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### ► To cite this version:

Laurent-Emmanuel Monfoulet, Sylvie Mercier, Desislava Abadjieva, Elena Stoyanova, Liga Lauberte, et al.. Oregonin from *Alnus incana* preserves from atherosclerosis by preventing endothelial dysfunction through nutrigenomic and epigenetic regulations. 10th International Conference on Polyphenols and Health, Apr 2022, Londres, United Kingdom. hal-03687784

**HAL Id: hal-03687784**

**<https://hal.inrae.fr/hal-03687784>**

Submitted on 3 Jun 2022

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## Oregonin from *Alnus incana* preserves from atherosclerosis by preventing endothelial dysfunction through nutrigenomic and epigenetic regulations

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**Background:** Scientific evidence from experimental to clinical studies support a beneficial effect of polyphenols on cardiometabolic health. Oregonin is a polyphenol present in different parts of plants from genus *Alnus* that exhibits anti-inflammatory and anti-adipogenic properties. However, the underlying mechanisms of its effects are still not known. This research aimed to analyse pathways of oregonin effects on endothelial cells and its ability to preserve endothelial function under an inflammatory stress.

**Methods:** Human endothelial cells (HUVECs) were exposed to oregonin extract from bark of *Alnus incana* or control medium for 48 hours and then stimulated with tumor necrosis factor alpha (TNF- $\alpha$ ) for 4 hours. Expression of adhesion (ICAM-1, VCAM-1) as well as monocyte adhesion were investigated. Methylation specific PCR for analysing ICAM-1 and VCAM1 methylation indexes was applied. The expression of total DNA-methyltransferase-1 (DNMT1), and mitochondrial DNA-methyltransferase-1 (mtDNMT1) and mitochondrial transcription factor (TFAM) by RT-PCR was analysed.

**Results:** The increased expression of vCAM-1 was inhibited by 50% with a pre-incubation of HUVECs with 7.5  $\mu$ M oregonin while iCAM-1 expression did not change. Oregonin exposition significantly decreased the adhesion of monocytes to endothelial cell surface. A strong, and negatively dependent to oregonin concentration, correlation between monocyte adhesion and the expression of CAM proteins was observed. No differences were defined between methylation indexes of iCAM-1 and vCAM-1 in control and oregonin-exposed cells despite a significant decrease of DNMT1 in oregonin pre-incubated cells. The expression of DNMT1 was not changed after TNF- $\alpha$  cell activation. However, a significant decrease of TFAM and mtDNMT1 mRNA expression was established in oregonin exposed cells.

**Conclusion:** All together these results show the ability of oregonin to counteract endothelial inflammation by alleviating pro-inflammatory genes expression and monocyte adhesion, by and to regulating of DNMT1 and mtDNMT1 expression make this polyphenol an interesting candidate to prevent cell-specific epigenetic change in atherosclerosis.

The author(s) would like to acknowledge networking support by the COST Action FA 1403 POSITIVE (Interindividual variation in response to consumption of plant food bioactives and determinants involved), supported by COST (European Cooperation in Science and Technology) and the European Twinning Project PhenolAcTwin coordinated by the Tubitak Institute (Turkey) for supporting the attendance of L-Em. Monfoulet at ICPH 2022.