Peptide found to induce autophagy resulting in defense against diseases

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(Medical Xpress)—A multi-disciplined team of researchers from the United States and The Netherlands has found that introducing a certain type of peptide into mice cells induces autophagy, which in turn helps in fighting diseases. In their paper published in the journal *Nature*, the researchers describe how introducing the peptide Tat- Beclin 1 into mice cells resulted in a natural process known as autophagy becoming active, which in turn was found to help combat several types of diseases.

Autophagy is a natural process that occurs in cells. Its purpose is to remove material from the cell that is not needed – to clean things up. Scientists have known for some time that the process helps in the fight against infectious diseases. Up till now however, they have been forced to watch from the sidelines as the process came about naturally. In this new research, led by Beth Levine, the team found that a protein known as Tat- Beclin 1 can force the process to come about unnaturally.

The protein was discovered by another team led by Levine nearly 15 years ago and she and colleagues have been studying its properties and the way it is used in organisms ever since. In this new research, the team has discovered that its presence can induce the onset of autophagy in cells.

To find out if the onset of artificially induced autophagy in cells might actually lead to health benefits, the research team first added the protein to cell cultures in a dish in a lab. In so doing, they found it contributed to removing other proteins involved with Huntington's disease and also

increased the survival rate of cells infected with West Nile virus, HIV, and listeria.

Building on their initial success, the team then introduced the protein into living mice. In so doing they found that 37 percent of treated mice survived an infection of the chikungunya virus, compared to none for a control group. In another test, 20 percent of mice treated with the protein survived a West Nile infection, compared to zero in the control group. This is the first documented case of an agent being introduced into cells that induced autophagy and that also led to an increase in resistance to a disease.

Levine reports that she is currently looking for a pharmaceutical sponsor to take the protein into clinical development, which would of course eventually involve trials with human volunteers. Thus far, she and colleagues report no ill effects from treating mice with the protein, though they aren't ruling out the possibly just yet. More testing will have to be done.

More information: Identification of a candidate therapeutic autophagy-inducing peptide, *Nature* (2013) doi:10.1038/nature11866

Abstract
The lysosomal degradation pathway of autophagy has a crucial role in defence against infection, neurodegenerative disorders, cancer and ageing. Accordingly, agents that induce autophagy may have broad therapeutic applications. One approach to developing such agents is to exploit autophagy manipulation strategies used by microbial virulence factors. Here we show that a peptide, Tat–beclin 1—derived from a region of the autophagy protein, beclin 1, which binds human immunodeficiency virus (HIV)-1 Nef—is a potent inducer of autophagy, and interacts with a newly identified negative regulator of autophagy, GAPR-1 (also called GLIPR2). Tat–beclin 1 decreases the accumulation

of polyglutamine expansion protein aggregates and the replication of several pathogens (including HIV-1) in vitro, and reduces mortality in mice infected with chikungunya or West Nile virus. Thus, through the characterization of a domain of beclin 1 that interacts with HIV-1 Nef, we have developed an autophagy-inducing peptide that has potential efficacy in the treatment of human diseases.