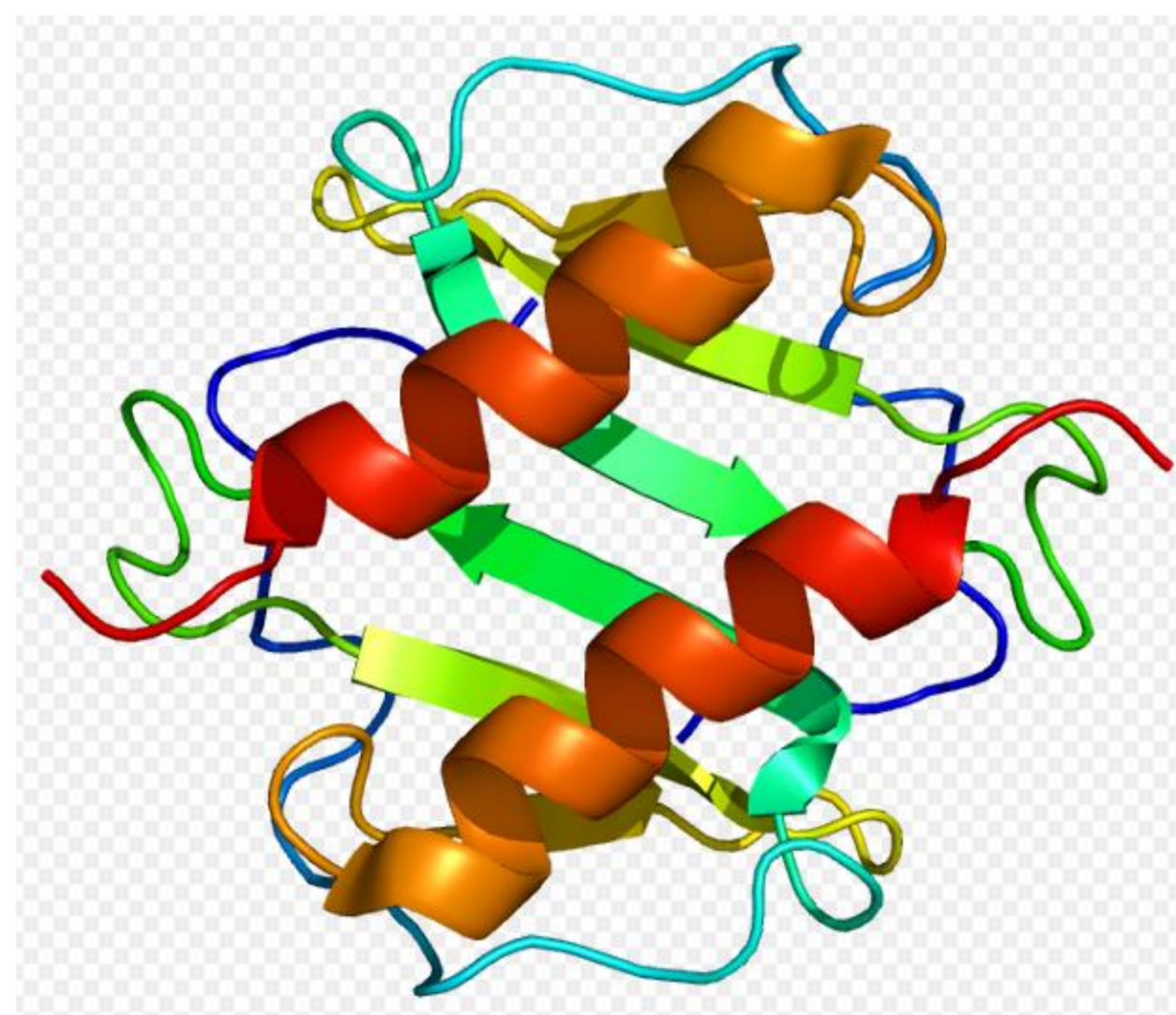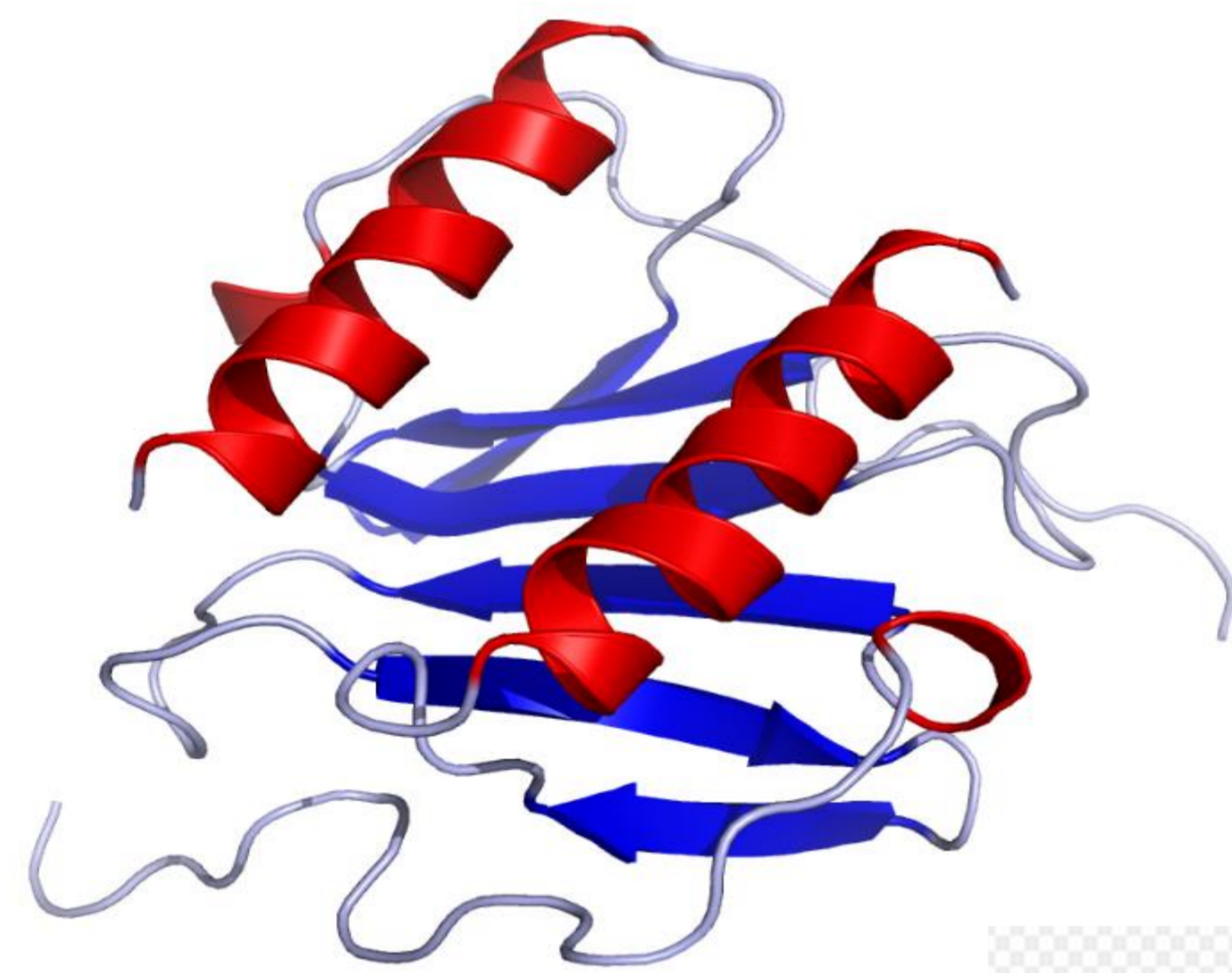# Chemokines and carotid intima-media thickness in a European population at high risk for cardiovascular events: Results from the IMPROVE study

Ilais Moreno , Anders Malarstig , Rona J. Strawbridge, Damiano Baldassarre , Fabrizio Veglia, Karin Leander, Angela Silveira, Rainer Rauramaa, Andries J. Smit , Philippe Giral , Elmo Mannarino, Elena Tremoli , Steve E. Humphries, Anders Lindén, Anders Hamsten, Ulf de Faire, Bruna Gigante.

CONCLUSIONS

The chemokine IL-8, but not GRO-α, is associated with baseline c-IMT in men at high risk of CV events. Furthermore, there is a European north-to-south gradient in chemokine levels.

New studies are warranted to disentangle potential differences between IL-8 and CV risk across sexes.

Introduction

Experimental studies indicate that two archetype chemokines circulating in the blood, IL-8 and GRO-α, are critical for atherogenesis. However, their association with measures of subclinical atherosclerosis has not been investigated previously.

Aim

To characterized the association between circulating IL-8 and GRO-α protein with the carotid artery intima media thickness (c-IMT) in a large prospective European multicenter study: *the c-IMT and c-IMT Progression as Predictors of Vascular Events in a High Risk European Population (IMPROVE) study*.

Methods

IMPROVE study participants (n=3,703), recruited in 5 European Countries (Sweden, Finland, the Netherlands, France and Italy), had at least three cardiovascular (CV) risk factors but not prevalent CV diseases. C-IMT (mm) (IMT maximum, IMT mean and IMT mean-maximum) was measured at baseline. Each measurement represent the average of 8 (4 left & 4 right) carotid segments. Concentrations of IL-8 and GRO-α proteins were quantified in plasma from 3,452 participants (women, n=1,784; men, n=1,668.

RESULTS

	Mean_8Max_IMT_dx_sx		Max_IMT_dx_sx		Mean_Imt_dx_sx	
	n	β 95 % CI	n	β 95 % CI	n	β 95 % CI
MEN						
Crude	1668	2.6×10^{-4} $1.0 \times 10^{-4} - 4.2 \times 10^{-4}$	1666	8.3×10^{-4} $3.7 \times 10^{-4} - 1.3 \times 10^{-3}$	1666	1.1×10^{-4} $8.4 \times 10^{-4} - 1.3 \times 10^{-2}$
Model 1	1637	1.9×10^{-4} $1.3 \times 10^{-4} - 2.5 \times 10^{-4}$	1635	6.4×10^{-4} $4.7 \times 10^{-4} - 8.1 \times 10^{-4}$	1635	1.0×10^{-4} $6.0 \times 10^{-5} - 1.4 \times 10^{-4}$
Model 2	1637	1.7×10^{-4} $1.3 \times 10^{-4} - 2.2 \times 10^{-4}$	1635	6.5×10^{-4} $4.8 \times 10^{-4} - 8.2 \times 10^{-4}$	1635	1.0×10^{-4} $6.5 \times 10^{-5} - 1.4 \times 10^{-4}$
WOMEN						
Crude	1784	1.7×10^{-4} $-6.9 \times 10^{-5} - 4.1 \times 10^{-4}$	1784	8.4×10^{-4} $-6.0 \times 10^{-5} - 1.7 \times 10^{-3}$	1784	1.2×10^{-4} $-2.9 \times 10^{-5} - 2.7 \times 10^{-4}$
Model 1	1757	8.8×10^{-5} $-1.6 \times 10^{-4} - 3.4 \times 10^{-4}$	1757	6.8×10^{-4} $-1.1 \times 10^{-4} - 1.5 \times 10^{-3}$	1757	6.4×10^{-5} $-1.2 \times 10^{-4} - 2.5 \times 10^{-4}$
Model 2	1757	1.0×10^{-4} $-1.5 \times 10^{-4} - 3.5 \times 10^{-4}$	1757	6.3×10^{-4} $-2.5 \times 10^{-4} - 1.5 \times 10^{-3}$	1757	-2.1×10^{-5} $-1.8 \times 10^{-4} - 1.4 \times 10^{-4}$
ALL						
Crude	3452	1.9×10^{-4} $1.2 \times 10^{-4} - 2.5 \times 10^{-4}$	3452	8.4×10^{-4} $4.9 \times 10^{-4} - 1.2 \times 10^{-3}$	3450	1.1×10^{-4} $7.1 \times 10^{-5} - 1.6 \times 10^{-4}$
Model 1	3392	1.9×10^{-4} $1.2 \times 10^{-4} - 2.7 \times 10^{-4}$	3392	6.6×10^{-4} $4.8 \times 10^{-4} - 8.6 \times 10^{-4}$	3392	1.1×10^{-4} $6.5 \times 10^{-5} - 1.6 \times 10^{-4}$
Model 2	3392	1.9×10^{-4} $1.3 \times 10^{-4} - 2.6 \times 10^{-4}$	3392	6.7×10^{-4} $4.5 \times 10^{-4} - 8.8 \times 10^{-4}$	3392	1.1×10^{-4} $2.6 \times 10^{-5} - 1.9 \times 10^{-4}$

Crude: adjusted by age. Model 1: crude + body mass index, hypertension, diabetes, current smokers and hypercholesterolemia.

Model 2: Model 1 + latitude.

We evaluated the association, expressed as beta coefficients and 95% confidence intervals (CI), between chemokines and baseline c-IMT using median regression. No association was observed between GRO-α and baseline IMT measurements.

Interleukin 8 (CXCL8) and GRO-α (CXCL1) belong to the sub-family of chemokines

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