**MOLECULAR MECHANISMS UNDERLYING THE ANTI-ATHEROGENIC ACTIONS OF NUTRACEUTICALS**

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**Objective:**To delineate the molecular mechanisms underlying the anti-atherogenic actions of nutraceuticals using *in vitro* and *in vivo* approaches.

**Background:**Atherosclerosisand its complications are responsible for most global deaths. Current therapies against atherosclerosis are associated with considerable residual risk for cardiovascular disease together with various side effects. In addition, there have been disappointing outcomes on several pharmaceutical agents against promising targets identified from various drug discovery programs. Nutraceuticals represent promising alternatives for the prevention and treatment of atherosclerosis. However, the molecular mechanisms underlying the protective actions of nutraceuticals in atherosclerosis are poorly understood. This aspect was therefore investigated with particular focus on macrophages, which are involved in all the different stages of the disease.

**Methods:**A combination of cell lines and primary cultures together with C57BL/6 and LDL receptor deficient mice fed a high fat diet were used as model systems. Gene expression was monitored by RT-qPCR and atherosclerosis profiler arrays. The plasma levels of LDL/VLDL, ROS, HDL and triacylglycerol were determined using kits from Abcam. Cell based assays included: monocytic migration; ROS production; phagocytosis; uptake of fluorescently labelled modified LDL; cholesterol efflux; and activation of the inflammasome.

**Results:**The actions of several nutraceuticals were investigated, including polyunsaturated fatty acids, flavanols, polyphenols and probiotics. These nutraceuticals regulated several cellular processes associated with the progression of atherosclerosis, including monocytic migration, ROS production, inflammasome activation, pro-inflammatory gene expression, uptake of modified LDL, macropinocytosis and cholesterol efflux. In addition, the levels of several atherosclerosis-associated markers were attenuated by the nutraceuticals *in vivo*. The potential underlying mechanisms are currently being determined and will be presented.

**Conclusion:**The studies provide new insights into the anti-atherogenic actions of nutraceuticals.