International Journal of Solids and Structures 48 (2011) 388–395

Contents lists available at ScienceDirect

International Journal of Solids and Structures

journal homepage: www.elsevier.com/locate/ijsolstr

Specific adhesion of vesicles to compliant bio-adhesive substrates

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ARTICLE INFO

Article history:
Received 20 April 2010
Received in revised form 27 September 2010
Available online 16 October 2010

Keywords:
Vesicle
Bio-adhesion
Rigidity
Thermodynamics
Gibbs free energy

ABSTRACT

Cell behavior is mediated by variety of physiochemical properties of the extracellular matrix (ECM). Mechanical stiffness of ECM, in particular, is found to be a major regulator for the multiple aspects of cellular function. Experiments show that cells generally exhibit an apparent adhesion preference for stiffer substrates. The effect of substrate elasticity is also found to be strongly coupled with adhesivity of the substrate. To understand the underlying physics of rigidity sensing mechanism in cells, in this study we use a vesicle-substrate system to model cell adhesion as a first order approximation. Within this framework, an equilibrium thermodynamic analysis is undertaken to elucidate the interplay between substrate compliance and equilibrium configuration of an adherent vesicle. The equilibrium adhesion is assumed to ensure minimization of the free energy contributed by substrate deformation and interfacial adhesive and repulsive interactions between the membrane and substrate. The predictions of this purely mechanistic model are found to be qualitatively analogous to some of the characteristic features of cell adhesion to compliant bio-adhesive substrates. This observation suggests that the physical aspects of the membrane–substrate interfacial interactions could passively contribute in regulation of the rigidity sensing by cells.

1. Introduction

Cell behavior is mediated by variety of physiochemical properties of extracellular matrix (ECM). Surface chemistry (Liu et al., 2007; Morgenthaler et al., 2008), roughness (Martin et al., 1995; Lampin et al., 1998) and distribution pattern of cell adhesive proteins (Chen et al., 1998; Christman et al., 2006; Cavalcanti-Adam et al., 2007) are among the ECM properties which are known to modulate various cellular physiological functions. Mechanical stiffness of ECM is also found to be a major regulator for multiple aspects of cellular function, ranging from cell motility to the lineage commitment and differentiation (Discher et al., 2005). Quantification of migration speed of motile cells cultured on substrate with variable stiffness reveals a biphasic dependence on substrate compliance, suggesting the existence of an optimal stiffness capable of supporting maximal speed of migration (Peyton and Putnam, 2005). Contractile cells, such as vascular smooth muscle cells (VSMC), become more proliferative and less apoptotic in response to the increasing the substrate stiffness (McDaniel et al., 2007). Other studies have demonstrated the strong influence of substrate elasticity on the lineage commitment of naive stem cells and driving their differentiation to variety of mature cells (Engler et al., 2004a, 2006).

The acute molecular basis of the sensory mechanism through which the tissue cells sense the ECM elasticity and translate it into a downstream response is largely unknown. It is currently believed that the downstream signaling in response to the matrix stiffness should be started at the molecular level and by transmembrane integrin *receptors* present on the surface of adherent cells. These mobile proteins can selectively associate with the complementary adhesive *ligand* molecules of ECM, providing not only the adhesion between the cell membrane and the matrix, but also a pathway of force transmission from inside the cell to the elastic substrate. The cytoskeletal force exerted on the ligand–receptor anchorage sites can deform the soft substrate and trigger the action of signaling molecules and mechano-transducers (Schwarz and Bischofs, 2005). Considering the role of these receptor-mediated linkages in initiation of the elasto-sensitivity, one could expect that substrate stiffness may also regulate the state of cellular adhesion. Pelham and Wang (1997) in a seminal study reported that the adhesion of rat kidney epithelial and 3T3 fibroblastic cells are strongly regulated by the rigidity of the underlying collagen coated polyacrylamide substrates. Subsequent and more quantitative works with different elastic substrates showed that cells in general, exhibit an apparent adhesion preference for stiffer substrates with a more organized cytoskeleton and a larger but saturable projected spread area with increasing the substrate stiffness (Lo et al., 2000; Engler et al., 2004b).

How stiffness couples with adhesiveness of the substrate to upregulate the cellular adhesion is a question raised recently with

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doi:10.1016/j.ijsolstr.2010.10.011