European Journal of Cancer 91 (2018) 107–115

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Fatty acid profile in peri-prostatic adipose tissue and prostate cancer aggressiveness in African–Caribbean and Caucasian patients

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Received 16 August 2017; received in revised form 29 November 2017; accepted 11 December 2017

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https://doi.org/10.1016/j.ejca.2017.12.017

KEYWORDS
Peri-prostatic adipose tissue;
Fatty acids;
Prostate cancer;
Cancer aggressiveness;
Linoleic acid

Abstract ***Background:*** Genetic and nutritional factors have been linked to the risk of aggressive prostate cancer (PCa). The fatty acid (FA) composition of peri-prostatic adipose tissue (PPAT), which reflects the past FA intake, is potentially involved in PCa progression. We analysed the FA composition of PPAT, in correlation with the ethno-geographical origin of the patients and markers of tumour aggressiveness.
Methods: From a cohort of 1000 men treated for PCa by radical prostatectomy, FA composition of PPAT was analysed in 156 patients (106 Caucasians and 50 African–Caribbeans), 78 with an indolent tumour (ISUP group 1 + pT2 + PSA <10 ng/mL) and 78 with an aggressive tumour (ISUP group 4–5 + pT3). The effect of FA extracted from PPAT on *in-vitro* migration of PCa cells DU145 was studied in 72 patients, 36 Caucasians, and 36 African–Caribbeans.
Results: FA composition differed according to the ethno-geographical origin. Linoleic acid, an essential n-6 FA, was 2-fold higher in African–Caribbeans compared with Caucasian patients, regardless of disease aggressiveness. In African–Caribbeans, the FA profile associated with PCa aggressiveness was characterised by low level of linoleic acid along with high levels of saturates. In Caucasians, a weak and negative association was observed between eicosapentaenoic acid level (an n-3 FA) and disease aggressiveness. *In-vitro* migration of PCa cells using PPAT from African–Caribbean patients was associated with lower content of linoleic acid.
Conclusion: These results highlight an important ethno-geographical variation of PPAT, in both their FA content and association with tumour aggressiveness.

1. Introduction

Important ethnic disparities have been reported for prostate cancer (PCa) risk, with a higher incidence among African–American men compared with European–Americans [1]. Similarly, in the French West Indies, where at least 90% of inhabitants are of African descent, the incidence of PCa is twice as high as in the rest of France [2].

Both genetic and environmental factors have been linked to the risk of aggressive disease. The ethnic origin is likely to play a role, since the proportion of cases diagnosed at the metastatic stage is reported to be higher for African–American patients than for European–Americans, with a 2.4-fold higher mortality rate in the former population [1]. Together with genetic parameters, environmental factors including dietary intake have been suggested to play a role in PCa progression [3].

Among nutrients, dietary lipids and particularly essential fatty acids (FAs), are important determinants of the lipid composition of white adipose tissue (WAT) [4,5]. Among FA, essential polyunsaturated fatty acids (PUFAs) are a subclass of bioactive components. The n-6 PUFA include the precursor linoleic acid (LA, 18:2n-6), and arachidonic acid (AA, 20:4n-6), a substrate to form inflammatory mediators. The n-3 series include the precursor alpha-linolenic acid (ALA, 18:3n-3) and highly unsaturated long chain derivatives.

Epidemiologic studies have widely studied the relationship between dietary fat and PCa. There is only weak evidence of an increased risk of aggressive PCa associated with total fat or saturated fatty acids (SFAs) [6–8]. A meta-analysis concluded to the absence of a clear relationship between circulating FA and PCa risk and aggressiveness, with a high heterogeneity amongst studies [9]. In contrast, animal and *in-vitro* experiments have suggested that n-6 PUFA stimulate, whereas n-3 PUFA inhibit PCa growth [10–13].

Most of the previous studies are based on food questionnaires or FA measurement in blood. Evaluation by food questionnaires is limited by subjectivity and difficulties in assessing the portion size. When compared with circulating FA, measurement of FA composition in WAT may provide a more accurate assessment of dietary intake, because it is a marker of essential FA consumption over the previous years [14]. In addition, prior studies have been primarily carried out in Caucasians, so the impact of the ethno-geographical origins on the association between FA and PCa aggressiveness remains poorly understood.

WAT is now recognised to be a metabolically active organ, secreting a variety of biologically active mediators. Several studies have supported an important role of peri-prostatic adipose tissue (PPAT) in the modulation of PCa progression. Increased thickness of PPAT has been associated with disease aggressiveness [15], and adipocytes from PPAT have been shown to increase PCa cell migration through adipokine release [16,17]. Other mediators, such as FA, are also likely to play a role in the crosstalk between adipocytes and cancer cells.

The objective of the study is to analyse the FA composition of PPAT in PCa patients from different