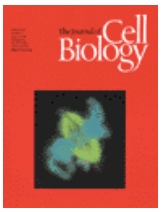

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A Role for Cdc42 in Macrophage Chemotaxis

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Three members of the Rho family, Cdc42, Rac, and Rho are known to regulate the organization of actin-based cytoskeletal structures. In Bac1.2F5 macrophages, we have shown that Rho regulates cell contraction, whereas Rac and Cdc42 regulate the formation of lamellipodia and filopodia, respectively. We have now tested the roles of Cdc42, Rac, and Rho in colony stimulating factor-1 (CSF-1)–induced macrophage migration and chemotaxis using the Dunn chemotaxis chamber. Microinjection of constitutively activated RhoA, Rac1, or Cdc42 inhibited cell migration, presumably because the cells were unable to polarize significantly in response to CSF-1. Both Rho and Rac were required for CSF-1–induced migration, since migration speed was reduced to background levels in cells injected with C3 transferase, an inhibitor of Rho, or with the dominant-negative Rac mutant, N17Rac1. In contrast, cells injected with the dominant-negative Cdc42 mutant, N17Cdc42, were able to migrate but did not polarize in the direction of the gradient, and chemotaxis towards CSF-1 was abolished.

We conclude that Rho and Rac are required for the process of cell migration, whereas Cdc42 is required for cells to respond to a gradient of CSF-1 but is not essential for cell locomotion.

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