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Editorial – referring to the article published on pp. x–y of this issue

The Influence of Lipid Metabolism on Prostate Cancer Development and Progression: Is it Time for a Closer Look?

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In December 2006 the BBC in London ran a major news article reporting the prediction by the research organisation, Cancer Research UK (CRUK) that soaring obesity levels would inevitably lead to a significant increase in “weight related” cancers [1]. The prediction was that there would be a 14% increase in obesity by 2010 and that this would cause an increase of 1500 extra cancers per year in a population of 60 million. Whilst this report relates to the UK, it is a reflection of a pan-European problem which, in turn, follows in the footsteps of the obesity related issues reported widely in North America. This is a problem which affects a number of cancers (eg renal cancer) but it is particularly manifest in endocrine cancers such as those arising in the breast and prostate. There is a gathering body of research in this field but notwithstanding this, our knowledge of the inter-relationship between lipid and cancer and particularly prostate cancer development and progression is poor. This review article by Mistry et al is therefore timely, as it will help to stimulate the urological clinical and scientific community to think a little more carefully about research in this area [2].

The authors concentrate much of their effort in this review on 4 “adipokines” and in particular, on the potential inter-relation between 2 specific ones: leptin (stimulatory when high) and adiponectin (inhibitory when high). This is an interesting focus for study as the influence of these adipokines in

control of the lipid milieu seems to be important both in the way that they control Body Mass Index (BMI) but also for their secondary effects on specific cytokine levels such as IL-6 and VEGF, both of which are implicated in prostate cancer development. However, in the area of cancer proliferation, apoptosis and metastatic migration the types of lipid which seem to be influential are numerous and their effects are complex. It may therefore be too simplistic to think that there is such a straightforward relationship between these 2 types of adipokine and that these are the only major controllers of prostate cancer behaviour in relation to lipid metabolism. After all, BMI may be important in this area but it is not necessarily an absolute pre-determinant for development of aggressive prostate cancer in all populations: witness the absence of high levels of aggressive CaP in groups of men with subpopulations with a high BMI in countries such as Japan.

The specific adipokines discussed may be important in prostate cancer biology but the influence of specific intra cellular fatty acid levels and their effect on intra-cellular signalling needs to be studied much more rigorously. The intracellular fatty acid profile is related to the dietary intake of certain types of lipid and high levels of poly-unsaturated fats such as Omega-6 lipid seem to have an adverse effect on cancer behaviour. There is evidence from in vitro studies that the influence of unsaturated fats on

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prostate cancer migrational signalling are especially influential [3]. It is also important to consider the fact that adipocytes in different anatomical locations may have differential effects. It is well known that prostate cancer metastases to subcutaneous fat deposits are rare but prostate cancer cells have been shown to migrate to adipocytes within red bone marrow [4], where metastases are very common. Furthermore, chemical analysis of the prostate cancer interface with bone marrow adipocytes has shown that the prostate cancer cell takes up lipid directly as an energy source in early metastatic development *in vitro* [5]. A recent report by Platz et al in relation to the use of Statins provides further clinical evidence for the importance of lipids in prostate cancer progression, showing that there was a 50% reduction in CaP mortality in men taking HMG CoA inhibitors (statins) [6]. This evidence brings together the *in vitro* and *in vivo* threads, suggesting that the lipid signalling effect in prostate cancer may relate strongly to cellular migration and aggressive metastatic behaviour, rather than simply to local proliferation. This might explain why studies looking at Statin use or lipid intake and prostate cancer incidence have not yielded consistent results. Rather, these studies might have looked more carefully at the rate of progression and metastasis.

Thus, it is becoming increasingly clear that lipids are important in the development and progression of prostate cancer. A closer investigation of adipokines and other lipid related cancer pathways would be a potentially fruitful exercise and it is perhaps one which prostate cancer research groups might usefully consider pursuing.

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