

This clinical study reports that blood levels of the pro-inflammatory mediator platelet-activating factor (PAF) did not change in colorectal cancer patients. In contrast, plasma levels of two enzymatic activities, one implicated in PAF production (i.e. phospholipase A₂) and one in PAF degradation (i.e. PAF acetylhydrolase activity) were significantly elevated.

Key words: Platelet-activating factor, Phospholipase A₂, Acetylhydrolase activity, Colorectal cancer

Elevated plasma phospholipase A₂ and platelet-activating factor acetylhydrolase activity in colorectal cancer

Yves Denizot^{1,CA}, Véronique Truffinet¹,
Stéphane Bouvier², Alain Gainant²,
Pierre Cubertafond² and Muriel Mathonnet²

¹UMR CNRS 6101, Laboratoire d'immunologie, Faculté de Médecine, 2 rue Dr. Marcland, 87025 Limoges, France and ²Service de Chirurgie Digestive, Endocrinienne et Générale, 2 avenue M. Luther King, 87025 Limoges, France

^{CA}Corresponding author
Tel: +33 5 55 43 58 96
Fax: +33 5 55 43 58 97
E-mail: yves.denizot@unilim.fr

Platelet-activating factor (PAF) is a lipidic molecule that sparks a wide range of immunoregulatory actions.¹ PAF derives from membrane precursors, 1-alkyl-2-acyl-glycero-3-phosphocholine. The action of a phospholipase A₂ (PLA₂)-dependent process generates the lyso-PAF precursor, and the subsequent acetylation of the lyso compound results in the PAF molecule. PAF concentrations are regulated by an acetylhydrolase activity (AHA) found both in plasma and in serum.¹ Despite no evident role in lung cancer, its potential role in breast cancer is suggested.² Recently elevated levels of AHA and PLA₂ have been found in tumour tissues of colorectal cancer patients.³ PAF can generate biological responses detectable at levels of 10 fM. It is thus of evidence that regulating PAF levels is important since elevated or decreased levels of PAF might result in pathological effects. The present study was designed to determine whether investigating circulating levels of PAF, soluble PLA₂, and AHA might be of clinical interest for colorectal cancer patients.

This study followed the rules edited by the French National Ethics Committee, and the Local Ethics Committee has approved them. This was a prospective study including 29 patients with a newly diagnosed and histologically confirmed primary colorectal cancer. There were 18 men and 11 women with a median age of 76 years (range, 45–95 years). No patient received chemotherapy or irradiation before

surgery. Blood samples were harvested at the time surgery for PAF, PLA₂ and AHA determinations. Blood samples from 20 healthy subjects (14 men and six women; mean age, 75 years) were investigated as controls. Two millilitres of blood were ethanol extracted (80% final), purified, and assayed for PAF activity by aggregation of washed rabbit platelets.³ Plasma AHA levels (expressed as nanomoles of PAF degraded per minute per millilitre of plasma) was determined by investing the degradation of [³H]-labelled-PAF.³ Soluble PLA₂ plasma levels (expressed as units per millilitre) were assessed by enzyme-linked immunosorbent assay according to the manufacturer's recommendations (R&D Systems Europe, Ltd, Oxon, UK).³ Results are presented as the mean \pm standard error of the mean, and were subjected to a non-parametric Mann–Whitney U-test. $p < 0.05$ was considered significant.

As shown in Fig. 1, no significant difference ($p = 0.8$) was documented between blood PAF levels of colorectal patients (9.6 ± 2.1 pg/ml, $n = 29$) and healthy controls (10.4 ± 2.4 pg/ml, $n = 20$). In contrast, plasma AHA (the PAF catabolic enzyme) was significantly ($p = 0.0004$) enhanced in patients (65.3 ± 4.8 nmol/ml/min, $n = 29$) as compared with controls (43.8 ± 3.4 nmol/ml/min, $n = 20$). Their plasma soluble PLA₂ (the key enzyme for PAF biosynthesis) levels were also significantly ($p = 0.03$)

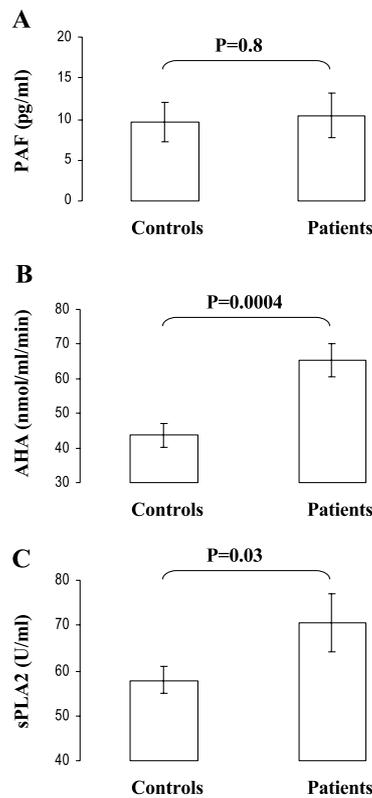


FIG. 1. Blood PAF (A), plasma AHA (B) and soluble PLA₂ (C) levels in colorectal cancer patients. Mean \pm standard error of the mean of 29 colorectal cancer patients and 20 healthy controls. Differences between groups were assessed using the Mann–Whitney U-test.

elevated (70.6 ± 6.5 U/ml versus 57.9 ± 3.1 U/ml for patients and controls, respectively).

Our results indicate that blood PAF amounts of colorectal cancer patients were not different at the time of surgery from those of healthy individuals. Since blood PAF has a half-life of few minutes *in vivo*, its circulating levels are reflective of the balance between its production and degradation. Two enzymatic activities, one implicated in PAF production (i.e. soluble PLA₂) and one in PAF degradation (i.e. AHA), were significantly elevated in colorectal cancer patients as compared with healthy individuals.

Previous data have reported elevated circulating PLA₂ levels in patients with advanced cancer.⁴ However, the plasma PLA₂ increase is modest and difficult to interpret since this enzyme is also elevated in a wide range of inflammatory diseases.⁵ Similarly to PLA₂, plasma AHA levels are elevated in colorectal cancer patients. However, the AHA increase is modest and sheds little light on its role in colorectal cancer patients since this enzyme is also elevated in numerous non-cancer diseases.¹ Whatever the origin of these elevated plasma PLA₂ and AHA levels, it is of evidence that assessment of their plasma concentrations cannot be used as a diagnostic and/or prognostic marker for colorectal cancer patients. In conclusion, and indirectly suggesting that PAF might play a role in colorectal cancer, plasma soluble PLA₂ and AHA levels were higher in patients as compared with healthy controls. These results strengthen recent data obtained with tumour tissues of colorectal cancer patients.³

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