Evidence of a causal association between C-reactive protein and adiposity in women.

[1]Bochud M., [1]Marquant F., [1]Marques-Vidal P.-M., [2]Vollenweider P., [3]Beckmann J., [4]Mooser V., [1]Paccaud F., [1]Rousson V.

IUMSP - CHUV[1], Internal Medicine - CHUV[2], Medical Genetics - CHUV[3], GlaxoSmithKline - USA[4]

Context: The link between C-reactive protein (CRP) and adiposity deserves to be further explored considering the diabetogenic role of CRP.

Objective: We explored the potential causal role of CRP on adiposity markers.

Design: We used a Mendelian randomization approach with the *CRP* and *LEPR* genes as instrumental variables in a cross-sectional Caucasian population-based study comprising 2526 men and 2836 women. Adiposity was measured using body mass index (BMI), fat and lean mass estimated by bioelectrical impedance, and waist circumference.

Results: Log-transformed CRP explained by the *rs7553007* SNP tagging the *CRP* gene was significantly associated with BMI (regression coefficient: 1.22 [0.18;2.25], P=0.02) and fat mass (2.67 [0.65;4.68], P=0.01), but not with lean mass in women, whereas no association was found in men. Log-transformed *CRP* explained by the *rs1805096 LEPR* SNP, located within exon 20, tended to be associated with BMI (0.70[-0.17;1.57], P=0.11) and fat mass (1.35[-0.32;3.02], P=0.11) in women, but not in men. The combined *CRP-LEPR* instrument explained 2.24% and 0.77% of CRP variance in women and in men, respectively. Log-transformed CRP explained by this combined instrument was significantly associated with BMI (0.98 [0.32 ;1.63], P=0.004), fat mass (2.07 [0.79 ;3.34], P=0.001) and waist (2.09 [0.39 ;3.78], P=0.01) in women, but not in men.

Conclusion: Our results suggest that CRP is causally positively related to BMI in women, and that this is mainly due to fat mass. The similar results observed for the *LEPR* gene suggest that leptin may play a key role in the association between CRP and adiposity.

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Couverture : Yannick Krempp, Département de Biologie Cellulaire et de Morphologie – UNIL

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Manuela Weier and Henrik Kaessmann of the Centre Intégratif de Génomique - CIG
and Jérôme Thomas of the Lausanne DNA Array Facility, Centre Intégratif de Génomique - CIG

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