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## VEGF-A, a potential biomarker for systems medicine

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Vascular endothelial growth factor-A (VEGF-A) is implicated in angiogenesis, lymphangiogenesis, vascular permeability and haematopoiesis. It is associated with numerous pathologies including cardio-vascular diseases and several types of cancer. We specifically developed an integrative systems biology strategy for clinical improvement of this biomarker.


A high heritability of this trait, 60% was estimated in the STANISLAS cohort giving us the needed arguments to continue for a deep characterization of the genetic component of VEGF-A levels. Therefore, we searched, by a Genome Wide Association Study (GWAS), the VEGF-A genetic variants and the inter-connexions of these biomarkers with other disease-associated molecules in healthy populations. Functional transcriptomic analyses were performed in peripheral blood mononuclear cells (PBMCs). Four polymorphisms (rs6921438,

rs4416670, rs6993770, rs10738760) explaining ~50% of VEGF-A heritability were identified. These variants, directly or via gene x environment interactions had significant effects on HDL, LDL, TNF-a, IL-6, E selectin and ICAM-1 plasma levels. SNP rs6993770 was shown to increase VEGF121 mRNA levels and rs4416670 was associated with L-selectin expression.

Recently, thanks to a meta-GWAS, we identified 6 additional rs further explaining VEGF-A levels variability and ongoing investigations focus on clinical implementation of the 'omics' determinants of this biomarker.

Our integrative strategy illustrates an improved exemple to be applied for every biomarker with high heritability levels, consequently with potential interest in personalised medicine

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