Chapter 9

POLYUNSATURATED FATTY ACIDS AND THEIR ROLE IN CANCER INVASION AND METASTASIS

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Abstract: Highly unsaturated fatty acids (HUFAs) have been demonstrated to have anticancer functions in the past decade. Recently, these fatty acids have been shown to exert a regulatory action on tumour cell motility, invasion and metastatic behaviour via such mechanisms as regulation of cell-cell adhesion, tumour suppressor molecules and motility related signal transduction pathways, and angiogenesis. Clinical studies based on laboratory results have recently been carried out and early indications show promise in extending the survival of patients with cancer.

The relationship between diet lipids and the incidence of cancer has been established. This is best demonstrated in Eskimos, who consume essential fatty acid (EFA)-rich diets and enjoy a low incidence of cancer (1). Similarly, other populations with high EFA intake also show a low incidence of female breast cancer (2). The early eighties saw the establishment of the knowledge that EFAs also exerted toxic effects on malignant cells (3-5). The role of EFAs in cancer has since been extensively explored. Recently, another important aspect of fatty acids on cancer emerges, i.e. the anti-invasion and anti-metastasis property of these lipids.

ESSENTIAL FATTY ACIDS AND POLYUNSATURATED FATTY ACIDS

There are four families of polyunsaturated fatty acids (n-9, n-7, n-6, and n-3) (figure 1), of which only the n-6 and n-3 are essential fatty acid (EFA) series. Thus all the EFAs are polyunsaturated and only include linoleic acid (LA) (n-6) and alpha-linolenic acid (ALA) (n-3), due to the fact
**Figure 1.** Polyunsaturated and essential fatty acids (n-3, 6, 7, 9). There exist four series of PUFAs, with n-3 and n-6 being essential. The n-3 series starts from alpha linolenic acid (ALA) and the n-6 from linoleic acid (LA). Both LA and ALA are obtained from the diet. These two fatty acids are firstly desaturated by delta-6-desaturase and then elongated by elongase. n-7 and n-9 series are non-essential and their parent fatty acids are firstly converted by delta-9-desaturase as opposed to delta-6-desaturase in the essential series. The desaturated steps are slow compared with elongation and thus are rate limiting in their metabolism. Those EFAs toxic to cancer cells are highly unsaturated with more than two double carbon-carbon bonds and have been underlined.