Journal club

TO ADHERE OR NOT TO ADHERE?

Three papers, from different generations and technologies, all go against the prevailing notion — a view that might be distorted by two-dimensional (2D) migration models — that stringent adhesion is required for migration. Indeed, there are now clear examples of a type of non-adhesive cell migration in 3D tissues.

A key paper, by Lammermann *et al.* in 2008, shows by a *tour de force* using a quadruple knockout of all the integrins expressed by dendritic cells (β1, β2, β3 and β7 integrins; transmembrane proteins that bind adhesion proteins in the extracellular matrix (ECM)) that these cells move independently of integrins in 3D collagen gels and *in vivo*. Whatever the authors did to these cells, the cells moved in their typical amoeboid leukocyte-like migration mode, as long as actin turnover and myosin II function were normal. This suggests that actin forward flow and myosin II-mediated rear retraction are sufficient for dendritic cell migration.

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By 1982, Haston *et al.*, led by a pioneer in the leukocyte migration field, Peter Wilkinson, had already discovered that although T cells are non-adhesive on 2D collagen (easily washed away with the supernatant), they migrate normally in 3D collagen lattices. Friedl *et al.* (my group during my Ph.D. studies) showed, using quadruple antibody-mediated integrin inhibition, that T cells in 3D collagen lattices never form focal adhesion structures and they move at the same rate even after all their integrins are blocked — results that differ from most other cells studied.

However, only the genetic approach of Lammermann *et al.* provides proof that no residual low-level integrin binding is contributing to non-adhesive cell migration in 3D tissues. Now that this blockbuster paper is published, it is up to lively debate and future studies to determine how this non-adhesive migration works. The non-adhesive cell could have a fluid but rigid body that enables it to ‘wiggle’ through a 3D matrix but loses this and flows around on a 2D surface. Alternatively, other adhesion moieties could be at work that weakly bind to the ECM, such as syndecans or discoidin domain receptors. Cell migration is such an important, versatile process that several mechanisms are probably active at the same time, such that evolution has decided on our behalf that integrins are one of the ways, but not the only way, forward.

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ORIGINAL RESEARCH PAPERS
Lammermann, T. *et al.* Rapid leukocyte migration by integrin-independent flowing and squeezing. *Nature*, **453**, 51–55 (2008) | Haston, W. S. *et al.* Lymphocyte locomotion and attachment on two-dimensional surfaces and in three-dimensional matrices. *J. Cell Biol.* **92**, 747–752 (1982) | Friedl, P. F. *et al.* CD4$^+$ T lymphocytes migrating in three-dimensional collagen lattices lack focal adhesions and utilize β1 integrin-independent strategies for polarization, interaction with collagen fibers and locomotion. *Eur. J. Immunol.* **28**, 2331–2343 (1998)