Abstract

Retinoic acid, the active metabolite of Vitamin A is known to play a major role in embryonic growth and differentiation during development. It has been shown that either excess or deficiency of retinoic acid during embryogenesis can be teratogenic. In order to study the teratogenic effects of retinoic acid, the aim of the present study was therefore to investigate the effect of all-*trans* retinoic acid on the migration and fate of neural crest cells *in vitro* and *in vivo*. In addition, the study investigated the effect of retinoic acid on the cytoskeletal elements of neural crest cells and on Rac and Rho, two members of the Rho family of GTPases. The neural tubes containing neural crest cells of quail embryos were removed at cranial levels and cultured on fibronectin as a substrate. The neural tubes were cultured in either Dulbecco's minimal essential medium (DMEM) or in DMEM+Dimethylsulphoxide (DMSO) as controls. In order to test the effect of retinoic acid, the neural tubes were cultured in 10^{-5}M all-*trans* retinoic acid (RA) which was reconstituted in DMSO. The distance of migration of the cultured quail neural crest cells was measured and compared between the controls and the experimentals. To study the effect of RA on the cell actin cytoskeleton *in vitro*, cultured neural crest cells were stained with rhodamine phalloidin. In addition, following 24 hours of culture, the quail neural crest cells were brought into suspension and micro-injected into 36 hour-old chick hosts. While the migration of neural crest cells was extensive in the control cultures *in vitro*, migration was inhibited in the retinoic acid-treated neural crest cells. In addition, retinoic-acid treated neural crest cells showed pigmentation and neuronal processes earlier than did the control neural crest cells. Retinoic acid-treated neural crest cells showed a disarray of the cytoskeletal elements as they were devoid of stress fibres and focal adhesions. In addition, retinoic acid appears to decrease the expression of Rac and Rho of cultured quail neural crest cells. Following micro-injection of cultured control and RA-treated quail neural crest into the cranial region of chick hosts, the control cells populated the beak area, whereas the retinoic acid-treated quail neural crest cells migrated to the retina of the eye, a region they normally do not populate. These results suggest that retinoic acid disturbs the migration of neural crest cells. It appears to do this by affecting the cytoskeletal elements of neural crest cells and the genes that are involved in forming these elements.