S18: Nanostructures in disease and health

S18-1 malaria parasites, host-erythrocytes and blood circulation

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Malaria deadly threats ensue when Plasmodium parasites massively infect erythrocytes, instigating their massive adhesion in capillaries and obstructing blood circulation to vital organs, such as brain and placenta. However, not everybody will die on the infection; sickle cell patients carry a mutation to hemoglobin that prevents the fatal cytoadhesion. By using cryo electron tomography, Mössbauer spectroscopy and related techniques we unravelled the molecular basis of sickle cell protection. We showed that irreversibly oxidized sickle hemoglobin interferes with actin dynamics and hinders the transport of adhesins to host-cell surface, thus thwarting the severe outcomes of malaria. We further propose a novel strategy for antimalarial intervention by which the protective trait would be drug-induced also in the erythrocytes of malaria vulnerable patients.

S18-2 Polyhedrocytes in type 2 diabetes

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Little is known about the composition and structure of contracted blood clots, particularly polyhedral erythrocytes (polyhedrocytes). We investigated the content of polyhedrocytes formed in blood clots and its determinants in type 2 diabetes (T2D) patients. In 97 patients with T2D and cardiovascular disease (aged 41-85 years, median HbA1c of 6.4% [interquartile range, 5.9-7.8]), we measured in vitro the composition of blood clots, including a clot area covered by polyhedrocytes using scanning electron microscopy. Additionally, we measured plasma fibrin clot permeability (Ks), clot lysis time (CLT), thrombin generation, oxidative stress (Total Protein Carbonyl and Thiobarbituric Acid Reactive Substances), P-selectin (CD62P) and platelet factor-4 (PF4) were also determined. Patients who generated > 5% polyhedrocytes within clots (n=83, 85.6%; high polyhedrocytes group) had higher glucose (+15.7%, P=0.018), fibrinogen (+16.6%, P=0.004), lower red blood cell distribution width (RDW) (-8.8%, p=0.034), reduced plasma clot density (-21.8% Ks, p=0.011) and impaired fibrinolysis (+6.5% CLT, p=0.037) compared to the low polyhedrocytes group. Glucose ≥ 6 mmol/L increased odds for the high polyhedrocytes formation (OR=4.81, 95% CI 1.49-16.40, P=0.009) when compared with lower glycaemia.

The content of polyhedrocytes positively correlated with fibrinogen, glucose, HbA1c and total cholesterol. In the in vitro experiment, increase of glucose concentration by 10 mmol/L was associated with 97% increased polyhedrocytes content (p=0.031). Moreover, in the linear regression analysis of T2D patients, an increase in TBARS, total PC, P-selectin, PF4, was associated with the increased content of polyhedrocytes in the blood clots of T2D patients. The content of polyhedrocytes reflected as percent of clot area covered by polyhedrocytes in blood clots generated in T2D patients is determined by glucose level, platelet activation, and oxidative stress.

S18-3 Differentiation between various melanomas based on biophysical characterization of their properties

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Cancer remains the second leading cause of death worldwide. That is why, there is still an urgent need for the development of various scientific methods that increase the chance to detect cancers of different organs and tissues. One of the emerging directions is to correlate cellular biomechanics with biochemical properties of single cancer cells. It can be achieved by the combination of two methods, Atomic Force Microscopy (AFM) and Time-of-Flight Secondary Ion Mass Spectrometry (ToF SIMS). By means of AFM, the nanomechanical properties of cancerous cells were investigated [1]. To study biochemical alterations at the single cell level, ToF SIMS was employed [2,3]. High resolution mass spectra were analyzed by means of Principal Component Analysis (PCA) [4]. The combination of AFM and ToF SIMS gives the information about the alterations between different cancer cells and it may be applied to monitor the effectivity of anticancer drugs. In this way, these two techniques are excellent tools for a complex analysis of cancerous cells.

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[2] J. Gostek et al., Analytical Chemistry 87(6), 2015, 3195–3201.

[3] J. Bobrowska et al., Analyst 141, 2016, 6217-6225.

[4] J. Bobrowska et al., Analytical Biochemistry 511, 2016, 52-60.

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S18-4 Endothelial nanomechanics in vascular diseases - an ex vivo AFM nanoindentation study

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The progressive dysfunction of the endothelium in diabetes leads to vascular injury and to the development of the cardiovascular disease. Recent studies have reported endothelium stiffening as an important symptom of the endothelium dysfunction in hyperglycemia. Other studies have shown that the degradation of the glycocalyx, which is a brush-like layer on the endothelium, coincide with the endothelial dysfunction in hyperglycemia. In this talk, we will demonstrate that atomic force microscope (AFM) is a valuable tool for studying nanomechanical properties of the endothelium. By means of this method we were able to evaluate the nanomechanical changes of endothelium in both in vitro [1] end ex vivo experiments [2].
In particular, ex vivo study of endothelium from mouse aorta enabled to quantitatively evaluate the changes in glycocalyx degradation and mechanical properties of the endothelium in progression of diabetes. We observed a local spatial redistribution of the glycocalyx and its progressive global degradation in the studied period of diabetes. The measured apparent elastic modulus of the endothelial layer increased for regions covered by glycocalyx and, in the same age-dependent way, for the whole endothelium layer. These results may indicate that the degradation of the glycocalyx is tightly related to endothelium stiffening and is a consequence of the endothelial dysfunction caused by the long lasting hyperglycemia.

[1] Targosz-Korecka M, Brzezinka G, Malek K, Stępień E, Szymonski M, 2013, Cardiovascular Diabetology12:96

[2] Targosz-Korecka M, Jaglarz M, Malek-Zietek KE, Gregorius A, Zakrzewska A, Sitek B, Rajfur Z, Chlopicki S, Szymonski M, 2017, Scientific Reports 7(1):15951

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