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The role of endothelial biomarkers in breast cancer metastasis

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Statement of the Problem: Metastatic cancers are the main cause of cancer-related death in the world. For this reason identification of novel treatment targets is warranted. Study of breast cancer metastasis is limited due to poor knowledge in progression of breast tumor and varied heterogeneity. Breast cancer metastasis is a complicated process in which each step is modulated by a complex network of signaling pathways. In recent years attention is paid to the significance of vascular endothelium in cancer metastasis and abundant evidence suggests that endothelial inflammation plays an important pathogenetic role in the development of metastasis. The purpose of this study was to describe changes in endothelium in mouse model of 4T1 metastatic breast cancer at various stages of disease progression with the use of the multi-protein panel of endothelial biomarkers.

Methodology & Theoretical Orientation: The panel contains proteins of glycocalyx disruption: syndecan-1 (SDC-1) and endocan (ESM-1); pro-inflammatory molecules: soluble intercellular adhesion molecule 1 (sICAM-1), soluble vascular cell adhesion molecule 1 (sVCAM-1) and soluble form of E-selectin (sE-sel); pro-thrombotic molecule: von Willebrand factor (vWF); fibrinolytic molecules: plasminogen activator inhibitor 1 (PAI-1) and tissue plasminogen activator (t-PA); pro-angiogenic molecules: the soluble form of the fms-like tyrosine kinase 1 (sFlt-1), angiopoietin 2 (Angpt-2) and adrenomedullin (ADM), and protein secreted by adipocytes - adiponectin (ADN). The biomarkers were determined using the liquid chromatography/mass spectrometry-multiple reaction monitoring-based method (LC/MS-MRM).

Findings: Some of these proteins altered during breast cancer progression. Using a panel of selected molecules was enabled to identify endothelial biomarkers for early and late metastatic phase.

Conclusion & Significance: Endothelial dysfunction in cancer confirms the hypothesis that condition of endothelium is a key step for disease development. The simultaneous analysis of many biomarkers in one sample enables for multidimensional screening of endothelial function in mouse 4T1 breast cancer.

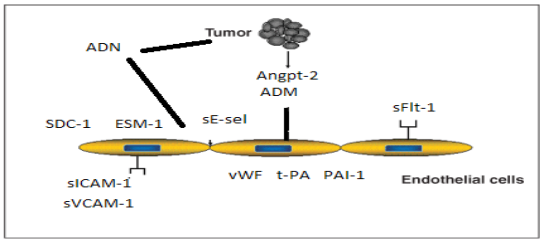

Figure 1. Endothelial biomarkers involved in breast cancer metastasis.

Biography

Maria Walczak has graduated from the Faculty of Pharmacy, Medical Academy in Krakow. She has obtained her PhD degree from the Faculty of Pharmacy, Jagiellonian University Medical College (UJ CM), Krakow in 2001 and habilitation thesis in Pharmacokinetics in 2014. Since 2001, she worked at the Department of Pharmacokinetics and Physical Pharmacy UJ CM as a Lecturer, since 2010 at the Jagiellonian Centre for Experimental Therapeutics (JCET) as a Manager of the Laboratory of Analytics and Pharmacokinetics, and since 2015 as a Head of Chair at Department of Toxicology, Faculty of Pharmacy UJ CM. Her scientific work refers to pharmacokinetic and toxicokinetic profiling, metabolite screening, assessment of protein binding of bioactive compounds and pharmacology of endothelium. She is keen in bioanalysis of novel compounds and biomarkers related to cancer metastasis using LC/MS/MS and CE techniques. She is a specialist in clinical pharmacy issues.

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