Medical Xpress

Discovery points way for new treatment for aneurysms

January 27 2010

New research findings from a team at the Providence Heart + Lung Institute at St. Paul's Hospital and the University of British Columbia (UBC) may lead to new treatment options for abdominal aortic aneurysms (AAA) - a potentially fatal disease that currently has no pharmacological treatments.

An aortic aneurysm is a bulging of the aorta, the largest blood vessel in the body. If the aneurysm ruptures, it causes rapid blood loss and a high risk of death. About 75 per cent of all aortic aneurysms occur in the part of the aorta that is located in the abdomen, which supplies blood to the lower limbs.

Published in today's American Journal of Pathology, a study led by Dr. David Granville, a researcher with UBC and the Providence Heart + Lung Institute, reveals a novel therapeutic target for AAA that could have a major impact on the treatment of this disease.

Using experimental models of AAA, Dr. Granville and his team identified a protein-degrading enzyme called Granzyme B that is abundant in aneurysms. To determine whether Granzyme B was contributing to aneurysms, the enzyme was genetically knocked out.

"When we removed Granzyme B, we found that it not only slowed the progression of aneurysms, but also markedly improved survival," says Dr. Granville. "This suggests that drugs designed specifically to target Granzyme B could be an effective means of treating aneurysms."

Granzyme B is released by many types of immune cells to target and destroy unwanted or virus-infected cells.

Until recently, it was thought that immune cells delivered Granzyme B directly into cells targeted for destruction, but Dr. Granville's team demonstrates that, in certain conditions, this protein can leak out into the space surrounding healthy cells and in the blood stream. As it builds up outside of cells it starts breaking down structural proteins that maintain tissue integrity - similar to a termites eating away at the infrastructure of a home. In the case of the aorta, this can lead to a weakening of the structure, ballooning of the aorta (creating an aneurysm) and ultimately, the rupturing of the aneurysm.

Currently the 13th leading cause of death in North America, AAA has an 80 - 90 per cent chance of fatality if the aneurysm ruptures. Ruptured AAA and complications of surgical treatment are responsible for at least 15,000 deaths each year in the United States. However, as autopsies are not routinely performed for people over the age of 60, it is suggested that the actual rate may be as high as 30,000 deaths per year - a mortality rate close to that of prostate and breast cancers. Currently, the only effective treatment interventions involve surgical repair at late stages of disease. There are no treatments for smaller, earlier-stage aneurysms beyond basic monitoring of progression.

"As an aging-related disease, the incidence of AAA is on the rise, yet there are currently no early treatment options beyond basic monitoring of progression and surgery when the risk of rupture is greater than the risk of surgery," says Dr. Granville. "Our latest findings about Granzyme B could lead to the development of pharmaceuticals geared towards slowing or preventing aneurysm progression and rupture - helping those with AAA avoid surgical treatment, and possibly death."