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ROLE OF LIPID RAFTS IN ORGANIZATION OF RECEPTOR COMPLEXES

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Lipid microdomains enriched in glycosphingolipids (GSL) and cholesterol, also named as "lipid rafts", may form in the plasma membrane. Definition of these lipid rafts highly depends upon the techniques (biochemical or biophysical) applied to detect them. According to the present status, GSLs form small, ordered microdomains, (so called "liquid ordered phase") which are further stabilized by cholesterol. Existence of such domains results in lateral phase separation which may promote compartmentation of raft-associated proteins and their spatial segregation from proteins excluded from rats. These properties suggest that lipid rafts existing in the plasma membrane may be critically important players in signal transductions processes by bringing together receptors with theirs signal transmitting/converting/amplifying molecules wile temporarily excluding others (e.g. negative regulator proteins) from these compartments. Biophysical techniques applied for detection and characterization of raft domains comprise atomic force microscopy, scanning near-field microscopy, single particle tracking, single dye tracing, optical trapping, confocal microscopy and various forms of fluorescence resonance energy transfer methods. Combined approaches can reveal biological and physicochemical factors controlling raft dynamics. Lipid rafts have crucial role in organizing receptor complexes and affecting their signal transduction processes, as an example the effect of rafts on signal transduction of tyrosine kinase receptors (e.g. epidermal growth factor receptor, ErbB2 and ErbB3) will be discussed in more detail. Clusters of ErbB2 colocalized with lipid rafts identified by the GM1-binding B subunit of cholera toxin. Pixel-by-pixel analysis of fluorescence resonance energy transfer between labeled antibodies indicated that the homoassociation (homodimerization) of ErbB2 was inversely proportional to the density of the raft-specific lipid GM1. Crosslinking lipid rafts with the B subunit of cholera toxin caused dissociation of the rafts and ErbB2 clusters, an effect that was independent of the cytoskeletal anchoring of ErbB2. Crosslinking also decreased ErbB2-ErbB3 heteroassociation and the EGF- and heregulin-induced tyrosine phosphorylation of Shc. When cells were treated with the anti-ErbB2 monoclonal antibody 4D5 (parent murine version of Trastuzumab used in the immunotherapy of breast cancer), internalization of the antibody was inhibited by crosslinking of lipid rafts, but the antiproliferative activity of 4D5 was retained and even enhanced. We conclude that local densities of ErbB2 and ErbB3, as well as the lipid environment profoundly influence the association properties and biological function of ErbB2.

1230–1400
Poster Presentations
(See abstracts beginning on page 111)

1615–1800
ISAC Business Meeting

Wednesday, 26 May

0800–0945

Parallel Session 6: Image Cytometry II

Chair: Laszlo Matyus

96967

THE SONIFICATION OF CYTOLOGIC IMAGES

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Texture analysis is mainly based on mathematical principles which are sometimes rather difficult to transmit to students. Therefore we looked for a more intuitive way of teaching texture analysis applying principles of synesthesia. We tried to create various ways of sonifcations equivalent to different techniques of texture analysis. Two main forms of sonification can be differentiated and will be explained using cell nuclei of routine cytologic preparations: 1. Sound equivalent to 1D gray level signals obtained by peel-off scanning: This method consits of a transformation of the original digitalized 2-D gray-scale image into a 1-D signal (of about 5000 to 8000 pixels) by means of a spiral scan algorithm beginning at the periphery and finishing in the central part. This 1D-diagram can be transformed in sound by two different ways: 1 a .The gray levels represent the acoustic pressure while performing at high speed (8000 pixels/s). Variations of object size and texture create different sounds. 1 b. Frequencies are attributed to each pixel by multiplying its gray value with a factor while performing at low speed (about 2– 8 pixels/s). 2. Sound equivalent to the Fast Fourier (FFT)Image : Gray level transformed images were FFT-transformed and regional maxima extracted by geodesic reconstruction. In order to get the time dimension, a vector was defined which moves, like a pointer of a clock, from the zero to the six hour position of the FFT image. The sound is played when the vector strikes a pixel. Frequency is defined by the distance of the pixel from the center of the FFT image and the amplitude is equivalent to the gray value (moment of inertia). Thus each microscopic image is represented by a short sound clip. Normal bronchial mucosa and adenocarcinoma cells are easily discernible, because chromatin condensations in carcinoma cells create a spectrum with lower frequencies and high amplitudes both in the FFT image and in the sound. In summary different types of sound can be created from an image equivalent to the kind of texture analysis performed. The sonification of the chromatin texture can be regarded as an equivalent sound of the nucleus, with complete reproducibility. This method can be regarded as a synesthetic way for understanding both principles of texture analysis and microscopic structures, since the auditory system can be used for pattern recognition. Finally an interface between science and art is created, which can contribute to humanization of technology. Supported by FAPESP, CNPq.