PINHEAD (pi): A NEW MUTANT GENE AFFECTING CRANIOFACIAL DEVELOPMENT IN THE AXOLOTL

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Introduction

Craniofacial development has been investigated by amphibian embryologists since the beginning of experimental embryology. Utilizing embryonic manipulations (Adelman , 1937) and chemical agents (Lehmann, 1938, Burgess, 1985) ,for example, craniofacial developmental defects have been induced in amphibian embryos. We feel, however, that the research advances in amphibian craniofacial development have reached a plateau due to the lack of mutant genes which affect craniofacial development. The present report describes the discovery and preliminary characterization of a new conditional (cold sensitive) mutation which affects craniofacial development in the Mexican axolotl (Ambystoma mexicanum). This new gene was named 'pinhead' (pi) because it is characteristically associated with reduced rostral head mass and reduced interocular distance.

Discovery

This new mutation was discovered in 1979 in the so-called Tompkins - DeLanney (Justus) line, when embryos in spawning #4885 of the Indiana University Axolotl Colony exhibited abnormal craniofacial development. In this spawning 20% (13) of the fertile eggs reared at 10°C exhibited craniofacial developmental defects when observed at the prehatching stage (stage 41-42). All the defective embryos hatched but eventually died, presumably because they could not feed. The siblings maintained at room temperature (20-22°C), however, developed normally to sexual maturity. The lineage of the pi gene is discussed in an accompanying report by Susan Duhon.

Phenotype

The pinhead phenotype is characterized at the prehatching and newly hatched stage (stage 41-44) by a dramatic reduction in rostral head mass, reduced interocular distance (including cases of cyclopia perfecta), and oral cavity defects. The rest of the embryo from the caudal head region (hindbrain) posterially appears normal (Figure 1). Histological analysis of pi prehatching embryos also reveals developmental abnormalities associated with the rostral head region. There is a wide range of developmental defects ranging from a slight decrease in interocular distance to embryos with synophthalmia and cyclopia

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perfecta. The more reduced the interocular distance, the more severe the abnormalities of the olfactory bulbs (including fused and single bulbs), abnormalities of the forebrain (including single telencephalon with structural disorganization), abnormalities of the diencephalon (disorganization), and abnormalities of the oral cavity (including cases with no oral cavities). In contrast the pharynx, gills, hindbrain, parachordal cartilages, notochord, and otic vesicles and the rest of the embryo appear relatively normal.

Figure 1. Gross morphology of the pi phenotype. Dorsal views of stage 42 axolotl larvae. Top - normal (control) morphology. Middle - typical pi phenotype showing reduced rostral head mass and reduced interocular distance. Lower - extreme pi phenotype with cyclopia perfecta showing severe reduced rostral head mass and reduced pigmentation typical of cyclopic pi larvae. Note the relatively normal caudal morpholgy of the pi mutants beginning with the hindbrain and the gills. Bar = 1mm.

Genetics

The pi gene appears to be recessive with incomplete penetrance. In twelve test spawnings (1979 through 1985) grown at temperatures ranging from 10°C to 25°C, 12.9% (3.2-21.5) of the embryos expressed the pi phenotype. The pi gene appears to be temperature sensitive (cold sensitive). Penetrance of the pi phenotype is increased by incubating fertile eggs at a cooler temperature until the prehatching stage. In seven test spawnings 17.6% (0.0 -35.8) of the embryos reared at 10°C showed the pi phenotype while only 5.6% (0.0-14.3) of the embryos incubated at 18-25°C expressed the pi phenotype.

Bibliography

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