Many have advocated that agricultural biotech graduate from the first generation of transgenic crops, exemplified by the expression of heterologous genes conferring pesticide and herbicide resistance, to a class of crops engineered to meet the growing demand for food, feed, fiber, fuels and biomaterials. The study by Zhang *et al.*[1] illustrates the promise of the next generation of transgenic crops.

COMPETING FINANCIAL INTERESTS
The authors declare no competing financial interests.

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A self-assembling retina

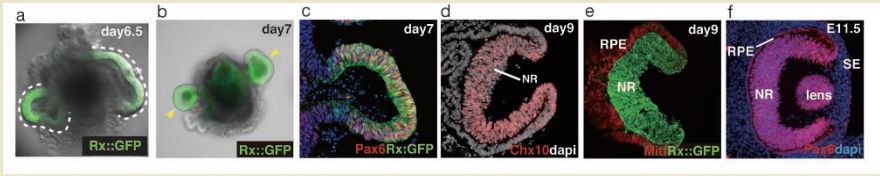

Figure 1 Stages in the generation of a mouse retina *in vitro*. NR, neural retina; SE, surface ectoderm.

Unlike the eye of mollusks, the vertebrate eye is oriented upside down[1]. Light-sensitive cells—the rods and cones—are located in the outermost layer of the neurosensory retina, furthest from the eye chamber and the incoming light. The inner retinal layers, closest to the light, contain the interneurons and ganglia that transmit optical signals to the brain, on the far side of the photoreceptor layer. In a new study[2] that marks an exciting advance in the use of embryonic stem cells (ESCs) to mimic development, this distinctive retinal structure has now been shown to emerge spontaneously *in vitro* starting with little more than mouse ESCs, the growth factor activin/nodal and a bit of extracellular matrix.

ESCs have already been differentiated into cells that resemble many of the cell types in the retina, including photoreceptors, neural cells and retinal pigment epithelium (RPE). But how can cells of different types be assembled *in vitro* into a complex organ such as the eye? For the self-assembling retina, all that was needed were slight modifications of the differentiation conditions. The critical new component was Matrigel or purified extracellular matrix proteins, which were added because they are known to promote the growth of epithelial structure.

As Eiraku *et al.*[2] show in time-lapse images taken over 9 days of culture, an *in vitro*–generated retina begins as a floating aggregate of ESCs. Soon, in the presence of extracellular matrix, the cells begin to express Rx, a marker of the retinal anlage. By day 6, the aggregate becomes a hollow sphere of polarized epithelial cells, and the Rx^+ cells self-associate into distinct Rx^+ islands (**Fig. 1a**). By day 7, the Rx^+ islands form vesicles that project out from the hollow sphere (**Fig. 1b**) and that express the retinal marker Pax6 (**Fig. 1c**).

Over the next three days, the vesicle involutes, creating the double-walled C shape of the developing retina (**Fig. 1d**). The outer wall expresses markers of RPE (**Fig. 1e**) and becomes pigmented, similar to the embryonic outer retina, and the inner wall expresses additional makers of the inner, neurosensory retina (**Fig. 1d**). Overall, the structure bears a striking resemblance to the mouse embryonic optic cup (**Fig. 1f**).

In the last stage, over days 20–24, the inner wall stratifies, revealing the characteristic upside-down architecture of the neurosensory retina. Markers of many of the expected cell types appear in their appropriate anatomical locations—photoreceptors (largely rods) on the outside, adjacent to the RPE, and ganglia, bipolar cells, horizontal cells, amacrine cells and Muller glia on the inside.

The generation of self-assembling retinas raises intriguing questions for future research. Are the retinas functional? What drives the self-assembly process at the molecular level? Can the method be adapted to human cells or to other organs? The work is also likely to have therapeutic implications if *in vitro*–generated retinas can be used for disease modeling and drug screening or as a source of cells for transplantation.

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