

ISTITUTO PASTEUR – FONDAZIONE CENCI BOLOGNETTI
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Research area: Molecular genetics of Eukaryotes.

Research project: Specification and maintenance of retinal stem cells.

Abstract

The developing eye is a favoured model system to study formation of the central nervous system (CNS), due to its accessible peripheral position, and to its simple and well-characterized structure. The mature retina consists of only six cell classes, identifiable by their morphology and molecular markers. Several vision-impairing diseases, such as retinitis pigmentosa and macular degeneration, are due to the loss of retinal cells. Studies in animals suggest that they may be treatable by transplantation of healthy retinal cells, but obtaining a sufficient number of suitable donor cells remains a major problem. This has propelled stem cell based approaches to generate pure populations of retinal cells in vitro, to be used for cell-replacement therapy.

Retinal stem cells (RSCs) are specified early in development as a result of three consecutive steps. First, the neuroectoderm is induced in the dorsal part of the embryo. Subsequently, the neuroectoderm is patterned along the embryonic antero-posterior (AP) axis, specifying forebrain, midbrain, hindbrain and spinal cord at different AP levels. Finally, a subset of the forebrain is specified as the eye field, containing the RSCs, while neighbouring regions take on alternative fates, such as telencephalon and diencephalon. Several pathways controlling neural induction and patterning have been identified. Yet, our understanding of their mechanisms of action and their precise roles during RSC specification is very incomplete. In whole organisms, it is difficult to distinguish among potential multiple roles of the same pathway, which can be more easily dissected using in vitro systems.

We are using mammalian pluripotent stem cells, such as embryonic stem cells, epiblast stem cells and induced pluripotent stem cells, as experimental in vitro systems to study the signalling systems controlling neural induction and patterning and the specification of RSCs. In order to address whether RSCs derived from pluripotent cells in vitro are equivalent to RSCs in the developing eye and that the specification pathways reconstructed in vitro recapitulate those acting in vivo, we are also isolating RSCs from the mouse embryonic eye to compare them with RSCs obtained in vitro.