EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 9
Issue: 6
99-103
Year: 2022

CELLULAR TOPOGRAOHY: EFFECTS OF PATHOLOGICAL CONDITIONS AND NANOMATERIALS

Y. K. Lahir*[1,2]

[1]Department of Biophysics, University of Mumbai, Santa Cruz (east), Mumbai-400098, India.
[2]Department of Zoology, Thakur College of Science and Commerce (Autonomous), Kandivli (east), Mumbai-400 101, India.

***Corresponding Author: Dr. Y. K. Lahir**
India.

Article Received on 23/03/2022 **Article Revised on 13/04/2022** **Article Accepted on 03/05/2022**

CELL AND ITS OVERALL FUNCTIONALITY

Cells are mostly fixed and well-set to constitute an organ among multicellular biosystems. Red blood cells, leukocytes, lymphocytes, and fibroblast, are free to move from one location to other to meet emergencies, like, transportation, microbial invasion, immune interactions, eliminating toxic and unwanted metabolites. These cells exhibit cellular topography that facilitates such functions. The cellular topography plays structural and functional roles during fertilization, development (embryonic and growth), cell migration, intercellular signaling, repairing of wounds, metastasis, invasive movements of cancer along with aligned fine layers of collagen (Walter and Israel, 1987, Curtis and Clark, 1990, Harrison 2011, Lahir, 2021). The cell membrane has been the target of investigation from the beginning of cytological studies. It is one of the most functional complex cell components and needs more consideration. The morphological folded appearance and other topographic features of cell membrane are mostly ignored but are of functional significant (Ingela and Onfelt, 2013). Cell membrane is non-elastic in their lateral plane, but it exhibits ability to stretch without any rupture. The membrane is able to form endocytic vesicles, blebs, protrusions, and ruffles, accommodate the changes in shape during migration, spreading, cell proliferation, formation of filopodia, pseudopodia, lamellipodium, and formation of immunological synapses involving B- or T-cells and NK-cells. There are frequent movements of cell surface receptors, signaling molecules, vesicles, curvature induced lipid rafts (Nichol and Hutter, 1996, Boucrot and Kirchhausen, 2007, Gauthier et al., 2009, Lahir and Chitre, 2021, Lahir et al., 2021).

The extracellular matrix and its chemistry and physicochemotactic components along with the cytoskeleton involve in such processes. The active roles of microfibers and other components of cytoskeleton are well established, and are very obvious during embryonic movements and development. The underlying mechanism involved topography during contact adherence is an elaborate process which regulates topographic functionalities (Weiss, 1945, Lahir, 2016). The alignment with proteins like collagen and fibronectin with the biological substrate fibrils is an important aspect. Possibly, fabricating method of topography can change the physicochemical aspects of surfaces involved and this may reflect on the mode of cellular interaction. One may coat the materials participating in cellular movements with titanium to change the chemistry or blankets etch the substratum prior to patterning of topography (Brunette et al., 1983, Curtis and Wilkinson, 1998, Hamilton et al., 2008). The neutrophils are one of the free moving blood cells and exhibit cellular spreading and phagocytosis. Both these processes depend on the available surface and in all probability; the wrinkled surface topography provides the extra area.

SOME OF THE FACTROS RELATED TO TOPORAPHY OF CELL

The physicochemical aspects of cell membrane are some of the prime factors affecting the topography of a cell membrane and plays significant role in the maintenance of physicochemotactic nature of cell surface. Cell membrane and cell surface, both are the mechanobiologial units of a biological cell. The mechanics of plasma membrane and membrane tension, both regulate the cellular activities and its behavior. Thus, cell membrane acts as a physicochemical set-up/system that exhibits various mechanical capabilities. These in turn, basically maintain specific surface mechanical control and polarity of a cell which helps to establish cellular activities like cellular retraction, adhesion, and maintenance of specific cellular identity (Sitarska and Diz-Munoz. 2020).

The common and basic conceptual components of cell membrane are lipid bilayers and trans-membrane specific proteins and sugars along with components of cytoskeleton like actinomycin or cortical cell skeleton. There are non-specific proteins like Ezrin, Radixin,

Moesin-(members of Myol family), are also structural and functional components of a cell membrane. The composition of members of Myol family) changes in different cell types, even the degree of spectrin net-work and intermediate filaments also fluctuates in different types of cells. There are three interactomes in a given cell membrane: (i)-Cell surface interactomes regulate the mechanism related to the cell membrane, and cytoskeleton interactions, (ii)-MCA-proteins (the mucin-like-carcinoma associated antigens, having molecular weight ranging within 350 to 500Kd) are present in serum. These can be detected readily using the 'Cobas core MCA-EIA test'. These proteins influence the mechanism of cell surface and bind with actin. This binding affects the degree of 'surface-viscous-drag'. Transmembrane proteins, directly or indirectly, interact with under-lying cytoskeleton involving MCA linkers. This interaction affects the diffusion process via plasma membrane, (iii)-The Bin/Amphiphysin/Rvs domain protein (BAR) regulates the dynamic remodelling of plasma membrane and actin cytoskeleton. The degree of sensing or generating curvature involving auxiliary domains likes SH_3 (SRC homology 3 domain consists of about 60 amino-acids residue, PX (a phosphoinositide bound structural domain that targets proteins of cell membrane), PH (a protein domain made of approximately 120 amino-acid residue, is found as a wide range of proteins which is used in intracellular signalling or acts as component of cytoskeleton), Rho-GEF (a domain with two distinct structural domains that have guanine nucleotide exchange factor and it regulates small GTPases in Rho family), and Rho-GAP (is an evolutionary conserved protein domain related to GTPase that enhances proteins concerning Rho/Rac/Cdc42- like small GTPase). Human proteins containing such domain relates with the remodelling of plasma membrane (Fig. no. 1) (Carman and Dominiquez, 2018; Sitarska and Diz-Munoz. 2020).

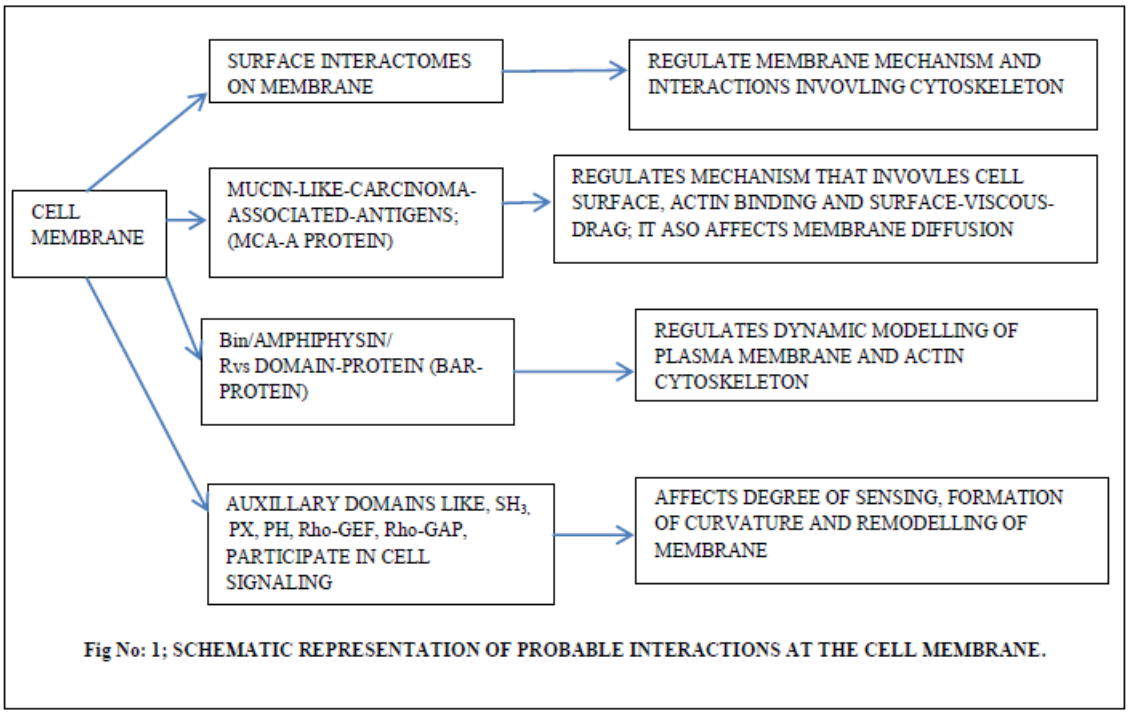

Fig No: 1; SCHEMATIC REPRESENTATION OF PROBABLE INTERACTIONS AT THE CELL MEMBRANE.

The cell membrane, in case of mammalian cells, is not very smooth and flat. Mostly, it exhibits irregular corrugated appearance. It appears that cells have more area than the required. In all probabilities, the extra cell membrane helps shape modification, cell migration, and signaling transduction. The common techniques, like, atomic force microscopy, scanning ion conductance microscopy, fluorescence polarization microscopy and linear dichroism elaborate more on the topography and folds on membrane. The mechanism involved in phenomena like instance colocalization, membrane organization and molecular clustering are still to be understood because these play significant role during cellular functions (Ingela and Onfelt, 2013).

The wrinkled surface topography of the cells may or may not impact the cellular behavior either during chemical expansion of cell membrane or cellular swelling during osmotic conditions. There is no or least cell spreading or shrinkage and even during phagocytosis in such cells under osmotic changes. The probable parameter responsible seems to be the initiating uncaging of inositol trisphosphate, (a phosphate signalling molecule) that triggers Ca^{++} signalling resulting in formation of tubular blebs but not readily cell spreading. The induced osmotic shrinkage due to phagocytic Ca^{++} signalling restricts phagocytosis at its cup stage. When neutrophils reach isotonic state then the process of phagocytosis gets accomplished. Thus, the wrinkled topography of neutrophils (osmotically hyperwrinkled topography) plays functional role in providing the needed space

during the cell spreading and phagocytosis. The uncaging of inositol trisphosphate plays an effective role in causing hyperwrinkled topographic state in neutrophils (Hemelaar et al., 2017).

Integrated functioning of musculoskeletal cells involves ambient physiological environment and varied external stimuli. The musculoskeletal tissue and primarily mechanosensitive functional aspect as far as locomotion concerns relates with the external physical cues (zeitgebers). This tissue senses cues like, stiffness of extracellular matrix, topographic and geometrical changes and convert them into intramuscular signalling cascades which induces numbers of successive cellular responses. The cell acknowledges these signalling cascades in the form of specific behavior during adhesion, maintenance of cellular phenotypes, reconstruction of cytoskeleton, and differentiating among stem cells. This cellular behavioural aspect and interface of cell matrix are of high significance in the field of tissue engineering and regenerative medicine (Bai et al., 2020).

The prognostic score studies concerning cancer cells are helpful. It is useful to adopt immunotec panel. The least absolute shrinkage and selection operator, LASSO-Cox regressor, can identify at least 13 types of immunocytes. The techniques like 'time dependent receiver operator (ROC) curve' and 'Kaplan-Meier survival estimation', and 'signature based immune marker', like, CD8 mRNA expression and CD8+expressing T-cells, are useful in such studies. The novel prognostic immune score based technique is also helpful to predict overall survival rate during colorectal cancer related investigations (Tang et al., 2021).

Blood platelets are the products of megakaryotes and are very active in the blood stream. These blood components exhibit changes in the distribution of the respective biomolecules. The allocation of biomolecules like thrombospondin, fibrinogen and glycoproteins IIb-IIIa and glycoprotein Ib is not same during the activation and resting phases of the platelets. The immunoelectron microscopy shows different allocation of thrombospondin and fibrinogen. Such alterations in the membrane due to the different distribution of such biomolecules may affect the functional topography of these blood structures (Asch et al., 1985)

The functioning of biochemical signals relates with chemistry, geometry, topography and physicochemical features of biomaterials, more so during specific ligand-receptor binding processes. Such interactions control the cell-matrix interactivity. The designing and the topography of nanoscale materials play significant role at cell-biomaterial interface. Consequently, the interactions between biological and nanomaterial interface influence the cellular topography, signaling process and cellular behavior (Di-Cio and Gautrot, 2016).

SOME COMMON PATHOLOGICAL CONDITIONS AND IMAPCTS OF NANOMATERIALS ON CELLULAR TOPOGRAPHY

Pituitary adenoma cells show blebs, wrinkles, microvilli, on their surface. The small uniform granules spread along the cell membrane; in case of normal cells these granules are much larger (Ilona et al., 2005). The surface of tumor cells, breast cancer cells is highly roughened. The proteins of cytoskeleton are more, probably adding to the roughness of cell membrane and affecting its topography. There is a disturbed gene expression for the skeletal proteins (Kaul-Ghanekar et al., 2009). The defense system of body responses to the injury and disease and involves cellular inflammation. The inflammatory cells are effective components of immune system and help in destruction of an agent that causes injury or disease. These cells also invite other inflammatory cells to participate and to remember the disease; this facilitates their response to the future infection. Specifically, those cells which present antibody like macrophages and dendritic cells participate in the immune response. This is also true in case of synthetic materials used in the implantation devices, drug delivery systems. Such interactions influence the processes of healing and inflammation. There are possible fluctuations in the biochemical, biophysical aspects and topography of the cells membrane when come in contact. These modifications critically involve in the pre, pro, and anti-inflammatory immune responses (Rustam et al., 2015).

The interactions between cells and the interacting substrate, (physical or biological) relate with the physical forces and cause changes in the structure of cell membrane, this involves topography also (Curtis and Wilkinson, 1998), and the mechanism involved needs through understanding. The multiple uses of nanomaterials in medical and biomedical sciences are the prime sources of their entry in biosystems and also large numbers of biomolecules are within the nanoscale which affects the cell membrane. Thus, biological cells have to interact with such nanoscaled materials (Curtis et al., 2001). Overall, nanomaterials because of the specific mechanisms affect cellular functions like proliferation, differentiation, signaling pathways, cell membrane and cytoskeleton (Abdal et al., 2018). TiO_2 nanoparticles impact functions of cell membrane and cytoskeleton (Hou et al., 2013). Barium-titanate nanoparticles affect proliferation of cells (2013). Glyco-chitosan coated barium titanate nanoparticles affect organization of cytoskeleton (Ciofani et al., 2013). TNT-TiO_2 nanoparticles influence cell surface area (Liu et al., 2015). These are some of the aspects that influence topography of cell membrane.

Thus, the reports reflect on the changed cellular topography due to pathological conditions and nanomaterials in a biosystem and existence of lacuna in understanding the mechanisms involved. There appears a

wide scope for further study related to cellular topography under various pathological conditions, in relation to nanodevices, pharmaceutics, and drug delivery. Such studies will better the insight of the processes like tissue regeneration, tissue engineering, senescence, and remedial techniques in the medical and biomedical engineering.

ACKNOWLEDGEMENT: Author gratefully acknowledges the encouragement from Dr. P M Dongre, Head, Department of Biophysics, University of Mumbai, and Author also conveys thanks to the Principle (Dr.) Chakraborti and Dr. Mohite, Head, Department of Zoology, Thakur College of Science and Commerce, Kandivli (east), Mumbai, India.

ONFLICTS OF INTREST: Author declares no conflict of the interest.

DECLARATION OF FUNDING: No funding required for this presentation.

REFERENCES

1. Abdal D A, Lee SB, and Cho SG, (2018) Impact of Metallic Nanoparticles on Stem Cell Proliferation and Differentiation, Nanomaterials (Basel, Switzerland, 8(10): 761. https://doi.org/10.3390/nano8100761
2. Asch AS, Leung LL, Polley MJ, and Nachman RL, (1985) Platelet membrane topography: colocalization of thrombospondin and fibrinogen with the glycoprotein IIb-IIIa complex, Blood, 66(4): 926–934. https://doi.org/10.1182/blood.V66.4.926.926
3. Bai M, Cai L, Li X, Ye L, and Xie J, (2020) Stiffness and topography of biomaterials dictate cell-matrix interaction in musculoskeletal cells at the bio-interface: A concise progress review, Journal of Biomed Mater Res B, Applied Biomaterial Research, 108(6): 2426-2440. doi: 10.1002/jbm.b.34575.
4. Brunette D M, Kenner GS, and Gould TRL, (1983) Grooved titanium surfaces orient growth and migration of cells from human gingival explants, J. Dental Research, 62(10): 1045-048. http://jdr.sagepub.com/content/62/10/1045 T
5. Boucrot E and Kirchhausen T, (2007) Endosomal recycling controls plasma membrane area during mitosis, PNAS, 104(09): 7939-7944. www. pnas.org/egi/doi/10.1073/pnas.0702511104
6. Carman PJ and Dominiquez R, (2018) BAR domain proteins- linkage between cellular membranes, signalling pathways, and actin cytoskeleton, Biophysical Reviews, 10(6): 1587-1604. DOI: 10.1007/s1255-018-0467-7
7. Ciofani G, Ricotti L, Canale C, D'Alessandro D, Berrettini S, Mazzolai B, and Mattoli V, (2013) Effects of barium-titanate nanoparticles on proliferation and differentiation of rat mesenchymal stem cells, Colloids Surf, B, 102: 312–320. doi: 10.1016/j.colsurfb.2012.08.001:
8. Curtis ASG and Clark P, (1990) The Effect of Topographic and Mechanical Properties of Materials on Cell Behaviour, Critical Reviews in Biocompatibility, 5: 343-362.
9. Curtis AS and Wilkinson CD, (1998) Reactions of cells to topography, J Biomater Sci Polym Ed, 9(12): 1313-1329. doi: 10.1163/156856298x00415.
10. Curtis AS, Casey B, Gallagher JO, Pasqui D, Wood MA, and Wilkinson CD. (2001) Substratum nanotopography and the adhesion of biological cells: Are symmetry or regularity of nanotopography important? Biophys Chem., 94(3): 275-283. doi: 10.1016/s0301-4622(01)00247-2.
11. Di Cio S, and Gautrot JE, (2016). Cell sensing of physical properties at the nanoscale: Mechanisms and control of cell adhesion and phenotype. Acta Biomaterialia, 30: 26-48. doi: 10.1016/j.actbio.2015.11.027
12. Gauthier NC, Rossier OM, Mathur A, Hone JC, and Sheetsz MP, (2009) Plasma membrane area increases with spread area by exocytosis of GPI anchored protein component, Molecular Biology of Cell, 20(14): 3261-3272. https://doi.org/10.1091/mbc.e09-01-0071
13. Hamilton DW, Ghrebi S, Kim H, Chehroudi B, and Brunette DM, (2008) Surface Topography and Cell Behavior, Encyclopedia of Biomaterials and Biomedical Engineering, DOI: 10.1081/E-EBBE-12004162
14. Harrison RG, (2011) On the stereotropism of embryonic cells. Science, 34(370): 279–381. DOI: 10.1126/science.34.870.279
15. Hemelaar SR, Nagl A, Bigot F, Rodríguez-García MM, de Vries MP, Chipaux M, and Schirhagl R, (2017) The interaction of fluorescent nanodiamond probes with cellular media, Mikrochimica acta, 184(4): 1001–1009. https://doi.org/10.1007/s00604-017-2086-6
16. Hou Y, Cai K, Li J, Chen X, Lai M, Hu Y, Luo Z, Ding X, and Xu D, (2013) Effects of titanium nanoparticles on adhesion, migration, proliferation, and differentiation of mesenchymal stem cells, International Journal of Nanomed, 8: 3619.
17. Ingela P and Onfelt B, (2013) Consequences of membrane topography, The Federation of European Biochemical society (FEBS) Journal, 280(12): 2775-2784. https://doi.org/10.1111/febs.12209
18. Ilona F, Hegedus B, Bacsy E, Kerekes E, Slowik F, Balint K, and Pasztor E, (2005) Characterization of human pituitary adenoma cell cultures by light and electron microscopic morphology and immunilabelling, Folia Histochemica et Cytobiologica, 43(2): 81-90. DOI: 10.5603/4617
19. Kaul-Ghanekar, R., Singh, S., Mamgain, H. Jalota-Badhwar A, Paknikar KM, and Chattopadhyay, (2009) Tumor suppressor protein SMAR1 modulates the roughness of cell surface: combined AFM and

SEM study, *BMC Cancer*, 9: 350. https://doi.org/10.1186/1471-2407-9-350

20. Lahir YK, (2016) Understanding the basic role of glycocalyx during Cancer, Journal of Radiation and Cancer Res, 7(3): 79-84. DOI: 104103/0973-0168.197974
21. Lahir YK, (2021) Do Cells of Biosystems Exhibit Intelligence? Innovations Tissue Engineering & Regeneration Medicine, 1(5), ITERM.000522.2021
22. Lahir YK and Chitre AV, (2021) Biochemical and physiological modulations on cell organelles induced by molecular crowding, World Journal of Pharmacy Research, 2021; 10(8): 723-747. DOI: 10.20959/wjpr20218-20947
23. Lahir YK, Avti P, and Chitre AV, (2021) Interactive Correlation between Exosomes and Nanomaterials, Advances in Clinical Toxicology; med win publishers, 2021; 6(4): 000227. DOI: 10.23880/act-16000227
24. Liu W, Su P, Chen S, Wang N, Wang J, Liu Y, Ma Y, Li H, Zhang Z, and Webster TJ, (2015), Antibacterial and osteogenic stem cell differentiation properties of photoinduced TiO_2 nanoparticle-decorated TiO_2 nanotubes, Nanomedicine, 10: 713–723. doi: 10.2217/nnm.14.183.
25. Sitraska E and Diz-Munoz A, (2020) Pay attention to membrane tension: Mechanobiologial of cell Surface, Current Opinion in Cell Biology, 66: 11-18. https://doi.org/10.1016/j.ceb.2020.04.001
26. Nichol JA and Hutter OF, (1996) Tensile strength and dialatational elasticity of giant sarcolemmal vesicles shed from rabbit muscle, Journal of Physiology, 493(1): 187-198. https://doi.org/10.1113/jphysiol.1996.sp021374
27. Rostam HM, Singh S, Vrana NE, Alexander MR, and Ghaemmaghami AM, (2015) Impact of surface chemistry and topography on the function of antigen presenting cells. Biomater Sci, 3(3): 424-441. doi: 10.1039/c4bm00375f.
28. Tang Z, Wu Y, Sun D, Xue X, and Qin L, (2021) A novel prognostic immunoscore based on The Cancer Genome Atlas to predict overall survival in colorectal cancer patients, Bioscience Reports, 2021; 41: BSR20210039. https://doi.org/10.1042/BSR20210039
29. Walter JB and Israel MS, (1987) M.S. General Pathology, 6th Ed, Churchill Livingstone: Edinburgh.
30. Weiss P, (1945) Experiments on cell and axon orientation in vitro: the role of colloidal exudates in tissue organization, J. Exp. Zool, 1945; 12/100: 353–386. ID PMID: 21010856