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EDITORIAL

Amino acids and autophagy: their crosstalk, interplay and interlock

Chien-An A. Hu[1] · Zhenlong Wu[2] · Junjun Wang[2]

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A long and well-established history has witnessed the study of amino acids and autophagy in both normal and pathophysiology of biological systems. The first amino acid identified and named was asparagine by Professors Vauquelin and Robiquet (1806; Fig. 1a), whereas the lysosome was discovered in 1955 (de Duve et al. 1955) and autophagy, a lysosome-dependent pathway, was identified and coined by Professor Christian de Duve at the CIBA Foundation Symposium on Lysosomes in 1963 (de Duve et al. 1955; Klionsky 2007). The crosstalk between amino acids and autophagy was first described by Professor Glenn Mortimore and colleagues indicating that amino acids inhibit autophagy and amino-acid deprivation induces autophagy in perfused rat liver (Neely et al. 1977; Mortimore and Schworer 1977). Professor AJ Meijer's group made some monumental findings between 1995 and 1997 revealing that (a) rapamycin, an inhibitor of mTOR, acts as an autophagy inducer (1995), (b) amino acids stimulate mTOR (Blommaart et al. 1995) and (c). Wortmanin and 3-methyladenine, both phosphatidylinositol 3-kinase (PI3K) inhibitors, inhibit autophagy (Blommaart et al. 1997). Since 1999, specific protein molecules, such as autophagy-related proteins (Atgs), Beclin 1 (Atg6) and mTORC1, protein complexes/interactomes and associated pathways, and autophagy-associated diseases have been systematically identified, characterized and functionally analyzed (Long et al. 2005; Klionsky 2007; Sancak et al. 2008, 2010; Zoncu et al. 2011; Efeyan et al. 2012; Jewell et al. 2013; Rebsamen et al. 2015; Meijer et al. 2015).

As summarized in Fig. 1b and other related figures of the manuscripts in this Special Issue (SI) of "Amino Acids and Autophagy", how amino acids regulate and fine tune autophagy is quite amazing and sophisticated, like a well-conducted molecular symphony that involves amino acids, growth factors, energy status, extra- and intracellular sensors, transcriptional factors, AKT, AMPK, mTORC1 complex, Atg proteins and a key organelle/conductor, the lysosome. Interestingly, amino acids are both regulators and products of autophagy, creating an intimate relationship between amino acids and autophagy.

So, what is the SI set to accomplish? First, we want to publish a range of excellent and stimulating papers including both review and research articles that document the role of amino acids and autophagy in (a) humans, mammals, plants, and yeast; (b) tissues such as brain, small intestine and liver; and (c) the interplay with apoptosis, the interplay of inflammation and tight junction barriers and the crosstalk of host immune response and pathogens. Second, we want to mandate that manuscripts in this SI are carefully written, rigidly peer-reviewed and then thoroughly revised. Third, we believe that this SI will serve as an educational asset for the junior scientists and students who are interested in this exciting research field. We sincerely hope that we have achieved and continue achieving these goals.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

✉ Chien-An A. Hu
ahu@salud.unm.edu

[1] Department of Biochemistry and Molecular Biology, University of New Mexico, Health Sciences Center, Albuquerque, NM 87131-0001, USA

[2] State Key Laboratory of Animal Nutrition, College of Animal Science and Technology, China Agricultural University, Beijing 100193, People's Republic of China

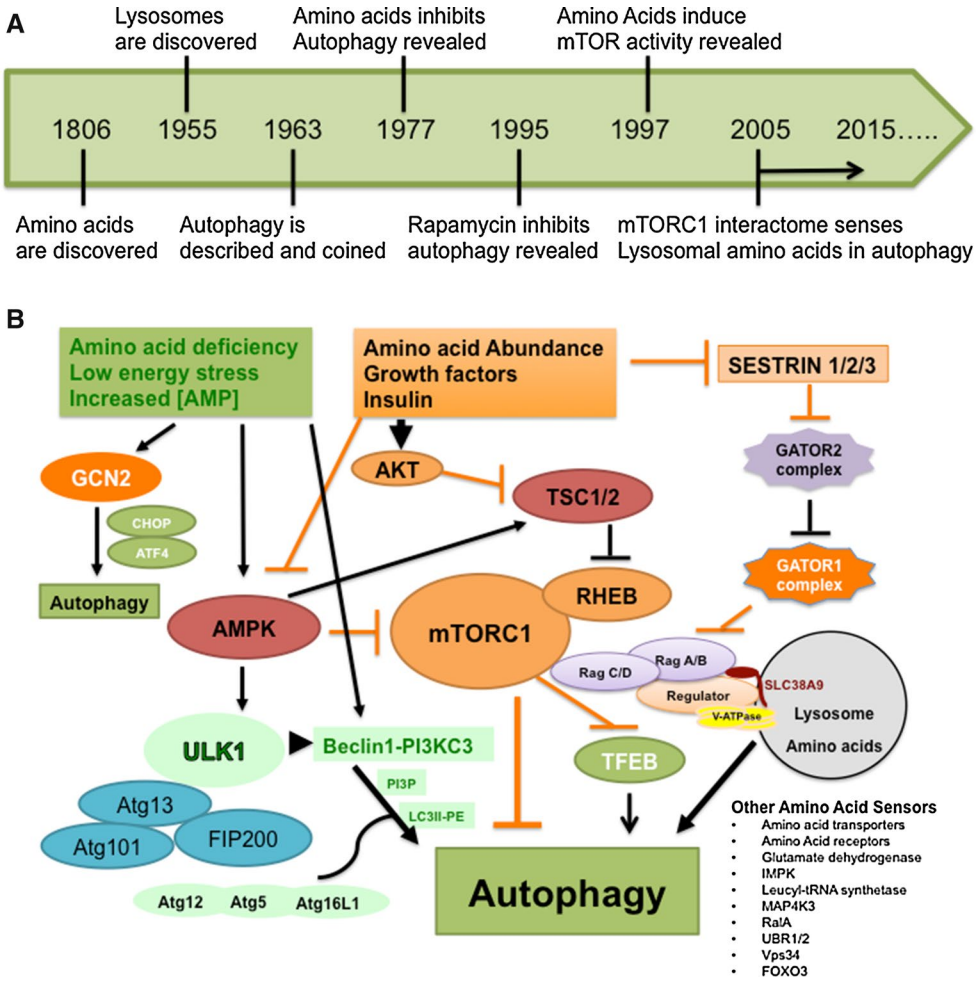

Fig. 1 **a** Timeline: a history of amino acids and autophagy. **b** Crosstalk between amino acids and autophagy. See text and the manuscripts in this Special Issue of "Amino Acids and Autophagy" for details. In essence, the autophagy signaling pathway is regulated by amino acid abundance, growth factors, insulin, and energy levels. In the presence of amino acids, mTORC1 is activated and AMPK is inactivated through various amino acid sensors, as indicated. Activation of mTORC1 by amino acid abundance represses autophagy in part through the inhibition of ULK1 activity. AMPK can inactivate mTORC1 when the intracellular ratio of AMP/ATP is significantly increased

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