Pigeons Provide Clue to Solving Common Problem in Heart Patients

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Through studying pigeons with genetic heart disease, researchers at Wake Forest University School of Medicine have discovered a clue about why some patients' heart vessels are prone to close back up after angioplasty.

"We identified a regulator of genes that controls the growth of artery smooth muscle cells," said William Wagner, Ph.D., senior researcher. "Learning to modulate the uncontrolled growth of these cells could potentially solve the problem of vessels re-closing after angioplasty."

The work is reported in the August issue of *Experimental and Molecular Pathology*.

Angioplasty uses a balloon-like device to crush the material blocking an artery. But, within three to six months, even if a stent is placed in the artery to keep it open, the vessel becomes re-blocked in about 25 percent to 30 percent of patients. This process, known as restenosis, has been described as "over exuberant" tissue healing and involves the smooth muscle cells. It is not known why this happens in some people and not in others, but many scientists believe that genes are to blame, Wagner said.

The researchers sought to find the answer in two breeds of pigeons – one that is genetically susceptible to heart attacks and heart vessel disease (white carneau) and one (show racer) that is resistant. A major difference between the two breeds is that smooth muscle cells from the heart vessels of white carneau pigeons are prone to uncontrolled growth.

“Understanding the factors that play a role in this increased cell growth may provide an opportunity to target its role in both the initial development of artery blockages and in the restenosis following angioplasty,” said Wagner, a professor of pathology and fellow of the American Heart Association.

Genes “express,” or produce, proteins that are used in building tissue. The process begins with “transcription,” or the copying of a gene’s DNA sequence.

It is not known which genes might control the pigeons’ heart vessel tissue-building process, so Wagner’s group focused on “transcription factors,” which regulate whether a gene is expressed and at what rate. The group’s aim was to see if certain transcription factors might be found in altered amounts in the smooth muscle cells of pigeons that are prone to atherosclerosis.

They screened 54 different transcription factors and found that one, known as STAT4, was 10 times higher in the white carneau pigeons with genetic heart disease. Further testing showed that stimulating STAT4 in smooth muscle cells in the laboratory resulted in a threefold increase in cell growth.

“We were very surprised,” said Wagner. “This is one of the first reports of this factor being found in smooth muscle cells.”

Wagner said the finding has potential for helping scientists solve the problem of restenosis.

“Interfering with these factors and the signaling pathways involving STAT4 may be potentially important in atherosclerosis therapy,” he said. “We may identify ways to reduce or block its effect and slow or stop the unwanted growth of cells.”

He said that by finding the transcription factor, researchers can concentrate on modifying its pathway, and won't need to know which or how many genes it affects.

Source: Wake Forest University Baptist Medical Center