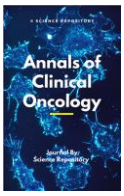

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Editorial

Tumor markers have biological functions that we should know. CEACAM1 as an example

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Tumor markers are substances widely used in the daily practice and its main clinical application generally lies, not in the diagnosis but in the patient's follow-up, because they are useful for early detection of a relapse/metastasis and to know the effectiveness of an established therapy. These markers have a main indication in daily practice, but almost all lack specificity because they can be elevated in different tumors. There are a number of aspects of tumor markers that we must know if we want to well understand them in regular practice: metabolism, half-life, hormonal dependence, temporary elevations by known or unknown causes, dosage moment, etc., all of which makes a tumor marker not just as a single biochemical parameter [1]. In that regard, we should recall that tumor markers have normal biological functions that often go unnoticed. With this in mind, we summarize in this editorial normal role of tumor markers (excluding any link with malignant proliferative function), using as example CEACAM1.

CEACAM1 (CD66a, BGP): carcinoembryonic antigen-related cell adhesion molecule 1 is a transmembrane molecule expressed on epithelial, hematopoietic, vascular, endothelial, human neutrophil, immune, activated T lymphocytes and NK cells. It is involved in tumorigenesis, in the inhibition of epithelial -mesenchymal transition in mammary carcinoma and is overexpressed in some tumors with different origin. A soluble form of CEACAM1 has found in different body fluids (serum, bile, saliva and seminal fluid), and elevated serum levels have been associated with some malignant tumors as osteosarcoma, melanoma, pancreatic, bladder, breast and non-small cell lung cancers.

Different authors have described some biological functions of CEACAM1 highlighting the following:

Structural Functions: an isoform (CEACAM1-L) controls the localization and organization of desmosomes in polarized epithelial cells [2]. It modulates epidermal growth factor receptor-mediated cell

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proliferation; its deficiency delays wound healing process; it is involved in apoptosis and inhibits cell-matrix adhesion also, it plays a critical role in the in vitro generation of prostate organoids, in the initiation of palatal fusion via epithelial cell adhesion, in mammary morphogenesis, and it is specifically expressed by the extra villous intermediate trophoblast [3].

Metabolic Features: it regulates insulin sensitivity by promoting hepatic insulin clearance its immunohistochemical liver expression is markedly decreased in the hepatocytes with macro-vesicular steatosis and obesity, with or without diabetes it plays a role in fatty acid metabolism, in modulation of bone metabolism and in the regulation of osteoclastogenesis [4, 5]. Serum levels are correlated with bone mineral density in postmenopausal women.

Immunological Functions: CEACAM1 isoforms alternatively inhibit and co-stimulate human T cell function; it negatively regulates the severity of autoimmune encephalomyelitis; CEACAM1 on activated NK cells inhibits NKG2D-mediated cytolytic function and signaling. Moreover, CEACAM1 mediates bacterial adherence and transcellular transcytosis, determining the suppression of immune cell activities and inflammatory responses; it is involved in central nervous system autoimmunity and in multiple sclerosis pathogenesis**.**

Role In Defense Against Infections: it serves as cellular receptor for a variety of Gram-negative bacterial pathogens associated with the human mucosa, and this recognition by bacterial pathogens is species-specific; its expression is essential for protective antiviral antibody production. Also, it is a receptor for *helicobacter*, and determines the outcome of *Neisseria gonorrhoeae* infection along the female reproductive tract [6].

Vascular/Blood/Coagulation Effects: it modulates vascular remodeling in vitro and in vivo as a negative regulator of platelet-collagen interactions and thrombus growth; also, it negatively regulates granulocyte colony-stimulating factor production and granulopoiesis, it is crucial for in vivo vascular integrity during ischemic neovascularization and a key regulator of vascular permeability. Likewise, it plays a role in tumor lymph-angiogenesis, vascular morphogenesis and endothelial barrier regulation, as well as in endothelial homeostasis in adult blood vessels [7].

Role In Pathogeny: it is a progression marker of high grade SIL (squamous intraepithelial lesions); in patients with acute rejection of human renal allografts, CEACAM1 is markedly up-regulated in tubular and/or glomerular cells and is an indicator of acute inflammatory processes in biopsy specimens; a reduction in mRNA and protein expression for CEACAM1 and 5 was observed in Crohn disease, but not in ulcerative colitis; it is expressed by keratinocytes and contributes to the pathophysiology of psoriasis; it regulates the secretion of matrix metalloproteinase 9 in neutrophils and protects the blood-brain barrier after ischemic stroke; CEACAM1 exacerbates hypoxic cardiomyocyte injury and post-infarction cardiac remodeling. Likewise, it is a novel serum biomarker for pericarditis [8, 9].

We can conclude that knowledge of the biological functions of tumor markers can help us to better understand their pathophysiology, non-specificity and possible elevations in non-neoplastic situations [10]. Only with this knowledge we will be able to use them in a more effective way and not consider them as a single biochemical parameter.

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