# CMX\_SEMINAR

## (神戸大学CMX創発医学講演会)

### Biomarkers of endothelial dysfunction

<内皮機能不全のバイオマーカー>

Speaker: Prof. Maria Walczak

「血管内皮機能」を大きなテーマとしてその機能不全に着目、 医薬品開発過程における候補物質の安全性評価において考慮されるべきことについて、臨床薬理学スペシャリストが最新の知見をご紹介下さいます。

日時: 2022. 12.6(火) 16:00-17:20 オンライン開催

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#### **Abstract:**

The strategic position of endothelium infers its indispensable role in controlling many biological processes, such as regulation of vascular tone, haemostasis and inflammation. A healthy endothelium is essential for the undisturbed functioning of the cardiovascular system, while an endothelial dysfunction is involved in the pathophysiology of multiple human diseases including atherothrombosis, diabetes, heart failure, sepsis, pulmonary hypertension, microangiopathies of neurodegenerative diseases, liver steatosis and cancer metastasis. As confirmed by numerous studies, the dysfunction of endothelium is either the cause or/and the effect of various diseases. Functional alterations of numerous endothelial mediators and mechanisms may contribute to the pathologies associated with the endothelial dysfunction. These include the loss of glycocalyx integrity, impairment of the production of vasoprotective mediators, activation of pro-thrombotic, anti-fibrynolytic and pro-inflammatory mechanisms. Taking into consideration the endothelium complexity, and the heterogeneous alterations of endothelial mediators in various diseases, we suspect that the simultaneous quantification of multiple biomarkers might enable a better insight into pathophysiology of the endothelial dysfunction and can provide a useful tool to stratify the risk as well as to monitor the efficacy of endothelium-oriented therapy. Many drugs used today have an impact on the endothelial function, and their therapeutic efficacy is linked to the endothelial function improvement. Altogether, evidence have accumulated that a significant number of drugs are withdrawn years or decades after being in the market. Endothelial toxicity might be the offender of the cardiovascular adverse effects observed for a significant number of drugs. In this regard, endothelium-dependent side effects should be taken into account in the safety assessment of a new drug candidate during the development process.

#### References:

- 1. **Walczak M**, Suraj J, Kus K, Kij A, Zakrzewska A, Chlopicki S: Towards a comprehensive endothelial biomarkers profiling and endothelium-guided pharmacotherapy. Pharmacol Rep. 2015 Aug;67(4):771-7. doi: 10.1016/j.pharep.2015.06.008.
- 2. Kurpińska A, Suraj J, Bonar E, Zakrzewska A, Stojak M, Sternak M, Jasztal A, **Walczak M**: Proteomic characterization of early lung response to breast cancer metastasis in mice. Exp Mol Pathol. 2019 Apr;107:129-140. doi: 10.1016/j.yexmp.2019.02.001.
- 3. Suraj J, Kurpińska A, Sternak M, Smolik M, Niedzielska-Andres E, Zakrzewska A, Sacha T, Kania A, Chlopicki S, **Walczak M**. Quantitative measurement of selected protein biomarkers of endothelial dysfunction in plasma by micro-liquid chromatography-tandem mass spectrometry based on stable isotope dilution method. Talanta. 2019 Mar 1;194:1005-1016. doi: 10.1016/j.talanta.2018.10.067.
- 4l. Suraj J, Kurpińska A, Zakrzewska A, Sternak M, Stojak M, Jasztal A, **Walczak M**, Chlopicki S: Early and late endothelial response in breast cancer metastasis in mice: simultaneous quantification of endothelial biomarkers using a mass spectrometry-based method. Dis Model Mech. 2019 Mar 1;12(3):dmm036269. doi: 10.1242/dmm.036269
- 5. Matyjaszczyk-Gwarda K, Kii A, Olkowicz M, Fels B, Kusche-Vihrog K, **Walczak M**. Chlopicki S: Simultaneous quantification of selected glycosaminoglycans by butanolysis-based derivatization and LC-SRM/MS analysis for assessing glycocalyx disruption in vitro and in vivo. Talanta. 2022 Feb 1;238(Pt 1):123008. doi: 10.1016/j.talanta.2021.123008.

#### Introducing the speaker (Self-introduction):

Maria Walczak has graduated at the Faculty of Pharmacy, Medical Academy in Krakow (Poland). She received her PhD degree and habilitation at the Faculty of Pharmacy, Jagiellonian University Medical College (UJ CM). Currently she is a head of the Chair and Department of Toxicology at the Faculty of Pharmacy UJ CM and a group leader at the Jagiellonian Centre for Experimental Therapeutics (JCET, UJ). Her research primaly focuses on the pharmacokinetic and toxicokinetic studies of bioactive compounds, metabolite identification, assessment of drug protein binding subsequently crucial for drug development. At the core of her work stands the bioanalysis of biomarkers related to civilisation deseases, as prognostic and diagnostic targets using mass spectrometry-based methods. She is a specialist in clinical pharmacy.

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