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The features of complex formation of poly(dG-dC).poly(dG-dC) with porphyrins

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The features of complex formation of water soluble cationic meso-tetra-(4N-oxyethylpyridyl) porphyrin (H_2TOEPyP4) and it's Cu- and Co-derivatives with synthetic double-stranded alternating polynu¬c¬le¬o¬tide poly(dG-dC).poly(dG-dC) was studied by UV/Vis and CD spectroscopes. All investigated porphyrins exhibit induced CD spectra (ICD) in visible range at interaction with poly(dG-dC).poly(dG-dC). Binding mode with DNA was determined by sign of ICD spectra. In the case of H2TOEPyP4 and CuTOEPyP4 observed both ICD: negative band at lower relative concentrations (intercalation, r<0.1) and positive band at higher relative concentrations (outside binding mode). In the case of co-derivatives observed strongly pronounced positive bands. These results suggest that H2TOEPyP4 and CuTOEPyP4 are intercalated into poly(dG-dC).poly(dG-dC), but CoTOEPyP4 binds only via external manner. But in high concentration range, all porphyrins preferably binds with duplex poly(dG-dC).poly(dG-dC) via outside self-stacking mode independent of the planarity of porphyrin molecules. The binding parameters (Kb and n) provides the additional evidences for the proposed models. The effectiveness of complex formation of investigated porphyrins with poly(dG-dC).poly(dG-dC) are arranged as follows: H_2TOEPyP4>CuTOEPyP4>CoTOEPyP4. The binding constants of the porphyrins with poly(dG-dC).poly(dG-dC) is comparable to those, obtained for the same cationic porphyrins upon interaction with DNA at the same conditions. These experimental results have demonstrated that the insertion of transition metal ions into H_2TOEPyP4 changes the polynucleotide duplex binding properties and the binding characteristics of metalloporphyrins to the DNA duplex are tuned by varying the metal center. This finding is important to get some insight into porphyrin–DNA interactions at the molecular level. All experiments were performed at room temperature in a phosphate buffer 0.1 BPSE, pH 7.0, [Na+]=0.02M.

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Optical bedside biomarkers of brain function

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Perinatal hypoxic-ischaemic (HI) brain injury in the infant remains a significant problem throughout the world. Neonatal encephalopathy (NE) is the clinical manifestation of the ensuing disordered neonatal brain function which can lead to serious consequences including death. The availability of markers of neuronal injury that correlate with disease severity and are predictive of neurodevelopmental disability in childhood would likely facilitate a more targeted therapeutic approach using adjunctive therapies. To meet the above clinical need, I have been developing optical technologies based on broadband near-infrared spectroscopy (or NIRS). Near-infrared (NIR) light (650-950 nm) can easily penetrate the skull and reach the brain. By measuring the light attenuation at different wavelengths, one can estimate the concentration of the oxygenated (HbO2) and the deoxygenated-haemoglobin (HHb). These two states of haemoglobin have different absorption spectra, which we can use for our spectroscopic measurements. Another strong NIR absorber is the terminal electron acceptor of the mitochondrial respiratory chain cytochrome-c-oxidase (CCO), which contains a unique Cu-Cu dimer (termed CuA). The NIR absorption spectrum of CCO depends on the redox state of CuA which in turns depends on the availability of oxygen in cells. For several years, I have been developing instrumentation and methodology that can non-invasively assess mitochondrial oxygenation through measurement of the changes in oxidation status of cytochrome-c-oxidase (oxCCO). In this talk, I will introduce the technology and emphasize several aspects in the instrumentation development. Finally, I will be discussing the deployment of the technology from the laboratory, to the preclinical environment and to the neonatal intensive care unit.

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