<Further Development 18_06>

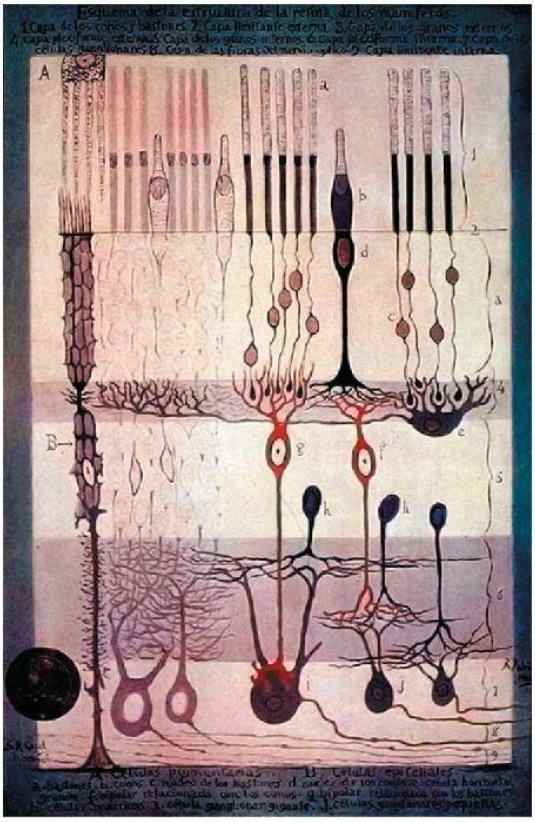
Neural Retina Differentiation

Like the cerebral and cerebellar cortices, the neural retina develops into a layered array of different neuronal types (Figure 1A). In mammals, these layers include the light- and color-sensitive photoreceptor cells (rods and cones); the cell bodies of the ganglion cells; and bipolar neurons that transmit electric stimuli from the rods and cones to the ganglion cells (Figure 1B). In addition, the retina contains numerous Müller glial cells that maintain its integrity, amacrine neurons (which lack large axons), and horizontal neurons that transmit electric impulses in the plane of the retina.

(A)

Courtesy of Andy J. Fischer.

(B)



Courtesy of the Instituto Cajal, CSIC, Madrid.

Figure 1 Retinal neurons sort out into functional layers during development. (A) Fluorescent labeled confocal micrograph of chick retina, showing the three layers of neurons and the synapses between them. (B) The mammalian retina as drawn and labeled by Santiago Ramón y Cajal in 1900. *Numerical labels:* 1, photoreceptor layer; 2, external limiting membrane; 3, outer granular layer; 4, outer plexiform layer; 5, inner granular layer; 6, inner plexiform layer; 7, ganglion cell layer; 8, optic nerve fiber layer; 9, internal limiting membrane. *Alphabetical labels:* A, pigmented cells; B, epithelial cells; a, rods; b, cones; c, rod nucleus; d, cone nucleus; e, large horizontal cell; f, cone-associated bipolar cell; g, rod-associated bipolar cell; h, amacrine cell; i, giant ganglion cell; j, small ganglion cell.

The neuroblasts of the retina appear to be competent to generate all the retinal cell types (Turner and Cepko 1987; Yang 2004). In amphibians, the type of neuron produced from a multipotent retinal stem cell appears to depend on the *timing* of gene translation. Photoreceptor neurons, for instance, are specified through expression of the *Xotx5b* gene, while *Xotx2* and *Xvsx1* expression is critical for specifying the bipolar neurons. Interestingly, these three genes are transcribed in all retinal cells, but

they are translated differently. Those *Xenopus* neurons whose birthday is at stage 30 translate *Xotx5b* mRNA and become photoreceptors, while those neurons forming later (birthdays at stage 35) translate the *Xotx2* and *Xvsx1* messages and become bipolar interneurons (Decembrini et al. 2006, 2009). This time-dependent regulation of translation is mediated by microRNAs.

Not all the cells of the optic cup become neural tissue. In addition to the pigmented epithelium that forms from the outer layer of the optic cup, the tips of the optic cup on either side of the lens develop into a pigmented ring of muscular tissue called the iris. The iris muscles control the size of the pupil (and give an individual his or her characteristic eye color). At the junction between the neural retina and the iris, the optic cup forms the ciliary body. This tissue secretes the aqueous humor, a fluid needed for the nutrition of the lens and for forming the pressure needed to stabilize the curvature of the eye and the constant distance between the lens and the cornea.

Literature Cited

Decembrini, S. and 9 others. 2009. MiRNAs couple cell fate and developmental timing in retinal histogenesis. *Proc. Natl. Acad. Sci. USA* 106: 21179–21184.
PubMed Link

Decembrini, S., M. Andreazzoli, R. Vignali, G. Barsacchi and F. Cremisi. 2006. Timing the generation of distinct retinal cells by homeobox proteins. *PLoS Biol*. 4: e272.
PubMed Link

Turner, D. L and C. L. Cepko. 1987. A common progenitor for neurons and glia persists in rat retina late in development. *Nature* 328: 131-136.
PubMed Link

Yang, X.-J. 2004. Roles of cell-extrinsic growth factors in vertebrate eye pattern formation and retinogenesis. *Sem. Cell Dev. Biol.* 15: 91–103.
PubMed Link