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Manipulation of selective macroautophagy by pathogens at a glance

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ABSTRACT

Macroautophagy (hereafter autophagy) is a highly conserved catabolic pathway, which mediates the delivery of unwanted cytoplasmic structures and organelles to lysosomes for degradation. In numerous situations, autophagy is highly selective and exclusively targets specific intracellular components. Selective types of autophagy are a central element of our cell-autonomous innate immunity as they can mediate the turnover of viruses or bacteria, that gain access to the cytoplasm of the cell. Selective autophagy also modulates other aspects of our immunity by turning over specific immunoregulators. Throughout evolution, however, the continuous interaction between this fundamental cellular pathway and pathogens has led several pathogens to develop exquisite mechanisms to inhibit or subvert selective types of autophagy, to promote their intracellular multiplication. This Cell Science at a Glance article and the accompanying poster provides an overview of the selective autophagy of both pathogens, known as xenophagy, and of immunoregulators, and highlights a few archetypal examples that illustrate molecular strategies developed by viruses and bacteria to manipulate selective autophagy for their own benefit.

KEY WORDS: Autophagy, Autophagy receptor, Immunity, Viruses, Bacteria, Subversion

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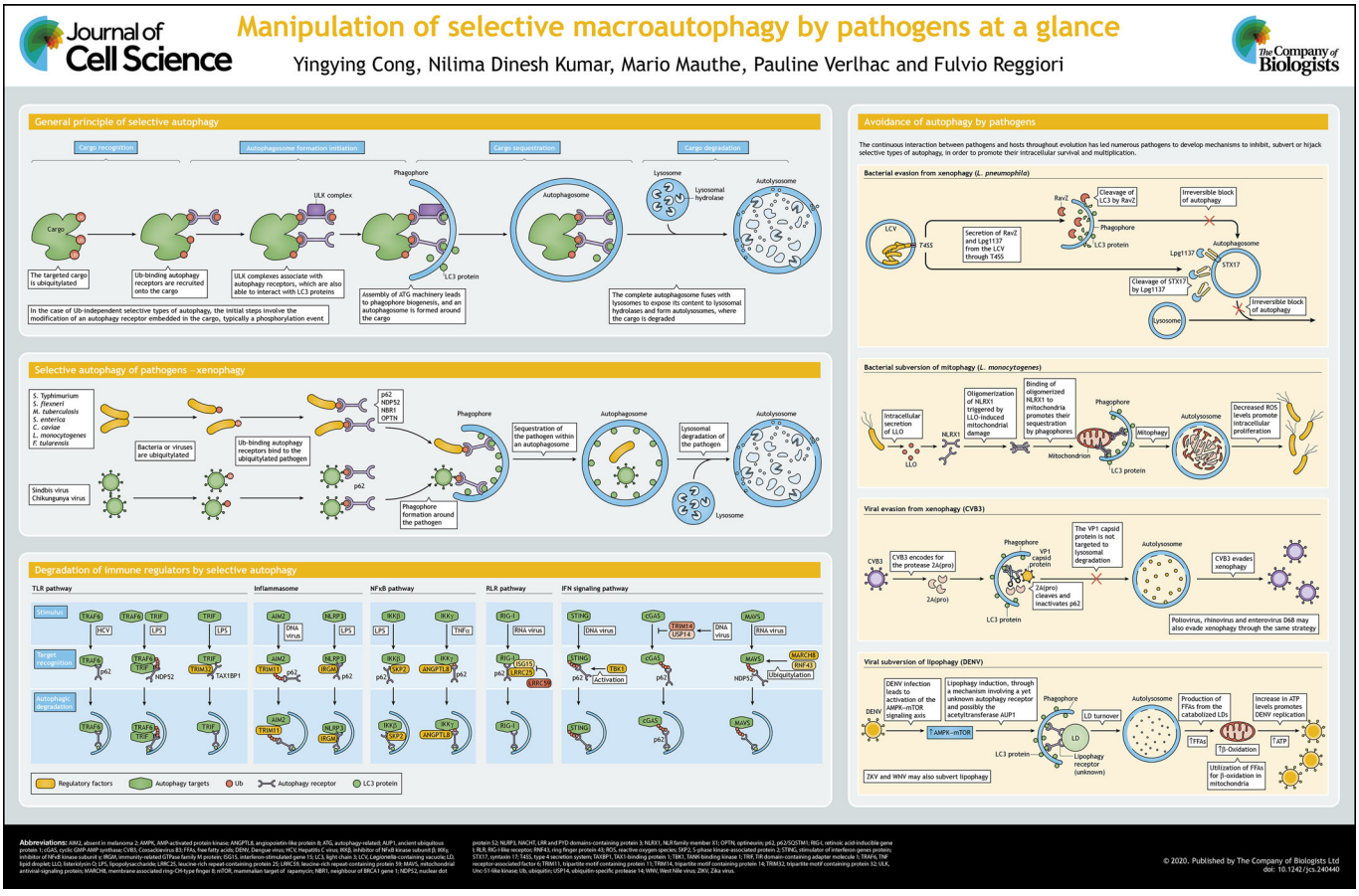

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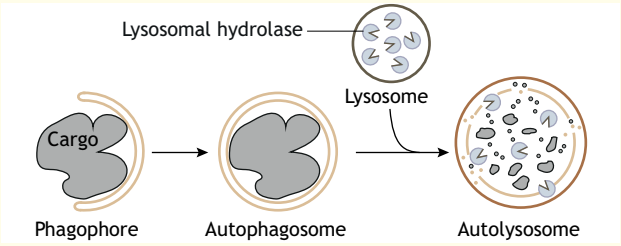
Introduction

Autophagy (see Box 1) is considered non-selective when the cargo molecules are heterogenous in their identity and appear to be sequestered randomly within autophagosomes. Selective types of autophagy, in contrast, are characterized by the exclusive degradation of specific structures. Distinctive terms have been coined to describe the selective degradation of organelles by autophagy, including mitophagy (mitochondria), lipophagy (lipid droplets), lysophagy (lysosomes), pexophagy (peroxisomes), nucleophagy (nucleus) and ER-phagy/reticulophagy (ER) (Kirkin and Rogov, 2019). Substrates of selective autophagy also include large protein complexes, such as ribosomes and midbodies, as well as single proteins, such as ferritin (Kraft et al., 2008; Mancias et al., 2014; Pohl and Jentsch, 2009; Wyant et al., 2018). Selective autophagy relies on so-called autophagy receptors, which allow both the *in situ* initiation of the formation of an autophagosome and the exclusive sequestration of cargoes within autophagosomes (Kirkin and Rogov, 2019). There are multiple autophagy receptors that can be broadly grouped into two categories based on how they recognize cargoes – ubiquitin (Ub)-dependent and Ub-independent autophagy receptors (Kirkin and Rogov, 2019). The principal Ub-dependent autophagy receptors are p62, also known as sequestosome 1 (SQSTM1), neighbour of BRCA1 gene 1 (NBR1), TAX1-binding protein 1 (TAX1BP1), nuclear dot protein 52 (NDP52, also known as CALCOCO2) and optineurin (OPTN). Ub-independent autophagy receptors are very often present on the cargo themselves, and examples are BCL2-interacting protein 3 (BNIP3), BCL2-interacting protein 3 like (BNIP3L, also known as NIX), FUN14 domain-containing protein 1 (FUNDC1), BCL2-like protein 13 (BCL2L13), FK506-binding protein 8 (FKBP8), prohibitin-2 (PHB2), 4-nitrophenylphosphatase domain and non-neuronal SNAP25-like protein homolog 1 (NIPSNAP1) and NIPSNAP2 for mitophagy, or family with sequence similarity 134 member B (FAM134B, also known as RETREG1), SEC62, reticulon-3 (RTN3), cell cycle progression 1 (CCPG1), alastin-3 (ATL3) and testis-expressed 264 (TEX264) for ER-phagy (Kirkin and Rogov, 2019). Binding of an autophagy receptor to the cargo modified with Ub moieties or the activation of a cargo-embedded autophagy receptor through a posttranslational modification (Farré and Subramani, 2016), leads to the recruitment and activation of the Unc-51-like kinase (ULK) complex (see poster) (Ravenhill et al., 2019; Turco et al., 2019; Vargas et al., 2019). The ULK complex is a key module of the highly conserved autophagy-related (ATG) machinery, and its activation leads to the assembly of the remaining ATG components (Dikic and Elazar, 2018). This event triggers the formation of a phagophore, the precursor intermediate of an autophagosome, which expands and sequesters the cargo targeted by the autophagy receptors (see poster). Exclusive cargo sequestration is also guaranteed by the direct interaction between the autophagy receptors and the Ub-like light chain 3 (LC3) proteins, which localize to the inner surface of the forming autophagosomes (Dikic and Elazar, 2018; Kirkin and Rogov, 2019). The LC3 proteins, which are the homologs of yeast Atg8, are part of a protein family that in humans comprises microtubule-associated protein LC3 member A (MAP1LC3A), MAP1LC3B, MAP1LC3C, γ-aminobutyric acid receptor-associated protein (GABARAP), GABARAP-like 1 (GABARAPL1) and GABARAPL2 (Shpilka et al., 2011). Upon autophagy induction, LC3 proteins are anchored onto the autophagosomal membrane by conjugation to phosphatidylethanolamine (PE), which requires the sequential action of ATG7 and ATG3, and the ATG12–ATG15–ATG16L1 complex (Dikic and Elazar, 2018; Shpilka et al., 2011).

Box 1. The general mechanism of autophagy

The basic mechanism of autophagy is the sequestration of structures destined to degradation by double-membrane vesicles called autophagosomes, which then fuse with lysosomes to form autolysosomes (see figure). In these organelles, the exposure of the cargo to lysosomal hydrolases leads to its degradation into basic metabolites, such as amino acids, nucleotides and fatty acids, which then are transported into the cytoplasm to be used as building blocks for the biosysnthesis of macromolecules or as a source of energy. Autophagosomes are formed by the nucleation, expansion and closure of a cistern that has been named phagophore or isolation membrane, a process that requires the function of the core ATG proteins.



Selective autophagy and immunity

A selective type of autophagy, known as xenophagy, plays a central role in innate immunity by targeting invading pathogens, bacteria and viruses for lysosomal degradation (Levine, 2005). In particular, pathogens that have gained access to the cytosol can become surrounded by phagophores and specifically sequestered within autophagosomes, before being delivered into lysosomes (Levine, 2005). The sequestration by phagophores requires the cytosolic bacteria to be ubiquitylated, a step that is essential for the subsequent recruitment of autophagy receptors, such as p62, NDP52, NBR1 and/or OPTN, and local activation of the ATG machinery (Kuo et al., 2018; Ravenhill et al., 2019) (see poster). Although multiple autophagy receptors are able to bind Ub, some bacteria are recognized by several autophagy receptors, whereas others are only recognized by a select few. The molecular bases underlying these differences, however, remain unclear.

The best-studied autophagy receptor, p62, is recruited to *Salmonella* Typhimurium, *Shigella flexneri* and *Mycobacterium tuberculosis*, and is crucial for the engulfment of these bacteria within autophagosomes (Chai et al., 2019; Mostowy et al., 2011; Thurston et al., 2009). NDP52 is responsible for the recognition of Ub-coated *Salmonella enterica* and *Chlamydia caviae* (Furtado et al., 2013; Thurston et al., 2009, 2012). Interestingly, although replication-deficient mutants of *Francisella tularensis* are cleared by xenophagy through p62 and NBR1, the wild-type bacterium has developed a strategy to avoid autophagic elimination (Chong et al., 2012). OPTN also promotes xenophagy of Ub-coated *Salmonella enterica* (Wild et al., 2011). Importantly, the interaction between OPTN and the ubiquitylated bacteria requires TANK-binding kinase 1 (TBK1)-mediated phosphorylation of OPTN at Ser177, which enhances the binding affinity of this autophagy receptor for LC3 proteins (Ravenhill et al., 2019; Wild et al., 2011). Phosphorylation of autophagy receptors by TBK1 appears to be a general requirement for selective types of autophagy (Kirkin and Rogov, 2019; Vargas et al., 2019). It must be noted that in addition to detecting ubiquitylated bacteria, selective autophagy can also indirectly eliminate some bacteria. For instance, when endosomal compartments are damaged by phagocytosed *S. flexneri*,

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S. Typhimurium or *Listeria monocytogenes*, cytosolic lectins, such as galectin-3 and galectin-8, are recruited by the then exposed glycans, which are typically present on the inner surface of the organelles of the endolysosomal system (Dupont et al., 2009; Paz et al., 2010; Thurston et al., 2012). Subsequent NDP52 binding to galectin-8 facilitates the autophagic degradation of the damaged compartment, including any bacteria that are still in its interior or in the vicinity (Thurston et al., 2012).

Most viruses disassemble while they fuse with the host cell membrane during infection, and, in most cases, xenophagy then clears specific viral components. For example, p62 is essential to control Sindbis virus (SINV) infection by favoring the lysosomal turnover of SINV capsid protein (Orvedahl et al., 2010). The selective targeting of the SINV capsid protein requires the HECT-domain containing E3 ubiquitin ligase SMAD ubiquitin regulatory factor 1 (SMURF1), which likely appends the Ub moieties to the SINV capsid protein that are then recognized by p62 (Orvedahl et al., 2011). SMURF1 can also promote the turnover of newly formed herpes simplex viral particles present in the cytoplasm, but the identity of the involved autophagy receptors remains to be unveiled (Orvedahl et al., 2011). Chikungunya virus (CHIKV) capsid protein is also targeted by p62 for autophagic degradation in an Ub-dependent manner (Judith et al., 2013).

The role of selective autophagy in immunity, however, is not exclusively linked to xenophagy as it also has a key role in modulating immune responses by turning over and thus deactivating the inflammasome or components of important immune regulatory pathways, including the toll-like receptor (TLR), interferon signaling, and the nuclear factor κ-light-chain-enhancer of activated B cells (NFκB) and the retinoic acid-inducible gene I (RIG-I)-like receptor (RLR) pathways (see poster) (Lim and Murthy, 2018; Trocoli and Djavaheri-Mergny, 2011; Wu and Cui, 2019). The components to be degraded are always recognized by selective autophagy receptors, but this interaction frequently requires adaptor proteins that mediate the interaction. For instance, the TLR pathway components TIR domain-containing adapter molecule 1 (TRIF) and TNF receptor-associated factor 6 (TRAF6) are recognized by TAX1BP1 and NDP52, and p62 and NDP52, respectively, and are degraded via autophagy, which inhibits the downstream NFκB and inflammatory signaling cascades (Chan et al., 2016; Inomata et al., 2012; Samie et al., 2018; Yang et al., 2017b). The downregulation of TRIF requires additionally tripartite motif containing protein 32 (TRIM32), which, independently of its ligase activity, physically connects TAX1BP1 to TRIF and initiates its degradation (Yang et al., 2017b). Furthermore, the inflammasome component NLRP3 (NACHT, LRR and PYD domains-containing protein 3) is recognized by NDP52 and p62 (Mehto et al., 2019), and this p62-mediated degradation depends on the immunity-related GTPase family M protein (IRGM), which promotes the association between NLRP3 and p62 (Mehto et al., 2019). Data obtained in microglia suggest that NLRP3 can also be recognized by NDP52 and targeted to autophagosomes (Houtman et al., 2019). Moreover, the inflammasome subunit absent in melanoma 2 (AIM2) interacts with tripartite motif containing protein 11 (TRIM11) upon infection by a DNA virus, and the subsequent self-polyubiquitylation of TRIM11 allows binding of p62 to AIM2 and its sequestration into autophagosomes (Liu et al., 2016; Shi et al., 2012). The main mechanism by which autophagy restricts inflammasome activation, however, is probably still by removing damaged mitochondria through mitophagy, in an ubiquitination- (carried out by the E3 ligase PARKIN) and p62-dependent manner (Zhong et al., 2016; Zhou et al., 2011). The autophagic turnover of cyclic GMP-AMP synthase (cGAS), stimulator of interferon genes protein 1 (STING1, also known simply as STING) and RIG-I (also known as DDX58), as well as the NFκB pathway components inhibitor of NFκB kinase subunit β and γ (IKKβ and IKKγ), are all mediated by p62 (Chen et al., 2016; Du et al., 2018; Liu et al., 2018; Zhang et al., 2017). The targeting of IKKβ and IKKγ, however, requires the specific adaptor proteins S-phase kinase-associated protein 2 (SKP2) and angiopoietin-like protein 8 (ANGPTL8), respectively, which act as a scaffold for their interaction to p62 (Liu et al., 2018; Zhang et al., 2017). RIG-I degradation requires two adaptor proteins, interferon-stimulated gene 15 (ISG15) and leucine-rich repeat-containing protein 25 (LRRC25), which bind in succession to promote its interaction with p62. The selective degradation of RIG-I is negatively controlled by leucine-rich repeat-containing protein 59 (LRRC59), which inhibits the binding of RIG-I to p62 (Du et al., 2018; Xian et al., 2019). Selective autophagy is also able to degrade factors that regulate interferon signaling, such as cGAS, STING and mitochondrial antiviral-signaling protein (MAVS). cGAS and STING are specifically ubiquitylated and this post-translation modification allows their direct recognition by p62 (Chen et al., 2016; Prabakaran et al., 2018). In the case of STING degradation, TBK1-mediated phosphorylation of p62 further enhances its binding to the Ub moiety, whereas tripartite motif containing protein 14 (TRIM14)-mediated recruitment of the deubiquitinating enzyme ubiquitin-specific protease 14 (USP14) to cGAS leads to a deubiquitylation of cGAS, which is required to inhibit p62 binding and thus lysosomal turnover (Chen et al., 2016; Prabakaran et al., 2018). The selective degradation of MAVS can be stimulated upon RNA virus infection through its ubiquitylation by two E3 ligases, mitochondrial membrane associated ring-CH-type finger 8 (MARCHF8) and cytoplasmic ring finger protein 43 (RNF43) (He et al., 2019; Jin et al., 2017). Ubiquitylated MAVS is then recognized by NDP52 and sequestered into autophagosomes.

Selective autophagy subversion by pathogens

As selective autophagy provides one of the first cell-autonomous lines of defense against pathogens and regulates several aspects of immune responses, the continuous co-evolution between hosts and pathogens has resulted in several virus and bacteria species having developed mechanisms to evade selective autophagic degradation, or to even use this process to facilitate their intracellular survival and proliferation. Here, we will discuss a few selected examples that illustrate the tactics adopted by bacteria and viruses to escape or exploit selective autophagy.

Legionella pneumophila is an opportunistic intracellular human pathogen that is responsible for a severe form of pneumonia called Legionnaires' disease (Brenner et al., 1979). *L. pneumophila* resides in a specialized vacuole, the *Legionella*-containing vacuole (LCV), which is formed inside the cytosol of infected cells. Using its type 4 secretion system (T4SS), *L. pneumophila* secretes around 300 virulence factors, and two of them, RavZ and Lpg1137, have been shown to inhibit autophagy, thereby protecting this bacterium from xenophagy (see poster). RavZ is a cysteine protease that irreversibly deconjugates LC3 proteins from PE preventing the formation of autophagosomes (Choy et al., 2012). RavZ contains three regions that directly bind to LC3 proteins, as well as a phosphatidylinositol-3-phosphate (PI3P)-binding domain, which together allow its interaction with lipidated LC3 proteins on PI3P-enriched autophagosomal membranes (Horenkamp et al., 2015; Yang et al., 2017a). Once bound to lipidated LC3 proteins, RavZ extracts them from the membrane by binding to the PE moiety via its

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lipid-binding motif, before its catalytic domain irreversibly cleaves the C-terminus to release the PE anchor (Yang et al., 2017a). As this cleavage also removes the lipid-modifiable C-terminal glycine residue, LC3 proteins can no longer be conjugated to PE and, consequently, they become autophagy incompetent. An additional strategy employed by *L. pneumophila* involves its serine protease Lpg1137, which can sever and thus inactivate syntaxin 17 (STX17) (Arasaki et al., 2017), a SNARE that is recruited onto complete autophagosomes and allows them to fuse with lysosomes (Itakura et al., 2012). Ectopic expression of Lpg1137, but not of a protease-dead variant, is sufficient to degrade STX17 with a concomitant inhibition of autophagy, whereas a *L. pneumophila* strain that lacks Lpg1137 is unable to cleave STX17 in infected cells (Arasaki et al., 2017). Thus, *L. pneumophila* blocks xenophagy by targeting both early and late steps in autophagy.

Listeria monocytogenes is a facultative intracellular bacterium that can replicate in the cytosol of macrophages and epithelial cells in humans. The interplay between *L. monocytogenes* and autophagy has been extensively studied and its various strategies to escape from xenophagy have been well documented. First, *L. monocytogenes* disguises its bacterial surface through its effector ActA to avoid recognition by autophagy receptors (Yoshikawa et al., 2009). Second, this bacterium also secretes lipases that degrade PI3P that is crucial for autophagosome formation (Tattoli et al., 2013). Finally, it can escape from the growing phagophore using actin-based mobility (Cheng et al., 2018). Recently, however, it has been shown that *L. monocytogenes* triggers mitophagy in macrophages by co-opting NLR family member X1 (NLRX1), a newly described mitophagy receptor, as cells lacking NLRX1 fail to induce mitophagy upon *L. monocytogenes* infection (see poster) (Zhang et al., 2019). Interestingly, Listeriolysin O (LLO), a virulence factor secreted in the cytosol of cells infected by *L. monocytogenes*, is sufficient to induce mitophagy, as a bacterial strain lacking LLO is unable to trigger this process (Zhang et al., 2019). LLO induces mitochondrial damage by inducing Ca^{2+} influx into this organelle; this triggers NLRX1 oligomerization, which in turn initiates its binding to LC3 proteins. *L. monocytogenes*-induced mitophagy decreases the levels of reactive oxygen species (ROS), thereby facilitating the proliferation of the bacterium in the cytoplasm of macrophages (Zhang et al., 2019). In accordance with this, treatment of macrophages with mitophagy inhibitors results in reduced *L. monocytogenes* proliferation (Zhang et al., 2019).

Viruses from the *Picornaviridae* family, including coxsackievirus (CVB3), poliovirus and enteroviruses, have been reported to exploit the autophagic machinery for replication (Jackson, 2015). Picornaviruses cause many human diseases ranging from encephalitis, over poliomyelitis, to hand, foot and mouth diseases (Tuthill et al., 2010). CVB3 avoids xenophagy by cleaving p62 with its 2A(pro) protease, which results in two fragments that can no longer function as autophagy receptors and thus fail to regulate NFκB signaling (see poster) (Shi et al., 2014, 2013). Additionally, CVB3 can also sever NDP52 with its 3C(pro) protease, and NBR1 with 2A(pro) and 3C(pro) proteases (Mohamud et al., 2019; Shi et al., 2014). Experimental evidence suggests that these events are strategies employed by CVB3 to escape xenophagy. Specifically, the CVB3 capsid protein VP1 is ubiquitylated and interacts with p62, and p62 knockdown increases the amounts of CVB3 viral proteins and viral titers (Mohamud et al., 2019). In addition to CVB3, other picornaviruses, including poliovirus, rhinovirus and enterovirus D68, sever p62 (Corona et al., 2018), but whether this cleavage is also employed to escape xenophagy needs further investigation.

A thus far unique case is that represented by viruses such as the Dengue, Zika and West Nile viruses, which belong to the family of *Flaviviridae*. Their NS3 protease and cofactor NS2B inhibit ER-phagy by cleaving reticulon-like FAM134B (Lennemann and Coyne, 2017), one of the specific ER-phagy receptors (Khaminets et al., 2015). NS3-mediated cleavage takes place in the cytoplasmic loop of FAM134B and generates two fragments that are unable to oligomerize (Lennemann and Coyne, 2017), which is crucial for inducing ER-membrane curvature and its subsequent pinching off during ER-phagy (Shibata et al., 2008). Importantly, knockdown of FAM134B promotes Dengue and Zika virus infection, whereas overexpression of this ER-phagy receptor causes a decrease in their infection (Lennemann and Coyne, 2017). It remains unclear, however, why ER-phagy is deleterious for flaviviruses. One explanation might be that, because replication and assembly of flaviviruses occurs on ER membranes, the ER stress this induces could trigger ER-phagy and thus turnover of part of the viral components.

Pathogens, including viruses, modulate the metabolism of host cells to establish conditions that favor their intracellular multiplication (Eisenreich et al., 2019; van der Meer-Janssen et al., 2010). Lipid droplets (LDs) are organelles involved in the storage of lipids, including triglycerides (Olzmann and Carvalho, 2019). Triglycerides can be mobilized and used to produce free fatty acids (FFAs) by lipophagy, a selective type of autophagy that mediates LDs turnover in lysosomes (Singh et al., 2009). FFAs can be further broken down by β-oxidation to generate ATP (Olzmann and Carvalho, 2019). Dengue virus (DENV), which causes dengue fever or dengue hemorrhagic fever, induces lipophagy (see poster) (Heaton and Randall, 2010; Jordan and Randall, 2017). This was uncovered based on the increased colocalization seen between GFP–LC3 and LDs in DENV-infected cells, as well as a decrease in LDs size and triglyceride levels in these cells (Heaton and Randall, 2010). FFAs that are generated as a result of lipophagy and enhanced β-oxidation are crucial for DENV infection because the supply of infected cells with FFAs circumvents the requirement for autophagy for viral replication (Heaton and Randall, 2010). DENV induces lipophagy by activating the AMP-activated protein kinase–mammalian target of rapamycin (AMPK–mTOR) signaling cascade; silencing of AMPK reduces DENV-induced lipophagy and leads to an inhibition of viral replication (Jordan and Randall, 2017). Interestingly, another study found that the acetyltransferase ancient ubiquitous protein 1 (AUP1), a LD-localized protein, also plays a crucial role in DENV-induced lipophagy (Zhang et al., 2018). AUP1 is mainly present in monoubiquitylated form, but during DENV infection, Ub is removed and deubiquitylated AUP1 relocalizes to GFP–LC3-positive autophagosomes. Importantly, lipophagy is induced in the $AUP1^{+/+}$ wild-type but not in the $AUP1^{-/-}$ cells or in cells expressing a variant of AUP1 that cannot be deubiquitylated (Zhang et al., 2018). Moreover, viral production is impaired in cells lacking *AUP1* or expressing the variant of AUP1 that cannot be deubiquitylated. Interestingly, when DENV NS4A and NS4B are co-expressed in cells, they interact with non-ubiquitylated conjugated AUP1 and activate the acyltransferase activity of AUP1, which result in an increase in lipophagy (Zhang et al., 2018). However, the exact mechanism of how AUP1 induces lipophagy remains unclear. Further investigations are also needed to determine which autophagy receptor is involved in DENV-induced lipophagy, including exploring whether the only known lipophagy receptor thus far, the adipose triglyceride lipase (ATGL) (Sathyanarayan et al., 2017), is required. As AUP1 deletion also impairs Zika and West Nile virus cell infection, it may be that other

flaiviruses subvert lipophagy (Zhang et al., 2018). This is another aspect that needs attention in the future.

Conclusions and perspectives

As pathogens exploit and manipulate cellular pathways to successfully survive and replicate in host cells, the study of their infections at the molecular level has been crucial for unveiling several new cellular processes as well as to determine the regulation and mechanism of others. During the past 15 years, after the initial ground-breaking work demonstrating that autophagy is part of innate immunity and that microbes can escape it (Nakagawa et al., 2004; Ogawa et al., 2005), investigations have shown that numerous bacteria and viruses manipulate this degradative route to promote their infection (Deretic and Levine, 2009; Dinesh Kumar et al., 2020; Kimmey and Stallings, 2016). Our understanding about the mechanism and regulation of selective autophagy has also expanded enormously during the last decade (Farré and Subramani, 2016; Kirkin and Rogov, 2019), and, as underlined in this article, this knowledge has been crucial to study the subversion of selective autophagy by pathogens. The manipulation of one or more selective types of autophagy has the ultimate advantage of not affecting the multitude of functions involving autophagy (Choi et al., 2013; Kroemer et al., 2010), which could hamper the survival of the host and consequently the invader itself. Thus, it is predictable that future research will reveal that numerous other viruses and bacteria have opted to manipulate selective autophagy. In this regard, it must be noted that past studies showing an alteration of autophagy during a specific infection may have detected an induction or inhibition of a selective type of autophagy. Therefore, some of these findings should be revisited in light of our current knowledge and tools to precisely address this question.

As some microbial strategies target autophagy receptors, such as p62 and NDP52, which in addition to xenophagy are also involved in immunoregulation (see poster), particular attention should be paid to establish whether cell autonomous immune responses are also altered when those autophagy receptors are inactivated. The expectation is that blocking the degradation of immunoregulators will enhance and/or prolong the immune response, and this will be inauspicious for the pathogen. However, several pathogens have also developed strategies to suppress immune responses, which would counteract such an approach. Understanding how the different pathogens counteract the enhancement of the immune responses caused by autophagy receptor inhibition, is key to obtaining a comprehensive view about the exquisite and detailed mechanism of selective autophagy subversion.

In conclusion, in addition to providing new antimicrobial targets, future studies on the interaction between pathogens and selective autophagy will be a valuable tool to not only understand the molecular principles of xenophagy but also the regulation of selective autophagy-mediated immune responses. Pathogens manipulating selective autophagy could also be a unique source of specific small molecules and proteins for the modulation of selective autophagy in experimental contexts, as well as possibly in medical interventions.

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Competing interests

The authors declare no competing or financial interests.

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Cell science at a glance

A high-resolution version of the poster and individual poster panels are available for downloading at http://jcs.biologists.org/lookup/doi/10.1242/jcs.240440.supplemental

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