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Immune activation, smoking, and vaccine response

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Understanding the factors that fuels inter-individual variability in vaccine response is important to improve vaccine efficiency. Here we tested the hypothesis that chronic immune activation might impair vaccine response. To this aim, we studied whether immune activation observed in HIV-1-infected patients [1] might reduce hepatitis B virus (HBV) vaccine efficiency.

We chose to quantify in peripheral blood soluble CD40L to evaluate platelet, endothelial and T cell activation, IgG, IgA, and IgM as a sign of B cell activation, soluble CD14 and CD163 to measure macrophage/monocyte activity, interleukin-6, soluble TNF receptor I (sTNFRI), and interferon gamma-induced protein 10 to estimate inflammation. We analyzed these markers before vaccination in 124 HIV-1-infected adults who received 3 intramuscular injections of GenHevac B Pasteur 20 µg in the course of ANRS HB03 trial [2]. Eighty-four (68%) patients were responders i.e. with anti-hepatitis B surface antigen (HBs) titers higher or equal to 10 mIU/mL one month after the third vaccine injection.

Among the tested markers, sTNFRI was the only one higher in non-responders than in responders (3.27±1.58 ng/mL and 2.50±1.13 ng/mL, p=0.016, Figure 1). The anti-HBs titers at week 28 tended to be inversely correlated with baseline sTNFRI levels (r=-0.168, p=0.061). A multivariate analysis adjusted on all the factors previously shown to be predictive (female sex, lower age, no active smoking, higher CD4 count and undetectable HIV-1 RNA at baseline [2]) and on nadir CD4 count confirmed the independent link between sTNFRI and vaccine response (odds-ratio (OR) 0.65 [95% CI 0.46-0.93], p = 0.019). Smoking did not remain associated with vaccine response when sTNFRI was introduced in the model (OR for smoking 0.46 [0.20-1.04]; p=0.06; OR for sTNFR1 0.67 [0.49-0.91], p=0.01), suggesting that the link between smoking and impaired response is mediated by immune activation. sTNFRI levels were higher in smokers than in non-smokers (3.10±1.36 ng/mL and 2.57±1.29 ng/mL,
p=0.028, Figure 1). Moreover, the association between sTNFRI levels and smoking remained significant after adjustment on age, sex, CD4 count, nadir CD4 T count and undetectable HIV RNA (p=0.037 in a multiple linear regression model). We show here that sTNFRI, a marker of inflammation, is predictive for vaccine response. Our data are in line with the observation that response to influenza vaccine is correlated with plasma TNFα levels [3]. This might open the way in the future for tailored vaccination adapted to each patient’s immune activation level. Of note, in clinical settings of long-lasting inflammation as chronic infections, autoimmune diseases, and aging, poor vaccine immunogenicity is often observed. Another finding of our work is the link between smoking and inflammation. This concurs with the link reported between T cell activation and tobacco smoking [4]. It raises the interesting hypothesis that tobacco might be pathogenic via immune activation.
References


**Figure legend.** Mean levels of sTNFRI in responders and non-responders to HBV vaccination and in smoking and non-smoking patients.
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