AUTHOR COMMENTARIES - From Special Topics

Autophagy - July 2009
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Isei Tanida

From the Special Topic of Autophagy

According to our Special Topics analysis on autophagy research over the past decade, the scientist whose work ranks at #9 by total citations is Dr. Isei Tanida, with 33 papers cited a total of 2,195 times. In Essential Science Indicators℠ *from Thomson Reuters, Dr. Tanida's record includes 37 papers, the majority of which are classified under Biology & Biochemistry, cited a total of 2,389 times between January 1, 1999 and June 30, 2009.*

Dr. Tanida is the Section Chief for the Laboratory of Biomembranes in the Department of Biochemistry and Cell Biology at the National Institute of Infectious Diseases in Tokyo, Japan.

In this interview, he talks with* ScienceWatch.com *about his research involving autophagy.

SW: Would you tell us a bit about your educational background and research experiences?

I majored in Biology at the University of Tokyo, where I received my Bachelor of Science degree in 1987. I also did my graduate work at the University of Tokyo, earning my Master of Science degree in Biology in 1989, and my Ph.D. in 1997.

My research career started in 1989 at the Tonen Corporation's Central Research Laboratory, where I worked as a Researcher in the Biotechnology Section until 1997. I then moved to the Juntendo University School of Medicine, where I was Assistant Professor in the Department of Biochemistry until October of 2006. From November of 2006 to the present, I have been with the National Institute of Infectious Diseases, where I am the Section Chief of the Laboratory of Biomembranes, in the Department of Biochemistry and Cell Biology.

SW: What first interested you in autophagy?

Autophagic body in the vacuole of yeast. When I visited Prof. Ohsumi's lab in 1991, Dr. Takeshige had just found this autophagic body, which was a novel structure. Thereafter, I was interested in the molecular mechanism of autophagy.

SW: One of your highly cited papers is the 1999 *Molecular Biology of the Cell* article, "Apg7p/Cvt2p: A novel protein-activating enzyme essential for autophagy" (10[5]: 1367-79, May 1999). Would you talk a little bit about this paper, its findings, and why it is so highly cited?

This is my first paper regarding autophagy. Cooperating with Dr. Ohsumi's lab, I was searching in the dark for the Atg7 protein and its mutant. One day, Dr. Ohsumi informed us that Dr. Mizushima (he is

now a professor at Tokyo Medical and Dental University) had found the Atg12-Atg5 conjugate, and that Atg7 is genetically essential for the conjugation.

One reason it is so highly cited is that Atg7 is a key enzyme for the formation of autophagosomes, and another is, from the standpoint of the ubiquitylation reaction, Atg7 is a unique E1-like enzyme that has at least two conjugations.

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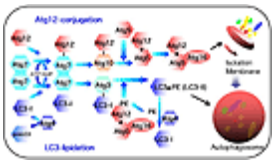

Atg conjugations essential for autophagy

SW: Another of your highly cited papers is the *Autophagy* article, "Lysosomal turnover, but not a cellular level, of endogenous LC3 is a marker for autophagy" (1[2]: 84-91, July-September 2005). Could you tell our readers something about this paper?

This paper focused on the lysosomal flux of LC3 during autophagy. Autophagy has at least a three-step reaction: autophagosome-formation for engulfing the cytosol, lysosome-autophagosome fusion, and lysosomal degradation of intra-autophagosomal contents. When autophagosome-formation is activated, LC3-II is increased, but simultaneously lysosomal degradation of LC3-II is activated.

At that time, many researchers were excited about the finding of LC3-II as a unique autophagosomal marker, but few people considered lysosomal degradation of LC3-II. Therefore, there was a confusion of translation of the amount of LC3 to autophagic activity. In this paper, we showed that lysosomal degradation of LC3-II is non-negligibly high during autophagy.

SW: How has our knowledge of autophagy changed over the past decade?

It has increased like the Big Bang. Ten years ago, few scientists knew about autophagy. Upon first hearing the term, many scientists asked me "What? Like phagosomes or like fuzzy logic?" One of the most amazing facts is that "autophagy" was employed as a key reaction in a gourmet adventure Manga "TO-RI-KO" of a famous Japanese weekly Manga magazine "SHONEN JUMP" several months ago. This means that now, even junior students know the word "autophagy" via this comic.

SW: Where would you like to take your research on autophagy in the next decade?

I will focus on the molecular mechanisms of autophagy, and autophagy on virus infection.

SW: What would you say the "take-home message" about your work should be?

Don't forget the lysosomal degradation of LC3-II during autophagy.

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Isei Tanida's current most-cited paper in *Essential Science Indicators*, with 386 cites:

Komatsu M, *et al*., "Loss of autophagy in the central nervous system causes neurodegeneration in mice," *Nature* 441(7095): 880-4, 15 June 2006. Source: *Essential Science Indicators* from Thomson Reuters.

KEYWORDS: AUTOPHAGY, YEAST, MOLECULAR MECHANISM, ATG7 PROTEIN, AUTOPHAGOSOMES, LYSOSOMAL FLUX, LC3, LYSOSOME-AUTOPHAGOSOME FUSION, LYSOSOMAL DEGRADATION, INTRA-AUTOPHAGOSOMAL CONTENTS, LC3-II.

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