

## All statins are not alike

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A study comparing two powerful cholesterol-lowering drugs has found that both are not equally effective. It was found that in patients taking pravastatin or Pravachol heart disease worsened slowly over 18 months. But the disease was halted in those who took the highest dose of atorvastatin, or Lipitor, another statin. The study was done on 502 patients and it was found that in those taking Atorvastatin the level of low-density lipoproteins (LDL), which carries cholesterol to arteries, dropped from 150 to 79 while those taking pravastatin it reduced to an average level of 110. After 18 months, the atorvastatin patients had no change in the plaque in their arteries, but plaque increased by 2.7 percent in pravastatin patients.

The study assessed the progression of atherosclerosis using a tiny ultrasound camera that was inserted into coronary arteries, allowing researchers to look directly at the growth of plaque. Though the study did not assess patient outcomes like heart attacks and deaths and additional studies will be needed to assess whether different statins would cause disparate reductions in clinical outcomes. But the study did raise a basic question that how low should the cholesterol go and how low is low enough.

Today with modern drugs it is possible to reduce the cholesterol to a very low level, but the impact in terms of costs of drugs, side effects of drugs and prevention of heart attacks is not known. Large studies are under way seeking to determine if more plaque growth means more heart attacks and deaths. Researchers suspect that it is the case, based on their recent understanding of how plaque in artery wall can kill. This opens a possibility of stopping the disease process and preventing most heart attacks from ever happening.

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## New psoriatic arthritis gene discovered

A new gene in psoriatic arthritis has been discovered by a Canadian research team. This offers hope for the development of targeted drug treatments and better diagnosis of the disease. Psoriatic arthritis is associated with psoriasis. It causes skin rashes and produces painful joint inflammation. It is a less common form of arthritis, occurring in 0.5 to 1 percent of the population. Psoriatic arthritis can occur in up to 20 to 30 percent of patients with psoriasis, and can range from being a mild disease to an illness associated with significant morbidity. At present there is no cure for psoriatic arthritis and patients are treated with anti-inflammatory drugs and occasionally drugs that alter their immune system. These therapies primarily focus on treating the symptoms of the condition, mainly because of a lack of understanding concerning the biology of the disease.

Now there is a growing body of evidence that psoriatic arthritis has a strong genetic component and often runs in families. The study resulted in the discovery of the CARD15 gene being associated with the disease. "For most such diseases there are usually multiple genes involved, so having one gene account for 30 percent of cases, which can be helpful for diagnosis. Especially in cases where the psoriasis, which normally occurs with psoriatic arthritis, has not yet developed," said Dr. Proton Rahman, a rheumatologist at Memorial University of Newfoundland, who headed the study. His initial study indicated that patients with CARD15 required more medication and had more surgeries than other people with psoriatic arthritis. His research team is now investigating whether the CARD15 gene is useful for predicting severe cases of psoriatic arthritis. If it does prove to be a "marker" for severe disease, it may lead to treating patients with the gene earlier and more aggressively to prevent their arthritis from progressing.

In a follow-up study to his initial research, Rahman said that his group is now trying to determine the function of the CARD15 gene, which at this stage has only been labeled a "susceptibility" gene – meaning it is not yet proven as a cause of the disease. He suspects the CARD15 gene has a much larger role to play in the development of psoriatic arthritis, and through further research he hopes to reveal the extent of that role. If it is confirmed that CARD15 affects the development of psoriatic arthritis, it could lead to new treatments for the disease. The gene could become a target for molecular-level drug therapies, which are designed to block the disease-influencing activity of specific genes. The Memorial University of Newfoundland has applied for an U.S. patent for the gene. The application focuses on the potential use of the gene to diagnose psoriatic arthritis.

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## Pyramiding insecticidal genes in crops for delayed resistance

Cornell University scientists have found that using crops bearing two different toxin genes in the same plant (pyramiding) can delay resistance development in the target pests. Today much of the biotech research is directed towards developing insect/pest resistant plants. These genetically modified plants containing insecticidal genes have the advantage of surviving the onslaught of insects, which in turn benefits the environment by reducing the use of chemical insecticides. But evolution of resistance to the insecticidal toxins in the target insects could nullify such gains.

Use of two different transgene plants grown sequentially, in mosaics or by mixing genetically engineered seeds, or by pyramiding can reduce the resistance build up in insects. Dr. Jian-Zhou Zhao, department of entomology, Cornell university and colleagues did an evaluation of the efficiency of various methods in delaying insect resistance in a model system and showed that by far the most efficient method is pyramiding. They developed a unique model system consisting of Bt transgenic broccoli plants and the diamondback moth, *Plutella xylostella*. Zhao along with his team conducted a greenhouse study using an artificial population of diamondback moths carrying genes for resistance to the Bt toxins Cry1Ac and Cry1C. They found that after 24 generations of selection, resistance to pyramided two-gene plants was significantly delayed as compared with resistance to single-gene plants deployed in mosaics. It was also observed that Cry1C resistance evolved more slowly than Cry1Ac resistance due to the multigene control of resistance for Cry1C as opposed to single autosomal inheritance for Cry1Ac. These results have implications for the current use of single transgene plants as well as for growing strategies in the future. The details of the study have been carried in the November 10 issue of Nature Biotechnology.

