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suffering from a particular disease. This approach is, therefore, perhaps uniquely able to contribute to the development of so-called "4P's medicine": Predictive, Preventive, Personalized and Participatory (2). Between 2007 and 2013, the EU's Framework 7 program invested some €207 million in its "Virtual Physiological Human" (VPH) initiative (3), funding over 50 multi-disciplinary biomedical research projects and support actions including ten in oncology. Crucially, each project team was required to include clinicians. The VPH Digital Patient initiative (4) was set up to develop a "roadmap" towards the ultimate exemplar of this approach: a computer model of an individual patient that is complex and precise enough to be used for prognosis prediction and clinical decision making. In this talk I will describe how these principles are being applied to oncology (5, 6) using examples from VPH projects in breast cancer, paediatric oncology and treatment planning, and illustrating the potential value of the "digital cancer patient" to oncologists.

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SCREENING FOR POTENTIAL HAZARD EFFECTS FROM MULTITARGET ANTHRACYCLINE ON THE CARDIOVASCULAR SYSTEM

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Conjugation of doxorubicin (DOX) with NO-releasing groups gives rise to novel multitarget anthracyclines, such as nitrooxy-DOX (NitDOX), capable to overcome drug resistance by decreasing the activity of ABC transporters *via* nitration of critical tyrosine residues on the pumps (1). In addition, NitDOX preferentially accumulates in mitochondria and affects their function, thus representing a prototype of novel multifunctional anthracyclines, which have cellular targets different from, and greater efficacy against, drug-resistant tumor cells than the parent compound (2). The widely described anthracycline toxicity, however, might limit their use. Therefore, the aim of this study was to investigate the NitDOX-induced cardiovascular effects, as potential hazard, by studying its functional and electrophysiological actions in rat aorta rings (3), Langendorff perfused rat heart (4) and A7r5 cells (5). DOX was used as reference compound. At concentrations ≥1 μM, NitDOX partially antagonized phenylephrine-induced contraction in freshly endothelium-denuded rings, while DOX was ineffective. Both drugs did not significantly affect the concentration-response curve to high KCl. In arteries cultured with both drugs for 7 days, NitDOX blocked both phenylephrine- and high KCl-induced contractions at concentrations 10-fold higher than that of DOX. Moreover, NitDOX exhibited L-type Ca^{2+} channel blocking activity in A7r5 cells. Preliminary results suggest that NitDOX did not affect the cardiac mechanical function and ECG in Langendorff perfused rat heart. In conclusion, NitDOX is a novel NO-releasing anthracycline devoid of significant acute cardiovascular properties, although endowed, at high concentrations of long-term effect on vasculature.

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EPIGENETIC CHANGES IN CANCER AND DEVELOPMENT OF COMBINATION THERPAY

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Multiple causes may result in uncontrolled growth, including inherited and somatic mutations, activation of oncogenes, silencing of tumor suppressor genes, environmental factors, and epigenetics. Transcriptional regulation by histone acetylation/ deacetylation and histone methylation/demethylation is a novel epigenetic mechanism of how gene expression is regulated. CpG residue methylation, hydroxymethylation in the upstream promoter and other regions of genes generate specific mechanisms of gene silencing in many types of cells, including stem cells and cancer cells. The prerequisite of the re-expression of silenced tumor suppressor genes should be the demethylation of these regions. We observed that histone deacetylase inhibitors (HDACi), down regulated DNA methyl transferase 1