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Immune activation, smoking, and vaccine response

Mehwish Younas¹, Fabrice Carrat^{2,3}, Sanae Finge⁴, Corinne Desaint^{5,6}, Odile Launay^{§ 5,6},
Pierre Corbeau^{§ 1,4,7}, for the ANRS HB03 VIH VAC-B Trial Group*

¹Institute of Human Genetics, CNRS UPR1142, Montpellier, France; ²Sorbonne Universités, UPMC Univ Paris 06, INSERM, Institut Pierre Louis d'épidémiologie et de Santé Publique (IPLESP UMRS 1136), Paris, France; ³Assistance Publique Hôpitaux de Paris (AP-HP), Hôpital Saint-Antoine, Public Health Unit, Paris France; ⁴University Hospital, Immunology Department, Nîmes, France; ⁵Université Paris Descartes, Sorbonne Paris Cité; AP-HP, CIC Cochin Pasteur, Hôpital Cochin, Paris, France ; ⁶Inserm, CIC 1417, Paris, F-CRIN, I – REIVAC, France; ⁷Montpellier University, Montpellier; France

* Study group members are listed after the text

Address correspondence to:

Professor Pierre Corbeau, Institut de Génétique Humaine CNRS UPR1142, 141 rue de la Cardonille, 34396 Montpellier cedex 5, France, Tel: +33 4 34 35 99 32, Fax: +33 4 34 35 99 01, E-mail: pierre.corbeau@igh.cnrs.fr

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§ OL and PC contributed equally to this work

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 TNF α 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.

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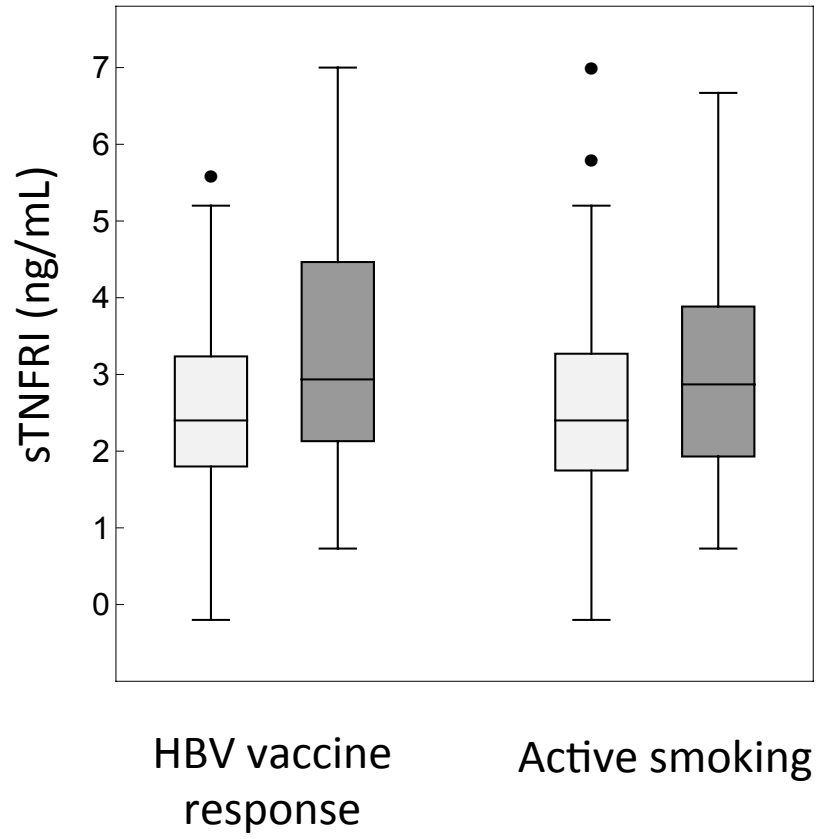


Figure legend. Mean levels of sTNFRI in responders and non-responders to HBV vaccination and in smoking and non-smoking patients.

ANRS HB03 VIH VAC-B Study group:

Anne Frésard (Hôpital Bellevue, Saint-Etienne); Caroline Lascoux (Hôpital Saint-Louis, Paris); Olivier Lortholary (Hôpital Necker-Enfants Malades, Paris); Elina Teicher (Hôpital Bicêtre, Le Kremlin-Bicêtre); Agathe Rami (Hôpital Lariboisière, Paris); Alain Lafeuillade (Hôpital Font-Pré, Toulon); Pierre de Truchis (Hôpital Raymond Poincaré, Garches); Vincent Jeantils (Hôpital Jean Verdier, Bondy); Daniel Vittecoq (Hôpital Paul Brousse, Villejuif); Laurence Slama, Gilles Pialoux (Hôpital Tenon, Paris); Sophie Abgrall (Hôpital Avicenne, Avicenne); Yves Levy (Hôpital Henri Mondor, Créteil); Marc-Antoine Valantin (Hôpital Pitié-Salpêtrière, Paris); Pierre-Marie Girard (Hôpital Saint-Antoine, AP-HPH, Paris); Jean-Michel Molina (Hôpital St-Louis, Paris); Didier Neau (Hôpital Pellegrin, Bordeaux); Patrick Miaillhes (Hôpital Hôtel-Dieu, Lyon); Isabelle Poizot-Martin (Hôpital Ste Marguerite, Marseille); Sophie Matheron (Hôpital Bichat, Paris); Jacques Reynes (Hôpital Gui de Chauliac, Montpellier); Bénédicte Bonnet (Hôpital Hôtel-Dieu, Nantes); Eric Rosenthal (Hôpital de l'Archet, Nice); David Rey, Patricia Fischer (Hôpital Civil, Strasbourg); Lise Cuzin (Hôpital Purpan, Toulouse); Renaud Verdon (Hôpital Côte de Nacre, Caen); Lionel Piroth (Hôpital du Bocage, Dijon); Pascale Leclercq (Hôpital A. Michallon, Grenoble); Faiza Ajana (Hôpital Gustave Dron, Tourcoing); Thierry May (Hôpital Brabois, Nancy); Agnès Lefort (Hôpital Beaujon, Clichy); Brigitte Elharrar (Centre Hospitalier Intercommunal, Créteil); Odile Launay (Hôpital Cochin, Paris); Jean-Paul Viard (Hôpital Hôtel-Dieu, Paris).