

Molecular forces at cell surface

Single cell force spectroscopy by AFM approach

Pierre-Henri Puech
puech@marseille.inserm.fr
Inserm 600 / CNRS 6212, Marseille – France

Abstract

[...] *The establishment of cell adhesion involves specific recognition events between individual cell-surface receptors and molecules of the cellular environment. However, characterizing single-molecule adhesion events in the context of a living cell presents an experimental challenge. The atomic force microscope (AFM) operated in force spectroscopy mode provides an ultrasensitive method to investigate cell adhesion forces at the level of single receptor-ligand bonds. With a living cell attached to the AFM cantilever, the number of cell-substrate interactions can be controlled and limited to the formation of single receptor-ligand bonds. From force-distance (F-D) curves recorded during cell detachment, the strength of single receptor-ligand bonds can be determined. Furthermore, by varying the rate of force application during bond rupture, a dynamic force spectrum (DFS) can be generated from which additional parameters that describe the energy landscape of the interaction, such as dissociation rate and energy barrier width, can be obtained. [...]*

In a first part, I will introduce the use of atomic force microscopy (AFM) in the force mode, and present the way the data is gained and analysed. Then I will introduce the pros and cons of analysing the recognition / adhesive events at cellular surface. I will then focus on the methodology and requirements to measure single molecule adhesive forces, starting with cell to “semi-artificial surfaces” interactions.

Based on published results, I will present the conclusions, both on the type and on the mechanisms of the measured recognition events. The need of a critical eye on the kind of controls that such a technique requires will be emphasized. The extension to the measure of single molecule forces between cells will be presented and perspectives will be drawn, in regards to cell mechanics and cytoskeletal interactions.

References

- [1] M. Krieg, Y. Arboleda1, P.-H. Puech, J. Käfer, F. Graner, D. J. Muller and C.-P. Heisenberg Tensile forces govern germ layer organization in zebrafish To appear in NATURE CELL BIOLOGY, feb. 2008
- [2] F. A. Fierro, A. Taubenberger, P.-H. Puech, G. Ehninger, M. Bornhauser, D. J. Muller and T. Illmer BCR/ABL expression of myeloid progenitors increases 1-integrin mediated adhesion to stromal cells JOURNAL OF MOLECULAR BIOLOGY Available online 5 February 2008
- [3] C. M. Franz, A. Taubenberger, P.-H. Puech, D. J. Muller Studying integrin-mediated cell adhesion at the single-molecule level using AFM force spectroscopy. SCIENCE STKE. 2007 Oct 2;2007(406):pl5.
- [4] Characterizing early steps of $\alpha_2\beta_1$ -integrin-mediated adhesion to collagen type I using single-cell AFM force spectroscopy Taubenberger A, Cisneros DA, Friedrichs J, Puech PH, Müller DJ, Franz CM Mol Biol Cell. 2007 Feb 21; PMID: 17314408
- [5] A new technical approach to quantify cell-cell adhesion forces by AFM Puech PH, Poole K, Knebel D and Muller DJ Ultramicroscopy. 2006 106(8-9):637-44..
- [6] Wnt11 Functions in Gastrulation by Controlling Cell Cohesion through Rab5c and E-Cadherin. Ulrich F, Krieg M, Schotz EM, Link V, Castanon I, Schnabel V, Taubenberger A, Müller DJ, Puech PH, Heisenberg CP. Dev Cell. 2005 9:555-64.
- [7] Measuring cell adhesion forces of primary gastrulating cells from zebrafish using atomic force microscopy. Puech PH, Taubenberger A, Ulrich F, Krieg M, Müller DJ, Heisenberg CP. J Cell Sci. 2005 Sep 15;118 :4199-206.