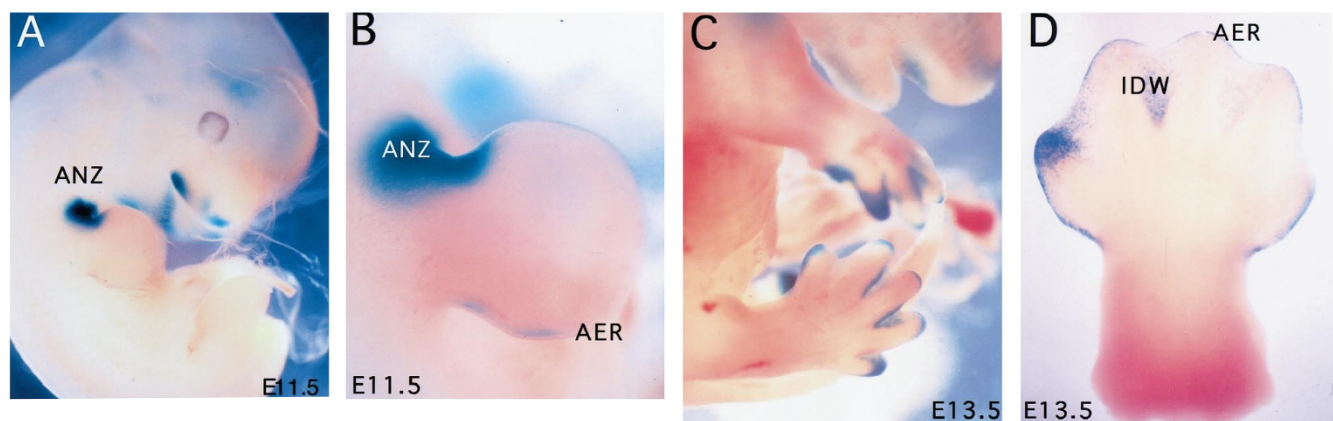


Educational corner

A transgenic mouse model for the study of apoptosis during limb development

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The expression and activation of the tissue transglutaminase gene is associated with apoptotic cell death in many cells and tissues. To gain insight into the regulation of this gene and the processes it is associated with we generated transgenic mouse lines.

The figure shows the expression pattern of the β -galactosidase marker gene under the control of a 3.8 kb fragment of the mouse tissue transglutaminase gene promoter in E11.5 and E13.5 mouse embryos stained with x-gal.

At E11.5 embryos of the lineage #26 showed β -galactosidase activity along the anterior edge of the proximal limb bud, in the craniofacial processes and in the mesenchyme of the developing cranium (panel A). Detailed evaluation of the anterior limb bud showed intense staining of cells in the region of the anterior necrotic zone (ANZ) with the faint appearance of transgene positive cells in the developing posterior necrotic zone and apical ectodermal ridge (AER) (Panel B). By E13.5 transgene expression in the limb is concentrated in the posterior necrotic zone, in the interdigital web and the apical ectodermal ridge (Panels C and D). Panel D shows a magnified view of the limb of an E13.5 embryo that demonstrates the presence of foci of β -galactosidase positive cells in both the posterior necrotic zone and in the interdigital web.

This lineage (#26) of transgenic mice shows a remarkably restricted pattern of transgene expression that parallels regions of apoptosis that occur during different stages of limb development. In the earliest embryos examined expression is restricted to the anterior margins

of the anterior limb bud. This region corresponds to the well characterized region of morphogenic apoptosis, the anterior necrotic zone (ANZ) described in detail in the chick. The expression is subsequently localized in the posterior and more distal aspects of the anterior limb bud. Ultimately expression of the transgene is limited to the interdigital zones and the posterior aspects of the developing hand-plate. The same pattern of transgene expression occurs in the hind-limb but delayed 24 h relative to the anterior limb.

The orderly and progressive expression of the transglutaminase transgene in the mouse limb and its remarkable coincidence with regions of apoptosis suggests this lineage may provide a useful model for investigating apoptosis during limb development.

Further reading

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