationships between viruses and autophagy, viruses modulate autophagy to their own profit for a myriad of purposes, some to improve their replication, to create a cellular environment conducive to their multiplication, others to help the viral particle to enter the cell, to exit, to acquire its envelope, or to be more stable. We also know that cells use autophagy to defend themselves against viruses, but we still barely know how. Xenophagy of viruses needs rigorous evaluation, in my opinion. I would love to discover how complete viruses can be recognized by autophagosomes during xenophagy. I think also that, thanks to viruses, as is often the case, we will further improve our understanding of selective autophagy and chaperone-mediated autophagy and will uncover novel properties of autophagic proteins.

Why is the field of autophagy important to you?

Modulations of autophagy represent promising therapeutic approaches in treating cancer, neurodegenerative diseases, and, why not, viral infections. However, the fact that this modulation can be beneficial or detrimental for viruses will complicate its use as an antiviral treatment.

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

Autophagy was already well recognized as cytoprotective, when Beth Levine, in PNAS in 2002, showed that a herpesvirus blocks autophagosome formation during infection. Indeed, HSV-1 both stimulates and represses it at the same time. For me, this represents an important milestone in the field because it opened up the possibility that autophagy can be reoriented by the cell to also protect itself against viruses. This is precisely what has

inspired me to see what was happening with HCMV.

Is teaching a substantial part of your current position? If so, what do you teach?

As an associate professor and a pharmacist, I spend half of my time teaching virology in a School of Pharmacy, and I love it. I'm responsible for several courses focusing on different aspects of medical virology, most of them focusing on pathology, diagnosis and treatment. I also participate in master's courses, where I teach about autophagy and microorganisms, of course! In addition, I am involved in the organization in Paris in 2015 of the 13th ULLA summer school (a European consortium for training in the field of pharmaceutical sciences).

Personal comments

Even though I will turn 40 this year, I had the chance to meet the man of my life 24 years ago, in high school! He's neither a scientist nor a pharmacist. He works as an engineer for Airbus, and more importantly he's very patient with my passion for my inspiring—but sometimes frustrating—job. We got married

just before we moved to the USA and we have now 2 charming kids (3 and 7). I love to ride my Dutch bike to go to work but I have to confess that I am not the athletic type and live, in fact, next to the lab…

Hans-Uwe Simon

Email: hus@pki.unibe.ch

Research focus

Role of autophagy in inflammation and cancer

Model system

Immune and cancer cells; mouse and human systems

Education and career

1980–1986, MD, medical faculty, University of Jena, Germany. 1986–1990, Specialization in immunology, University of Jena; advisor: Lothar Jäger. 1990–1992, postdoctoral fellowship, University of Toronto, Mount Sinai Hospital and Toronto General Hospital, Toronto, Canada; advisors: Katherine Siminovitch and Gordon B Mills. 1992–2000, principal investigator, University of Zurich, Swiss Institute of Allergy and Asthma Research (SIAF), Davos, Switzerland; 1996–2001, PhD, University of Jerusalem, Hadassah Medical School, Department of Pharmacy, Jerusalem, Israel; advisor: Francesca Levi-Schaffer; 2000–present, full professor, Pharmacology, and Chairman, Institute of Pharmacology, University of Bern, Bern, Switzerland. 2012–present, vice dean for research, medical faculty, University of Bern.

Why do you study autophagy?

I studied the role of apoptosis in the pathogenesis of inflammatory responses. We then discovered a crosstalk between apoptosis and autophagy, and since then my lab has been interested in the role of autophagy in inflammation and cancer.

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

I think that it is important to study autophagy in the context of the pathogenesis of diseases. A key question is how we can translate our knowledge into improved diagnostics and/or treatment of human diseases.

What do you hope to achieve in your scientific career?

I hope to be able to contribute to our understanding on the role of autophagy in human diseases. It would be great if my discovery could be beneficial for patients.

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

I think I would like to be an entrepreneur and establish my own company.

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?

We teach students studying medicine, dental medicine, biomedicine, biology, and pharmacy. Unfortunately, my research and teaching topics are not really related.

Personal comments

I like gardening, hiking, jogging, reading, and traveling. I enjoy good food and good wines. I like to watch movies and attend live performances (concerts and theater). I also frequently visit art exhibitions and organize art exhibitions.