does not change with carrier concentration, disorder, or temperature, of the electron fluid. It became clear that we are seeing a new state of matter now called the quantum Hall fluid. Thouless and coworkers showed that the robustness and precision of the quantized Hall conductance have a topological origin. The Hall conductance, a long length scale, global, property is proportional to a topological integer, called the Chern number. Properties such as the Hall conductance are 'topologically protected'. This is the basic characteristic of the state. It also turns out that there are necessarily zero energy modes present at the boundary between such a phase and another which is topologically different.

Duncan Haldane's pioneering journey started in an apparently obscure bylane. In 1983, he showed that a chain consisting of magnetic moments (spins) interacting with their nearest neighbours had very different properties depending on whether the spins were integral or half integral in units of $(h/2\pi)$ where h is the Planck's constant, the basic quantum constant. Both classes of systems lack long-range order. For the former there is no gap between the ground state and the lowest excited state, while for the latter, there is. This stunning result was not quite believed by experts. However, the Haldane gap exists; it has been measured experimentally. Presciently, he tracked down the origin of this gap; it is a direct consequence of a non-zero topological term in the effective action of the entire system, this action being expressed as a function of the spin field. So one has, in such chains, two different quantum fluids arising because of a topological distinction. A few years later, in unrelated work, he showed that even in the *absence* of an external magnetic field, a special two-dimensional lattice system is a topological quantum Hall fluid. Interestingly, such a system has been recently synthesized in a cold atom lattice (this consists of about fifty thousand potassium atoms hopping around in a special lattice generated by crossed laser beams, the whole thing being at a temperature of about 10^{-7} K above absolute zero). This creative work by Haldane was quite directly the inspiration for later developments of models of topological insulators, mentioned below.

These contributions had an enormous direct and indirect effect on the community of physicists, by pointing to the crucial (and unsuspected) role of topology in condensed matter systems, by stimulating the search for other kinds of topologically non-trivial matter, as well as by providing actual models and methods. One well-known instance of the far flung consequences of the work and ideas of the laureates has to do with topological insulators. These are semiconducting or insulating in the bulk, like so many other materials of that kind. However, because of a topological peculiarity in their electronic structure, they inevitably have a metallic surface; there are free electrons there. These electrons are quite unusual. Their intrinsic spin always points perpendicular to their direction of motion, in a specific sense. Bi_2Se_3 is one out of dozens of examples. There is great promise that these electronic states indicate even more unusual possibilities. There are many road maps for the realization of these. For example, it is likely that their nature will be the basis for robust, intrinsically quantum, ways of computing. We are in the middle of a great creative ferment. It is therefore wonderful that the physicists whose curiosity and work very clearly started it all, are recognized by their peers.

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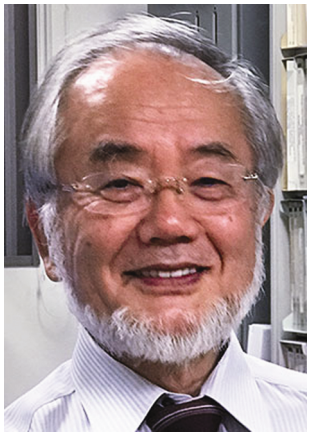
Nobel Prize in Physiology or Medicine 2016



The Nobel Prize in Physiology or Medicine 2016 was awarded to Yoshinori Ohsumi of the Tokyo Institute of Technology, Tokyo, Japan 'for his discoveries of mechanisms for autophagy' (http://www.nobelprize.org/nobel_prizes/medicine/laureates/2016/).

Autophagy is a commonly used word in biology. It derives from the Greek words 'auto' meaning oneself, 'phagy' meaning eating, and was coined by the Belgian scientist – Christian de Duve. The 1974 Nobel laureate for Physiology or Medicine, de Duve, had discovered cellular compartments, named *lysosomes*, in which most of the worn out biological material is degraded. Explained beautifully by Daniel Klionsky in a insightful video on 'Science and Art Collaboration' at the University of Michigan: 'Autophagy is the process in which our cells break down parts of themselves. As with many things, parts of cells wear out and how do the cells get rid of these things – that are no longer functional – is the process of autophagy'. However, digestion of its own components by cells remained enigmatic for a long time. Why would cells compel degradation of its own constituents? Moreover, what are the underlying molecular mechanisms of autophagy? These questions were addressed in a series of experiments since the early 1990s by Yoshinori Ohsumi. These experiments have led to the current understanding of autophagy and its immense physiological relevance. The press release of the Nobel committee (http://www.nobelprize.org/nobel_prizes/medicine/laureates/2016/press.html) states 'Ohsumi's discoveries led to a new

paradigm in our understanding of how the cell recycles its content. His discoveries opened the path to understanding the fundamental importance of autophagy in many physiological processes, such as in the adaptation to starvation or response to infection. Mutations in autophagy genes can cause disease, and the autophagic process is involved in several conditions including cancer and neurological disease.' Thus, autophagy is now believed to play an important role in many diverse cellular processes such as ageing, development, response to infections, neurodegeneration, etc.

Lysosomes are subcellular compartments, which serve as the workhorse for degradation of biological material. Cells have evolved clever molecular strategies for carrying the material destined for degradation to the lysosomes, and then enzymatically degrade the material. A remarkable step in this process is the formation of a new double membrane subcellular compartment called the autophagosome, concomitantly sequestering the material for degradation, which eventually fuses with the lysosomes and allows enzymes in the lysosomes to degrade the material. Ohsumi designed an elegant experimental strategy using Baker's yeast to test if these enzymes are inactivated, what would be the outcome? It was known that autophagy can be induced under nutrient starvation. Baker's yeast was a convenient model for use because it can be observed under a light microscope. Ohsumi used protease (enzymes that degrade proteins)-deficient strains of yeast and subjected these under nutrient starvation media to visual analysis under a microscope. He observed within a few hours that the vesicles within the lysosomes – the autophagic bodies – are not degraded, but rather get accumulated in the compartment[1]. This was the first instance that autophagy was being observed by any one. If the proteolytic enzymes were present, the cellular material would be degraded instantly, and the phenomenon would not be observed. Indeed no one had been able to observe this phenomenon earlier. Ohsumi acknowledges that his love for microscopes led him to make the fundamental observation (http://www.titech.ac.jp/english/research/stories/ohsumi.html). Thus, a combination of a clever experimental strategy, yeast as the model, and visual observation under a microscope led to the foundations of discovery of mechanisms of autophagy.

Discovery of autophagy in yeast within a short time led to the search of genes involved in this process. Ohsumi was once again at the forefront in the identification of these genes by conducting a genetic screen in yeast and analysing mutants which were autophagy-defective[2]. This was much before the importance of autophagy was recognized in physiology and disease. As of today, around 15 genes are known to be involved in autophagosome initiation and maturation, which comprise a cascade of events. This cascade includes formation of a double layered membrane isolating cellular components to be degraded under the appropriate conditions (autophagosomes), fusion of this vesicle with lysosomes, release or activation of lysosomal degradation enzymes into the vesicle, and finally degradation of biological macromolecules into their respective building blocks such as nucleotides, amino acids, etc. The degraded components are then recycled by the cells and thereby promote cell survival. Combined with Ohsumi's work and screens from other groups in the world, the genes which participate in all these processes of autophagy are now collectively termed as the *atg* genes[3].

The molecular mechanisms in autophagy have now been demonstrated to be conserved in many species, yeast to humans. In the past 15–20 years, there has been growing appreciation of autophagy in diverse cellular processes, but more importantly has been the realization of the correlation of dysfunctional autophagy to many different disease conditions. For example, loss of autophagy in central nervous system causes increased neurodegeneration in mice[4,5]. *beclin 1*, a mammalian autophagy gene, has been shown to inhibit tumorigenesis, thereby acting as a tumour suppressor in different cancers[6]. Similarly, decreased expression of many autophagy proteins is related to progression of tumours in humans. Thus, increasing realization of the link between autophagy and disease conditions has opened up avenues for understanding the disease processes and possible interventional strategies.

Thanks to the work of Ohsumi and others, progress in understanding autophagy in the last 20 years has revealed that autophagy is an important physiological process, required for recycling cellular components. It eliminates damaged biological macromolecules, thus providing a quality control mechanism. In the starving cells, autophagy provides fuel for cellular components. During invasion by foreign organisms, autophagy acts to eliminate the pathogen from the host. Autophagy also regulates cell growth, development and differentiation, and thereby provides an effective control over prevention of unregulated growth, as in cancer. All these correlations of autophagy and cellular processes can be traced to the initial discovery of Ohsumi in 1992.

Ohsumi remains steadfastly active in the field, passionately attempting to decipher the details of mechanisms of various steps of autophagy. On the website of Tokyo Institute of Technology, he has the following advice to offer to young researchers (http://www.titech.ac.jp/english/research/stories/ohsumi.html): 'So my message to all of you, who want to pursue a career in science, is to do what no one else is doing, and do what you find truly interesting. Research isn't easy. However, if you're really drawn to a subject and you're interested in it, you'll certainly overcome all the obstacles, even if, say, your work isn't appreciated for a time. You only live once. Others aren't interested in trivia. In the end, you have to want to taste the pleasures of success after all is said and done.'

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