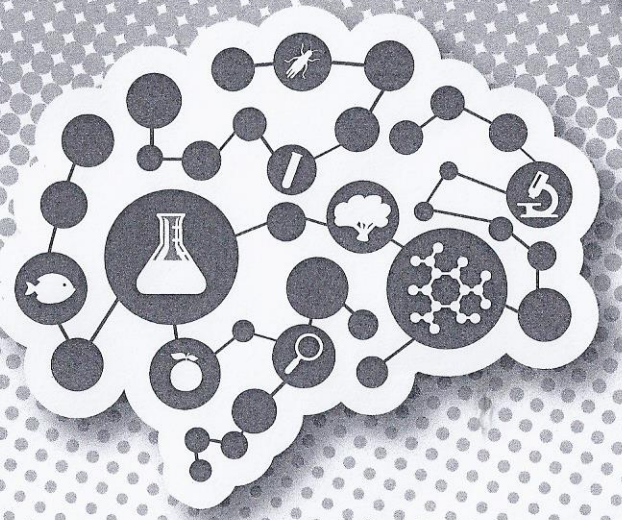
FROM DATA



TO KNOWLEDGE

5th International Conference on Foodomics

10-12 January 2018
Cesena-Italy

Abstract Book

4th Session

THE FOODOMICS APPROACH TO FOOD AND HEALTH

Multidisciplinary strategy to investigate new lupin peptide inhibitors of PCSK9 activity as useful approach for cardiovascular disease risk reduction

Carmen Lammi, Giovanni Grazioso, Giulio Vistoli, Gilda Aiello, Anna Arnoldi.
Department of Pharmaceutical Sciences, University of Milan, via Mangiagalli 25, 20133 Milan, Italy

Proprotein convertase subtilisin/kexin type 9 (PCSK9) has been recently identified as a new target for hypercholesterolemia treatment. The main role exploited by PCSK9 is the degradation of LDL receptor (LDLR) protein, leading to an increase of plasma cholesterol level. In this context, inhibition of PCSK9 is considered a good strategy for the treatment of hypercholesterolemia [1]. Recently, our research was focused mainly on lupin peptides, since in a recent paper it was shown that in hypercholesterolemic subjects, who had consumed dietary bars containing lupin protein for a month, the total cholesterol decrease was accompanied by a parallel decrement of circulating PCSK9 (-8.5%) versus the control group that had consumed casein bars [2]. For this reason, a multidisciplinary investigation was carried out in order to screen and develop new peptides, deriving from lupin protein hydrolysis and absorbable at intestinal level, which are able to modulate the PCSK9 target with a dual mechanism of action. More in details, lupin peptides reduce PCSK9 production and secretion through a decrease of HNF1-alpha in HepG2 cells and an absorbed lupin peptide, LILPKHSDAD (**P5**), is able to inhibit the protein-protein interaction (PPI) between PCSK9 and the LDLR with an IC_{50} value equal to 1.6±0.33 μM. In this context, a molecular docking analysis has allowed us to simulate the effects induced by **P5** on the binding of PCSK9 to the LDLR (Figure 1). In fact, the superimposition of **P5** on the EGF-A domain of LDLR co-crystallized with PCSK9 (PDB code 4NE9) showed a good overlapping, justifying the **P5** inhibitory property.

For the first time, we have provided evidences that lupin peptides may modulate PCSK9, contributing to explain the beneficial effects observed in clinical studies and opening a new area of investigation on plant proteins.

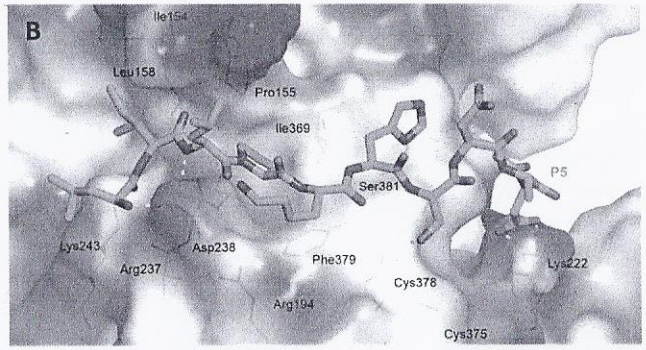


Figure 1. Simulation of the inhibitory binding of PCSK9 induced by P5.

References

[1] Horton JD, Cohen JC, Hobbs HH. Molecular biology of PCSK9: its role in LDL metabolism. Trends Biochem Sci. 2007;32(2):71-7.

[2] Lammi, 2016, Lupin protein exerts cholesterol-lowering effects targeting PCSK9: from clinical evidences to elucidation of the in vitro molecular mechanism using HepG2 cells J Funct Foods, 2016;(23):230-40

From metabolites to gene expression: fusing the postprandial response to dairy intake

Burton KJ, [1] Pimentel G,[1] Münger L,[1] Zangger N,[3] Portmann R,[1] Delorenzi M,[3] Pralong FP,[2] Vionnet N,[2] Vergères G.[1]

1 Federal Department of Economic Affairs, Education and Research EAER, Agroscope, Berne, Switzerland. 2 Service of Endocrinology, Diabetes and Metabolism, Lausanne University Hospital, 1011 Lausanne, Switzerland. 3 SIB Swiss Institute of Bioinformatics, Lausanne, Switzerland.

The dynamic postprandial response represents a unique opportunity to explore the metabolomic signatures associated with different foods. Blood transcriptomics can complement metabolomic analysis by revealing the impact of changing metabolite concentrations on the gene expression of circulating blood cells. Network analysis can be used to combine such complex datasets to support understanding of the overall effect of the food on the organism. To explore the postprandial effects of dairy products, we carried out a randomized cross-over study in ten healthy subjects to compare milk (600 mL), cheese (100 g) and non-dairy soy drink (600 mL). Blood sampling was completed during six hour postprandial tests to assess the serum metabolome (LC-MS) and the whole blood