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Free radicals theory questioned, as is cause of cancer and arthritis

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It is widely believed that free radicals, produced when our bodies fight infection, inflict damage on our tissues. There is a wide range of drugs designed to mop up these excessive amounts of free radicals. The reason they are given is to prevent damage and disease. This theory is now being questioned by researchers at University College London (UK). They think the theory could be wrong. They say their findings could change the way free radicals are treated. Standard theory believes that the molecules (free radicals) cause so much tissue damage that they are major contributory factors in many diseases such as cancer, arthritis and heart disease.

The drugs that mop up these free radicals are called antioxidants. For the last 30 years the pharmaceutical industry has developed antioxidants that stop the production of free radicals and/or mop them up so that they do not damage tissue. Some vitamins attack free radicals – mainly vitamins E and C.

The research team at University College London (UCL) say that their research shows that the evidence on which this theory was first based is wrong. Dr Tony Sega, one of the researchers, said: 'White blood cells produce oxygen free radicals, and the process by which they do so is essential for the efficient killing of microbes. However, people in whom this process is defective are prone to severe, chronic and often fatal infections. This fact has led to the presumption that the oxygen free radicals themselves are highly toxic, and that if they can kill organisms as tough as bacteria and fungi they can also damage human tissues. However, our work shows that the basic theory underlying the toxicity of oxygen radicals is flawed.'

The team found that it was not free radicals that make white blood cells so destructive. It was enzymes which digest foreign invaders. The flow of potassium within the cell triggers the production of these enzymes. They found that when they blocked this flow, the cells could not kill off foreign invaders any more. They used a chemical developed from scorpion venom to block this flow.

This shows, they say, that free radicals are not the toxic particles we all had assumed. The team said that we (the pharmaceutical industry) have spent billions on a red herring.

Dr. Sega said 'Many patients might be using expensive antioxidant drugs based upon completely invalid theories as to their therapeutic potential. All the theories relating to their causation of disease by oxygen free radicals, and the therapeutic value of antioxidants must, at the very least, be re-evaluated.'

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The verdict on oxygen free radicals: Innocent!

A new study in Nature suggests 30 years of research costing billions has been "fundamentally flawed"

BY TONY CRAIG

Decades of research and hundreds of millions of dollars have been wasted chasing the red herring of free radicals' role in disease, according to British scientists. And if they're right, beliefs about why some vitamins are good may also have to be jettisoned.

Oxygen free radicals, the sinister little atoms and molecules accused of causing diseases ranging from cancer to arthritis to arteritis, may not actually be causing any diseases at all.

In fact, according to a team from University College London (UCL), medicine has been barking up the wrong tree on this issue for 30 years. They said that medication based on antioxidants -- a major focus of drug research for decades -- are being developed on the basis of a fundamentally flawed theory.

Instead, the scientists suggested, we need to look at treatments regulating enzymes released from neutrophil leukocytes, the most numerous of the white blood cells.

"White blood cells produce oxygen free radicals, and the process by which they do so is essential for the efficient killing of microbes," said Dr Tony Segal of the Centre for Molecular Medicine within UCL's Department of Medicine, one of the authors of the research. But people in whom this process is defective are prone to severe, chronic and often fatal infections. This fact has led to the presumption that the oxygen free radicals themselves are highly toxic and that if they can kill organisms as tough as bacteria and fungi they can also damage human tissues. Free radicals are believed to be promoted by many agents, including smoking and atmospheric pollutants, and have been implicated in the production of conditions

such as cancer, and many others caused by an initial inflammation in which these neutrophil leukocytes accumulate.

"However," said Dr Segal, "our work shows that the basic theory underlying the toxicity of oxygen radicals is flawed. Tens, if not hundreds, of millions of pounds have been misspent by the pharmaceutical industry in chasing the red herring of the involvement of oxygen free radicals in the causation of many diseases. Many patients might be using expensive antioxidant drugs based on completely invalid theories as to their therapeutic potential," he added. "All the theories relating to their causation of disease by oxygen free radicals, and the therapeutic value of antioxidants must, at the very least, be re-evaluated".

Many vitamins, notably vitamin E and C, as well as other natural substances are regarded as healthy because they attack free radicals. In reality, said Segal, free radicals aren't the agents of destruction when white blood cells attack foreign particles. They found that mice whose white blood cells were altered to be deficient in enzymes called neutrophil-granule proteases, but were able to produce free radicals as usual, were unable to resist staphylococcal and candidal infections.

They discovered that neutrophil-granule proteases are the real agents of destruction in the white blood cells' antibacterial arsenal. Production of these enzymes is triggered by the flow of potassium within the cell. When this flow was blocked, using a chemical derived from scorpion venom, the cells were unable to kill off foreign invaders.

If it's indeed the proteases and not the oxygen free radicals that are responsible for the destruction of bacteria, this removes the main basis for the assumption that free radicals are highly toxic. It also knocks out the theoretical underpinning behind a great deal of drug research, especially in cancer and autoimmune diseases. The research is published in the February 26 issue of the journal *Nature*.

Scientists seek 'radical' rethink: A British research team argues hundreds of millions have been wasted on a free radical goose chase

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Roger Highfield, The Daily Telegraph

Thumb through years of scientific literature on cancer, heart disease and arthritis and you will, according to this story, find endless references to villains known as free radicals, a natural byproduct of the metabolism of cells.

They says that agents that neutralize them -- antioxidants -- have been under intensive study since the '70s.

Many vitamins, notably E and C, as well as other natural substances are regarded as healthy because they mop up free radicals. And fruit and vegetables are thought to be rich in radical scavengers and antioxidants, accounting for their well-known health effects.

The story says that now, however, a team at University College London has called for a radical rethink, warning that hundreds of millions of dollars may have been misspent on a wild radical chase.

Professor Tony Segal, head of UCL's Centre for Molecular Medicine and a fellow of the Royal Society, was cited as writing in the current issue of Nature that scientists have looked at countless diseases under the narrow illumination of the free radical idea, adding that, "Our work shows that the basic theory underlying the toxicity of oxygen radicals is flawed."

The story says that work published in the '60s and '70s showed that white blood cells called neutrophil leukocytes make the free radical superoxide. So it was thought that these white blood cells use oxygen free radicals to deliver a lethal blow to microbes. This in turn led to the belief that if they are capable of destroying organisms as tough as bacteria and fungi they can also damage human tissues.

Professor Segal was quoted as saying, "Everyone then climbed on the bandwagon. It was thought whenever you get inflammation in tissues, you would get the generation of oxygen free radicals and they played a role in damage in atherosclerosis [a disease which clogs arteries], arthritis, bowel disease, everything."

As a corollary, efforts to halt free radical damage or mop them up with antioxidants was thought to be able to treat these conditions.

But Professor Segal was cited as saying that laboratory experiments by his team indicate that the foundations of this belief are wrong because although free radicals are indeed produced, it is the associated pumping of potassium into the space around an invading microbe that triggers the activity of enzymes leading to its destruction.

Future research should focus less on free radicals and much more on how white blood cells release enzymes from a family called the proteases, which digest proteins.