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Press information

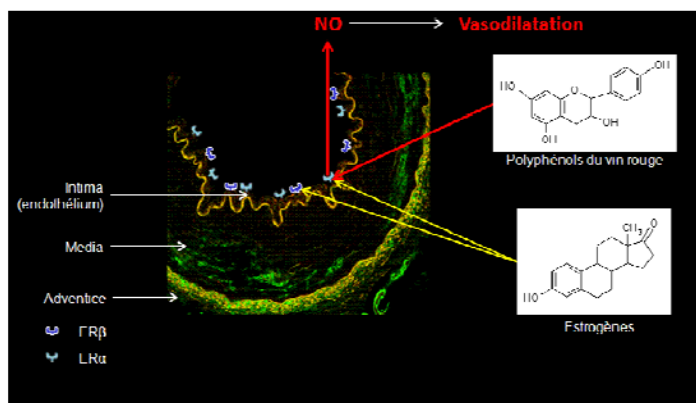
The “French Paradox” revealed

It has long been established by many epidemiological studies that moderate consumption of red wine reduces the risk of cardiovascular disease. The mechanisms behind polyphenol action, however, remained a mystery. A team of research scientists in Angers (Inserm UMR 771-University of Angers research unit “Integrated Neurovascular Biology”) has identified the alpha subtype of the oestrogen receptor as playing a key role in the transduction of wine polyphenols, thus providing an explanation for what has become known as the “French Paradox”. Their results have been published in the journal *PLoS ONE*.

Moderate consumption of wine – red wine in particular – is associated with reduced risk of cardiovascular disease. Until now, this strong suggestion was based solely on the results of an admittedly large number of epidemiological studies. Nothing was known, however, about the mechanism involved or the molecular target responsible for the protective effects that red wine has on the cardiovascular system. This premise still needed to be scientifically demonstrated.

Nonetheless, various studies, especially those conducted by the Angers team, have gradually led to the identification of a vasodilatory action of wine polyphenols through the production of nitric oxide (NO), also known as nitrogen monoxide, by endothelial cells.

For the latest study, the researchers used molecular biology techniques to determine the action mechanism of the polyphenols concerned. They felt that the oestrogen receptor was probably involved, since activation of the oestrogen receptor alpha subtype (ER α) is known to stimulate the NO pathway in endothelial cells.



Ramaroson Andriantsitohaina and his team therefore began with the assumption that an ER α activating compound would be enough to activate the NO pathway in endothelial cells and explain the reduced risk of cardiovascular disease observed.

Diagram illustrating the effects of red wine polyphenols on the endothelium of the vessel wall
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Experiments showed that while red wine polyphenols – especially delphinidin – led to epithelium-dependent vascular relaxation in the arteries of wild mice, they failed to induce

any vasodilatory effect dependent on the vascular epithelium in the arteries of ER α receptor-deficient mice.

This shows that the vasodilatory effect of polyphenols due to NO production by endothelial cells relies on the presence of the ER α receptor.

Furthermore, the use of an oestrogen-receptor antagonist known as fulvestrant, or an siRNA¹ that specifically targets ER α , prevents both NO production and the activation of the molecular transduction pathways responsible for this molecule's formation in human endothelial cells.

The team was able to confirm the direct interaction of delphinidin on the ER α receptor activation site by means of molecular modelling and specific linkage studies.

The polyphenol pharmacology results all provide a scientific basis for the assumptions made during epidemiological studies as to the protective effects on the cardiovascular system associated with moderate consumption of wine and other fruit and vegetables. This action is probably due to the ability of these products to activate the ER α oestrogen receptor.

For further information:

Source:

“ *Estrogen Receptor Alpha as a Key Target of Red Wine Polyphenols Action on the Endothelium* ”

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http://www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0008554?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+plosone%2FPLoSONE+%28PLoS+ONE+Alerts%3A+New+Articles%29

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¹ siRNA: small interfering RNA that can bind specifically to a messenger RNA sequence and thus inhibit gene expression by cleaving this RNA.