

Impact Objectives

- Tap into the huge potential of the biology of autophagy to combat diseases such as cancers, neurodegeneration and infection
- Further explore the possible environmental applications of autophagy, such as improving plant growth under stressful conditions including drought, and the development of innovative applications for optimal agro-food production and bio-energy production
- Use the TRANSAUTOPHAGY consortium as an example of how a collaborative view of science produces significant results

Nurturing a young field

Dr Caty Casas, Dr Patrice Codogno, Patricia Boya, Christian Behrends, Agnieszka Sirko, Benjamin Dehay, Walter Balduini, Sylviane Muller, Fulvio Reggiori and Sharon Tooze form part of the collaborative consortium TRANSAUTOPHAGY. Here they explain how its diverse study of basic and translational autophagy is shedding light on the ways in which the mechanism can be manipulated for use in healthcare and biotechnology

From what context did the European Network of Multidisciplinary Research and Translation of Autophagy Knowledge (TRANSAUTOPHAGY) emerge?

CC & PC: Beginning in 2010, many national autophagy research networks were created in Europe (France and the Nordic Countries were first, and thereafter Germany, Spain, and the UK created their own networks). The emergence of these national networks was contemporary with growing interest in research into autophagy.

The national networks provided a solid base with a critical mass of researchers to organise a field of research that developed very rapidly with different orientations in different European countries. In addition, the creation of a European consortium in the frame of the European research H2020 call appeared to be timely and important to give this field European and international visibility.

What are the network's objectives?

CC & PC: An important goal of TRANSAUTOPHAGY is to translate our growing knowledge of the basic biology of autophagy into applications to human health, such as the development of new therapies and biomarkers, and into environmental applications such as improving plant growth under stressful conditions such as drought.

Have you faced any challenges when bringing together researchers from diverse fields?

CC & PC: We did not encounter difficulties bringing together researchers with different academic and non-academic backgrounds in TRANSAUTOPHAGY. Autophagy is a common bedrock for more than 250 researchers in the consortium. Some of us were already collaborating with investigators from other disciplines also interested in the field. This allowed the exponential growth of the multidisciplinary network. In order to facilitate exchange between researchers we have created five working packages that generate aims that bring together researchers with different and complementary backgrounds.

Could you discuss your work with young researchers and efforts to produce a gender balance within the consortium?

PB & FR: Autophagy is a relatively young field, and probably for this reason the gender balance is very good. In particular, many female scientists are leading figures in this research area, and when organising conferences or collaborative networks, just picking the best scientists based on the quality of their research, without applying any sort of positive discrimination, results in a fair gender balance.

The TRANSAUTOPHAGY COST action is no exception to this, and there is gender balance of participants from approximately 40 per cent of the countries participating in this initiative. For the COST activities, such as the short-term scientific mission (STSM) evaluations, we always take into account

not only gender balance, but also country balance. Restrictions have not had to be applied so far, as the number of male versus female applications has been similar. Thus, although not forgotten, the gender balance issue is not a problem in the autophagy field and could represent an example of the target that needs to be achieved.

What does the future hold for the consortium?

CC & PC: We hope to leave a legacy of an imbricated social network of researchers with a collaborative view of science. We hope the TRANSAUTOPHAGY consortium will be the starting point for the creation of a European Society for Autophagy that will raise money for the organisation of meetings and will support European projects including postdoctoral and PhD programmes.

One goal of the consortium is to act as a platform to favour the creation of start-up companies. We already have four SMEs who helped found the consortium: Anaxomics Biotech, Prous Institut for biomedical research, Vivia Biotech SL and 2E Science di Emanuele Enzo. The presence of these companies highlights the keen interest of the field in the market and has helped develop different aspects of autophagy that have been incubated in the consortium, ultimately translating basic research findings into disease treatment and strategies to foster healthy ageing.

A powerful network

TRANSAUTOPHAGY is an innovative consortium of researchers seeking to forge footsteps in the untrodden path of autophagy. The team behind the project, including Chair Dr Caty Casas and Vice-chair Dr Patrice Codogno, alongside working group chairs Jon Lane, Tassula Proikas-Cezanne, Henri Batoko, Guillermo Velasco and Maria Moran believe the potential impact of the network's research is huge, with possible applications that span healthcare and biotechnology and could ultimately improve the lives of many

Autophagy is an essential mechanism that maintains homeostasis at cellular and organismal levels. It controls nutrient balance, and gets rid of excessive or damaged organelles, misfolded proteins and invading microorganisms. Furthermore, it has the potential to combat diseases such as cancers, neurodegeneration and infection, as well as the ability to slow the age-related decline of tissue. The mechanism's potential extends beyond healthcare, with possible application in biotechnology; for example, modulating autophagy unlocks the potential to obtain alternative sources from microalgae or develop innovative applications for optimal agro-food production. The field of autophagy is relatively young and with so much untapped potential, requires the attention of a skilled and dedicated troop of researchers. Enter the European Network of Multidisciplinary Research and Translation of Autophagy knowledge (TRANSAUTOPHAGY).

TRANSAUTOPHAGY is a highly collaborative and multidisciplinary consortium that acts as a platform for enterprises, stakeholders and researchers from diverse disciplines, including nanotechnologists, bioinformatics, physics, chemists, biologists and physicians. The network is striving to generate multidisciplinary breakthroughs about autophagy regulation and use this knowledge for biomedical and biotechnological purposes. Although the network is still in its early stages, the consortium expects a range of impressive outcomes, ranging from recommendations for healthy ageing or disease prevention, to the discovery of new therapies, bio-based components or nanodevices capable of selectively modulating autophagy. The hope is these exciting breakthroughs will have clinical potential, for example, as antineoplastic, neuroprotective, antimicrobial or immunomodulatory agents in healthcare, or in biotechnology, the potential to exploit plants and microorganisms for efficient crop and energy production.

A FAR-REACHING FIELD

TRANSAUTOPHAGY was approved in the framework of the Horizon 2020 Programme in November 2015 as a COST Action of the EU and will be sponsored for four years. The European research groups involved in the Network currently stands at 304 scientists from 31 countries and rising. Dr Caty Casas of the Universitat Autònoma de Barcelona, Spain, is Chair of the consortium and Dr Patrice Codogno of Paris Descartes University, France, is Vice-Chair. 'My personal interest in working in favour of the TRANSAUTOPHAGY framework is to make science more collaborative and to pave the way for translation opportunities in the field,' Casas reveals. This goal resonates with the rest of the consortium,

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including Codogno: 'I became involved with TRANSAUTOPHAGY when Caty asked me to join the crew to elaborate the consortium and bring my knowledge of the field,' he states. 'Since then it has been a great pleasure for me to collaborate with her and other members of the consortium.'

Some of the researchers the pair are working alongside are: Jon Lane (Working Group 1 Chair); Tassula Proikas-Cezanne (Working Group 2 Chair); Henri Batoko (Working Group 3 Chair); Agnieszka Sirko (Working Group 3 Vice-Chair); Guillermo Velasco (Working Group 4 Chair); Maria Moran (Working Group 5 Chair); Patricia Boya (Short-term scientific mission-STSM- coordination); Christian Behrends (Short-term scientific mission-STSM- coordination); Benjamin Dehay (Dissemination coordination); Walter Balduini (Translational Committee); Sylviane Muller (Translational Committee); Fulvio Reggiori (TRANSAUTOPHAGY

COST member); and Sharon Tooze (TRANSAUTOPHAGY COST member).

Casas and Codogno highlight the necessity of a multidisciplinary and collaborative approach to TRANSAUTOPHAGY: 'Due to the complex and transversal nature of the autophagy field, research must be highly collaborative, with interactions among disciplines and with a clear purpose to generate both breakthroughs in basic knowledge and products for translative activities,' they explain. According to the researchers, they provide the consortium with several tools to facilitate collaboration. For example, they hold periodic foresight workshops that welcome researchers from all countries, and which companies

interested in autophagy products attend. Additionally, the network comprises special Working Groups (WGs) assigned to execute different deliverables, while the Translational Committee acts as a think-tank to identify projects of high potential clinical or biotechnological value. 'Networking is the essence of TRANSAUTOPHAGY, as we seek to facilitate easy and fast exchange of advanced scientific discoveries, techniques and resources, and to foster innovation and new discoveries including ideas for spin-off generation and market opportunities,' Casas and Codogno emphasise.

THE FIVE PARTS OF THE WHOLE

The aim behind WG1 is an improvement in the understanding of the molecular mechanisms that underlie the autophagy process. According to WG1 Chair Jon Lane, it is concerned with the advancement of knowledge of the molecular mechanisms that underpin the autophagy process and with synthesis of this knowledge into a

Project Insights

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PROJECT COORDINATOR BIOS

Dr Caty Casas

Caty Casas has been an Associate Professor at the Universitat Autònoma de Barcelona, Spain since 2013. She entered the autophagy field in 2011. During her post-doc period, she worked at the Centre de Recherche de Maladie Neurodegenerative at Sanofi-Aventis Pharma in Paris, France where she developed, characterised and patented a new mouse model for Alzheimer's disease.

Dr Patrice Codogno

A Research Director at INSERM, Codogno is a group leader at the 'Institut Necker-Enfants Malades' in Paris, France. His research is dedicated to autophagy from basic research on the membrane dynamics in autophagosome formation to the role of autophagy in adaptation to stress situations and its targeting in cancer cells as a new therapeutic avenue.

unifying model of autophagy control, which can be disseminated to and exploited by researchers in the autophagy community and beyond. 'To this end, various members of WG1 will engage in studies addressing molecular pathways and signalling modulators (for example lipids, kinases, miRNAs) that control various distinct steps in non-selective and selective forms of autophagy,' Lane explains.

WG2 was created with a view to providing new strategies to assist the researchers with analysing and modulating autophagy. WG2 Chair Tassula Proikas-Cezanne, reveals more: 'The molecular understanding of the process of autophagy in human health and disease has advanced enormously in the last couple of years; however, limited progress was made with regard to autophagy analysis, in particular *in vivo*,' she explains. 'Recognising the urgent need for efficient and robust large-scale autophagy assessments, WG2 concentrates on providing recommendations for autophagy analysis and treatment opportunities for modulating autophagy from bench-to bedside.'

ACCELERATING KNOWLEDGE TRANSFER

Next is WG3, which sets out to investigate how autophagy – an essential process in plants that decisively impacts growth – modulation in plants could be useful regarding biotechnological applications for crop and energy production. 'WG3 aims to extend current knowledge on autophagy in phototrophic organisms, identifying critical gaps in knowledge and translating this knowledge into enhancing plant growth, optimising nutrient utilisation, improving food quality and modulating stress responses and immunity,' explains WG3 Chair Henri Batoko.

WG4 and WG5 are closely interrelated and their purpose is to develop preclinical research (WG4) that can be translated into clinical applications (WG5). 'It is well established that dysregulation of autophagy is associated with the development of

different diseases, including cancer and neurodegeneration,' states WG4 Chair Guillermo Velasco. 'However, in most cases it is not known what triggers this dysregulation, or its precise contribution to the development of each disease. Thus, one of the aims of WG4 is advancing knowledge of the precise mechanisms that are involved in the enhanced or decreased activation of autophagy that occurs in different pathological conditions.'

WG5 Chair Maria Moran adds that a key goal of biomedical research is to accelerate the transfer of basic knowledge into practical information that can be used in the field of disease management, as well as in the implementation of health promotion strategies, including those aiming to favour healthy ageing. 'Such an important goal can only be achieved through a close cooperation between basic and clinical researchers, allowing design of new clinical trials, of new drugs targeting autophagy-related signals, and of novel and more accurate diagnostic methods,' she highlights. 'This objective is addressed mainly by WG4 and WG5, with the support of WG1 and WG2, with the involvement of autophagy in the pathogenesis (and thus in potential treatment) of cancer and immunity being main areas of interest.'

A NEW PATH

Although still in its infancy, with such an abundance of knowledge and shared enthusiasm, TRANSAUTOPHAGY is set to make impressive headway, forging a path of discovery for the young field of autophagy. 'From the beginning of the formation of the consortium, the real success has been the enthusiasm with which many high-quality researchers have quickly adopted this vision and joined and worked hard in the consortium,' Casas enthuses. With such exciting possible applications spanning healthcare and biotechnology, this research has the potential to hugely impact on, and potentially even revolutionise, these fields. Watch this space!

