RAFTING IN THE MEMBRANE. A LESSON LEARNT FROM LYMPHOPROLIFERATIVE DISORDERS

Švec A.

Department of Cellular Pathology, James Cook University Hospital, Middlesbrough, United Kingdom

Summary

Lipid rafts are chemically distinct compartments of the plasma membrane. Their integrity is a prerequisite for vital cellular functions particularly for signalling and trafficking. Their perturbation is associated with development of a broad spectrum of diseases. Lipid rafts are also important for therapeutic effects of some drugs. Moreover, some of the raft associated molecules are useful immunohistochemical markers in routine histopathology.
Key words: lipid rafts – malignant lymphoma – anti-lymphoma drugs

Souhrn

Na raftu a na membráně. Jedna zkušenost z biologie lymfoproliferativních onemocnění

Lipidové rafty jsou zvláštním kompartmentem cytoplazmatické membrány vyznačující se charakteristickým chemickým složením. Jejich integrita má zásadní význam pro životně důležité buněčné funkce, zejména signální procesy a membránový transport. Narušení lipidových raftů bylo prokázáno u řady onemocnění. Lipidové rafty jsou rovněž významné pro terapeutické účinky některých léků a určité molekuly zakotvené v lipidových raftech jsou navíc užitečnými diagnostickými markery v rutinní histopatologické praxi.

Klíčová slova: lipidové rafty – maligní lymfom – proti-lymfomové léky

Čes.-slov. Patol., 44, 2008, No. 4, p. 96–99

Why just the rafts?

Pathology used to provide clinical medicine with 'the base of diseases' and deliver diagnoses on the grounds of information obtained by direct visual observations of morphological changes. Except for other methods, it was the introduction of immunohistochemistry that added a new dimension to pathological observation both in practice and research. This method makes it possible to detect an array of molecules which would otherwise remain hidden in the 'red and blue mosaic' of the conventional histological sections. This progress imposed a considerable pressure on pathologists to embrace a significant bulk of new knowledge about microscopically elusive substances such as molecules, their functions, mutual relations as well as their cellular location.

The following text brings elementary information about plasma membrane microdomains called lipid rafts or glycosphingolipid-enriched microdomains, the home site of a number of molecules significant both in health and disease.

What are the rafts like?

A text-book scheme of the biological membrane as a phospholipid bi-layer with in-built proteins known as Singer&Nicolson's fluid mosaic model has become complicated by the discovery of marked chemical and structural heterogeneity of the membrane where molecules are engaged in preferential interactions, clustering into microdomains capable of lateral movements. Lipid rafts represent such microdomains with special physical-chemical properties and physiological roles. They show a higher degree of physical organisation called a liquid-ordered phase distinguishing them from the liquid disordered non-raft membrane (8, 25). In a figurative sense, they could be viewed as small solid islands 'rafting' in the membrane with some restrictions resulting from interactions with intracellular and extracellular molecules, but are they, really?

Although lipid rafts have become a hot topic only in the current millennium (39), the lipid raft story started unwinding as early as 1953 when George E. Palade, 1974 Nobel Prize winner, presented his observations of spherical vesicles in endothelial cells at the 11th annual meeting of the Electron Microscope Society of America (30). The vesicles were considered identical to 'pit-like' and 'cave-like vesicles' observed in microvilli of rat gall bladder epithelium by Yamada in 1955 who called them caveolae intracellulares (48). These are currently recognized as a special example of lipid rafts referred to simply as caveolae, generally described as flask-shaped invaginations of the plasma membrane 50–100 nm in size. Later, it was shown that caveolae are associated with a family of proteins known as caveolins; interestingly, with both -COOH and -NH_2 ends facing the cell interior and having no extracellular domains. The caveolins turned out to be critical for caveolae formation. Functionally, they act as adaptor proteins recruiting other signalling molecules to the caveolae (10).

Caveolae are present in nearly all cell types particularly in the endothelium and type 1 pneumocytes but typically missing in haematopoetic cells which do not express caveolins (10).

As a result, haematopoietic cell membranes comprise lipid rafts morphologically indistinguishable but highly sophisticated methods allowing tracking single molecules were used to visualise them (33, 37). Lipid rafts defined biochemically are plasma membrane compartments characterised by an increased proportion of sphingolipids with long saturated fatty