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Global coordination of protrusive forces in migrating immune cells

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When migrating through mesenchymal tissues with fibrillar architecture, leukocytes rarely digest or permanently remodel their environment. Instead, they probe their vicinity to sense and select the path of least resistance. To do so they use their frontward-positioned nucleus as a gauge to choose larger pores over smaller ones.

We now show that in very dense tissues, where even the largest pores preclude free passage, cells push and laterally displace the surrounding matrix in order to transiently open a path for translocation of the cell body. To this end the cells revert from their usual amoeboid configuration, where the organelles like Golgi and Lysosomes are positioned behind the nucleus, to the mesenchymal configuration, where organelles are positioned towards the front. Associated with organelles we find a central actin pool that responds to mechanical compression and serves to laterally push into the surrounding matrix to transiently dilate a path. This central actin pool communicates with lamellipodial actin, which advances the cell body along the longitudinal axis, establishing a system that either creates space for passage or translocates forward. When we specifically delete the central actin pool, cells migrate faster in unrestricted environments because lamellipodial actin is enhanced. In complex 3D environments, locomotion is impaired because passage through constrictions depends on lateral pushing. Moreover, unleashed lamellipodial protrusion causes dissociation between leading edge and cell body, visible as actively detaching cell fragments that migrate away from the cell body.

Presenter: SIXT, Michael (Institute for Science and Technology Austria)