Gene 676 (2018) 171–183

Contents lists available at ScienceDirect

Gene

journal homepage: www.elsevier.com/locate/gene

Review

Diverse roles of fatty acid binding proteins (FABPs) in development and pathogenesis of cancers

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ARTICLE INFO

Keywords:
Cancer
Cell proliferation
Fatty acid binding proteins
Inflammatory response

ABSTRACT

One of the most importantly involved pathways in cancer development is fatty-acid signaling pathway. Synthesized lipids as energetic sources are consumed by cancer cells for proliferation, growth, survival, invasion and angiogenesis. Fatty acids as signaling compounds regulate metabolic and transcriptional networks, survival pathways and inflammatory responses. Aggregation of fatty acids with fatty acid binding proteins (FABPs) facilitates their transportation to different cell organelles. FABPs, a group of lipid binding proteins modulate fatty acid metabolism, cell growth and proliferation and cancer development. They may be used as tumor marker in some cancers. FABPs are expressed in most malignancies such as prostate, breast, liver, bladder and lung cancer which are associated with the incidence, proliferation, metastasis, invasion of tumors. This review introduces several isoforms of FABPs (FABP1–12) and summarizes their function and their possible roles in cancer development through some proposed mechanisms.

1. Introduction

Lipids may involve in cancer development through fatty-acid signaling pathway. Synthesized lipids and their movement from adipose tissue as a consequence of cachexia increase availability of cancer cells to lipids. Then lipids as energetic references are consumed in cancer cells for some phenotypes such as proliferation, growth, survival, invasion and angiogenesis (Santos and Schulze, 2012). Different fatty acids (FAs) perform various functions in the organism. They are significant sources of energy produced in muscles and liver and stored as

Abbreviations: A-FABP, Adipocyte fatty acid binding protein; ALBP, Adipocyte lipid-binding protein; aP2, adipocyte P2; AEA, Anandamide; BPH, benign prostatic hyperplasia; B-FABP, Brain fatty acid binding protein; BLBP, Brain lipid-binding protein; E-FABP, Epidermal fatty acid binding protein; EMT, Epithelial-mesenchymal transition; EGFR, Epithelial growth factor receptor; EAN, Experimental autoimmune neuritis; FA, Fatty acid; FAAH, Fatty acid amide hydrolase; FABPs, fatty acid-binding proteins; FASN, Fatty acid synthase; FAT, Fatty acid translocase; FATP, Fatty acid transport protein; FFAs, Free fatty acids; GPCR, G protein- coupled receptors; GBS, Guillain-Barré Syndrome; H-FABP, Heart fatty acid binding protein; HCC, Hepatocellular carcinoma; HIF1A, Hypoxia-induced factor; I-BABP, Ileal bile acid-binding protein; ILLBP, Ileal lipid-binding protein; I-FABP, Intestinal fatty acid-binding protein; IDC, Invasive ductal carcinoma; K-FABP, Keratinocyte-type fatty acid binding protein; KLBP, Keratinocyte-type lipid-binding protein; KLF2, Kruppel-like factor; L-FABP, Liver fatty acid binding protein; LCFAs, Long-chain fatty acids; MDGI, Mammary derived growth inhibitor; MRG, Mammary derived growth inhibitor-related gene; MSCs, Mesenchymal stem cells; MBP, Myelin basic protein; M-FABP, Myelin fatty acid binding protein; MP2, Myelin protein 2; NPY, Neuropeptide Y; NHRs, Nuclear hormone receptors; PP, Pancreatic polypeptide; PYY, Peptide tyrosine tyrosine; PMP2, Peripheral myelin protein 2; PPAR α/γ, Peroxisome proliferator-activated receptor α/γ; PPRE, Peroxisome proliferator response element; PMA, Phorbol-12-myristate-13-acetate; FABP-pm, Plasma membrane-associated FABP; PGs, Prostaglandins; PKC, Protein kinase C; PA-FABP, Psoriasis-associated fatty acid binding protein; RXR, Retinoid X receptors; SLCFA, Saturated long-chain fatty acid; SP1, Specific protein1; SREBP, Sterol responsive element binding protein; T-FABP, Testis fatty acid-binding protein; TLBP, Testis lipid-binding protein; ULCFA, Unsaturated long-chain fatty acid; vldlr, Very low-density lipoprotein receptor, vitellogenin receptor

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https://doi.org/10.1016/j.gene.2018.07.035
Received 27 May 2018; Received in revised form 4 July 2018; Accepted 12 July 2018
0378-1119/

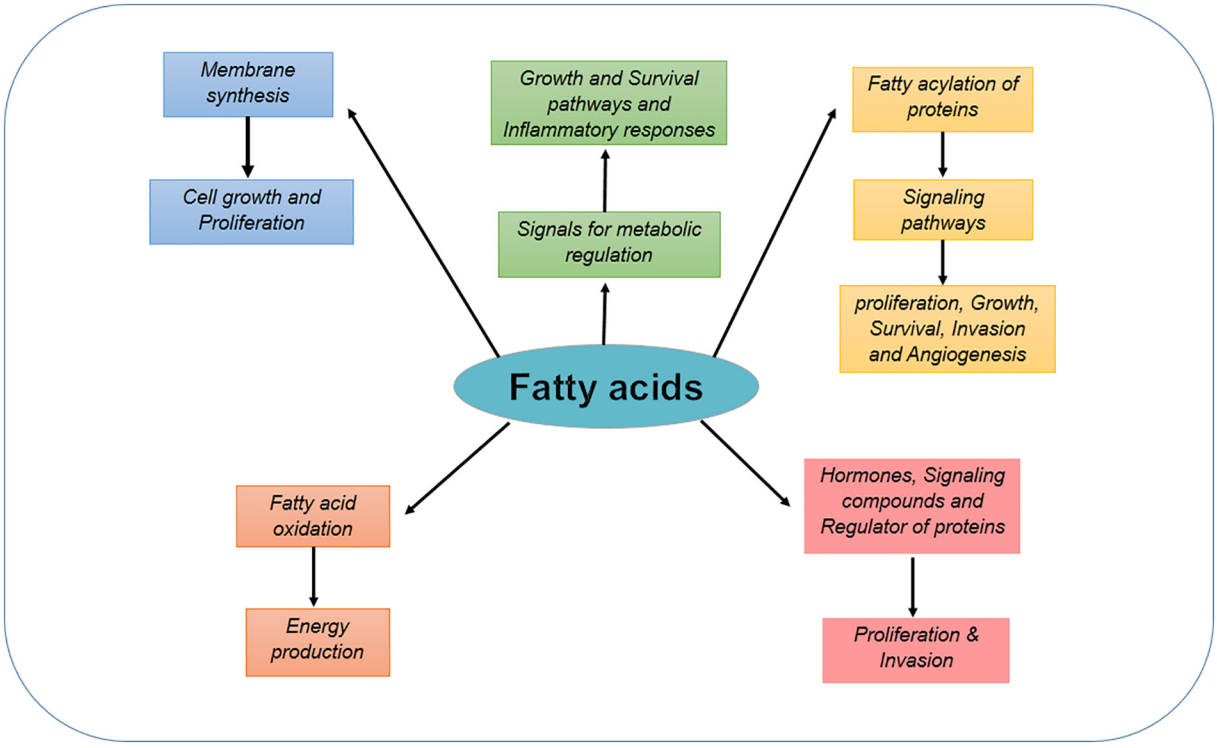

Fig. 1. Various function of fatty acids in organisms.

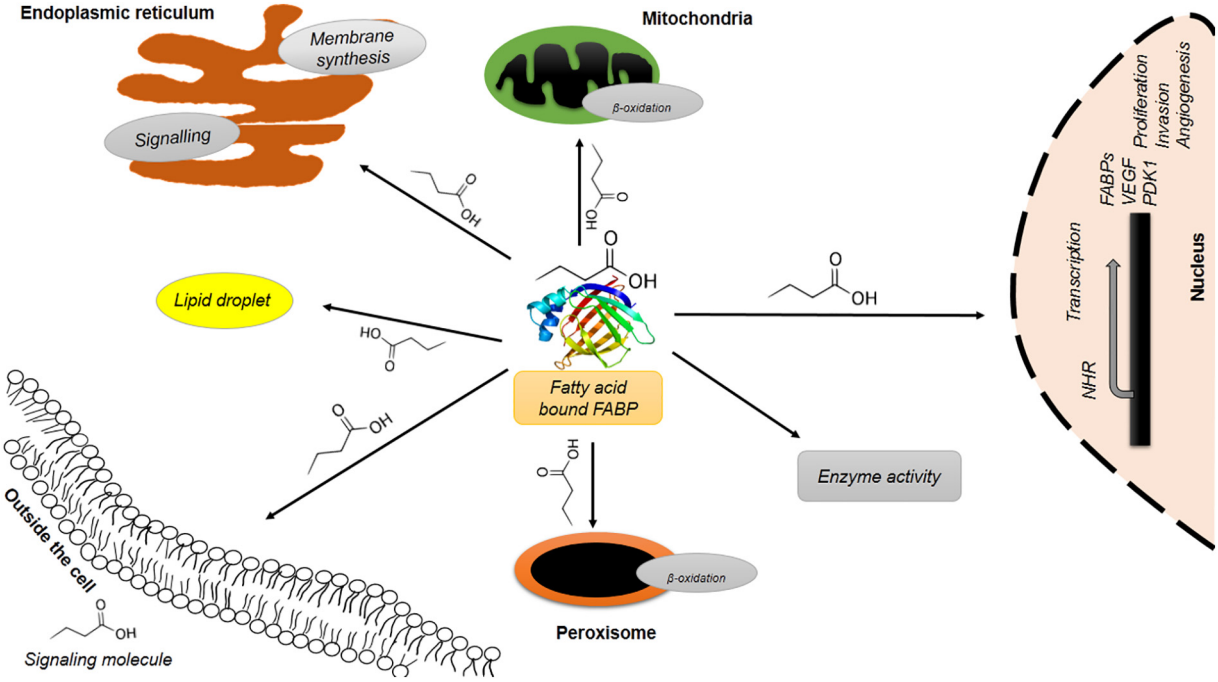

Fig. 2. Fatty-acid accompanies with fatty acid-binding proteins (FABPs) in the cell in order to biological responses. FABPs are involved in lipid transfer to some compartments in the cell including lipid droplet as a storage reference, endoplasmic reticulum for trafficking and signaling and membrane synthesis, mitochondria and peroxisome in order to β-oxidation, cytosol to regulate enzymes activity, nucleus to regulate transcription of genes related to lipids through binding nuclear hormone receptors (NHRs) and even outside the cell as a signaling molecule.

triacylglycerol. They are used for the formation of complex lipids, such as phospholipids and cholesterol as well as their role as hormones, signaling compounds and regulator of proteins. There are many functions performed by long-chain fatty acids in mammals. Their roles in energy production through fatty acid oxidation, fatty acylation of specific proteins, their function as signaling compounds have been reported (Chmurzyńska, 2006). They act as signals for metabolic regulation through enzymatic and transcriptional networks to modulate gene expression, growth and survival pathways and inflammatory responses (Lawrie et al., 2004) (Fig. 1). Furthermore, fatty acids, particularly arachidonic-acid can be metabolized into a family of lipid mediators such as eicosanoids, which can function as anti-inflammatory