

Antiangiogenic, antimigratory and antiinflammatory effects of 2-methoxyestradiol in zebrafish larvae

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Abstract

2-Methoxyestradiol (2ME), an endogenous metabolite of 17 β -estradiol, has been previously reported to possess antiangiogenic and antitumor properties. Herein, we demonstrate that the effects of this antiangiogenic steroid can be readily assayed in live zebrafish, introducing a convenient and robust new model system as a screening tool for both single cell and collective cell migration assays. Using the in vitro mammalian endothelial cell line EA.hy926, we first show that cell migration and angiogenesis, as estimated by wound assay and tube formation respectively, are antagonized by 2ME. In zebrafish (*Danio rerio*) larvae, dose-dependent exposure to 2ME diminishes (1) larval angiogenesis, (2) leukocyte recruitment to damaged lateral line neuromasts and (3) retards the lateral line primordium in its migration along the body. Our results indicate that 2ME has an effect on collective cell migration in vivo as well as previously reported anti-tumorigenic activity and suggests that the molecular mechanisms governing cell migration in a variety of contexts are conserved between fish and mammals. Moreover, we exemplify the versatility of the zebrafish larvae for testing diverse physiological processes and screening for antiangiogenic and antimigratory drugs in vivo..

Keywords

Angiogenesis, Neutrophil migration, Inflammation, Zebrafish, EA.hy926, Primordium, 2-methoxyestradiol.