

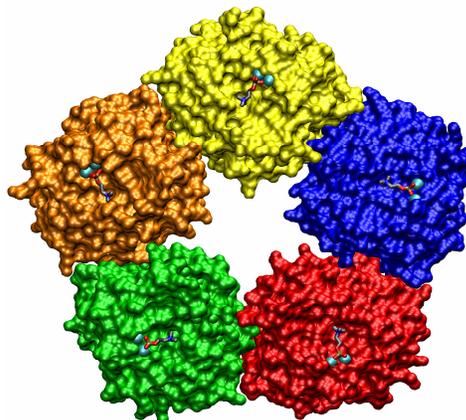
No more Christmas pudding?

Vivienne Baillie Gerritsen

Christmas and the New Year are almost forgotten. But has our body forgotten about the stuffing and the pudding, or the brandy butter and the chocolate truffles? Probably not. The cholesterol has been piling up slowly...and so have the chances of cardiovascular problems. We know that the levels of low-density lipoprotein (LDL) cholesterol in our blood can be an indicator of the potential for heart attacks. However, it looks as though a second molecule – C-reactive protein or CRP – is a far better indicator of cardiovascular disease. A study which has involved accompanying 28'000 women over a period of eight years, and previously 22'000 men over a shorter period, seems to point to a risk of heart attack when the levels of CRP are high – though the levels of cholesterol can be normal or even low.

No one wants to die of a heart attack or stroke, which is why so much energy is put into digging up risk factors that could foretell such a fate. Twenty years ago, over 240 risk factors for coronary heart disease had already been identified and the number never ceases to grow. Yet hundreds of thousands of men and women in our Western society are still dying of heart attacks every year. It is a tricky business to find one sole marker which could predict for sure the likelihood of a heart attack. C-reactive protein¹ may be a solution.

The cohort of 28'000 women was divided into categories depending on age and health, i.e. adjustments to the risk factor were made depending on whether the women smoked, whether they had diabetes, high blood pressure or were under hormone-replacement therapy. The result of the test was that a large portion of cardiovascular accidents occurred in women who had high CRP levels yet low LDL cholesterol levels; high CRP levels and high LDL cholesterol levels were also indicative. What this means is that women, and no doubt men, with LDL cholesterol levels which are below the threshold values for prevention or treatment are in fact not treated and could develop cardiovascular complications in the future.



Pentamer of C-reactive proteins

Courtesy of Fabrice David, SIB Geneva

CRP has been known for years. It makes an appearance in a variety of conditions: infections, inflammatory diseases, allograft rejections, malignant tumours, myocardial infarctions and traumas such as burns and fractures – to name a few. Hence, a high level of CRP is an indication that something is going on. What would this something be? Inflammation. Inflammation results from damage made to vascular connective tissue. CRP is expressed, exclusively, in the liver and is secreted within six hours of an acute inflammatory stimulus. Within eight hours, the level of CRP can double and it reaches a peak after fifty hours. Once

¹ So named because it reacts with the C polysaccharide of *Streptococcus pneumoniae*.

treated – or once the inflammatory stimulus has been checked – the levels of CRP drop rapidly, unless there is a liver impairment. Damaged blood vessels leading to the heart are part of the process which can lead to a heart attack, and in these instances CRP levels are higher than normal.

CRP is a pentamer of five identical and globular subunits, whose three-dimensional structure is reminiscent of a flower with five petals, such as a buttercup. When tissue is damaged CRP is secreted by the liver, and binds to the damaged tissue cell membranes via the phosphocholine head groups of the phospholipids and calcium ions, of which there is one per CRP subunit. In this way, aggregations of CRP are formed on the surface of damaged tissue. Once there, CRP activates host defence mechanisms and stimulates tissue-factor production. It may also have a direct role in inflammation as well as coagulation...two scenarios heart attacks thrive on. Indeed, the cholesterol plaque which lines an artery could break free in the event of inflammation resulting in a blood clot at the site

of rupture. Such a clot could block the normal blood flow in the artery thus setting the scene for a heart attack.

Should a test for CRP replace a test for LDL cholesterol? No. The level of cholesterol is indicative of the amount of plaque which is piling up in your arteries. The level of CRP could give an idea as to the odds of the plaque breaking free. So why not resort to both tests immediately? There is no evidence to date that CRP stimulates inflammation directly. It does perhaps have some predictive value but so far leads to no treatment strategy – unlike the existence of cholesterol in the blood. No one knows whether CRP is simply a marker, a cause or indeed a consequence of coronary heart disease – and this is not good enough to make CRP screening compulsory or even necessary. But the findings remain of particular interest. In the meantime, there is no need to set all our hopes on the identification of risk factors. Human levels of cholesterol and CRP can be kept at bay simply by smoking less, by eating healthily, and by getting regular exercise.

Cross-references to Swiss-Prot

C-reactive protein, *Homo sapiens* (Human): P02741
C-reactive protein, *Cavia porcellus* (Guinea pig) : P49254
C-reactive protein, *Mesocricetus auratus* (Golden hamster) : P49262
C-reactive protein, *Mus musculus* (Mouse) : P14847
C-reactive protein, *Oryctolagus cuniculus* : P02742
C-reactive protein, *Rattus norvegicus* (Rat) : P48199
C-reactive protein, *Xenopus laevis* (African clawed frog) : Q07203

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