PROFILES

Gordon Fishell: Oracle's gift to autism

BY **VIRGINIA HUGHES**

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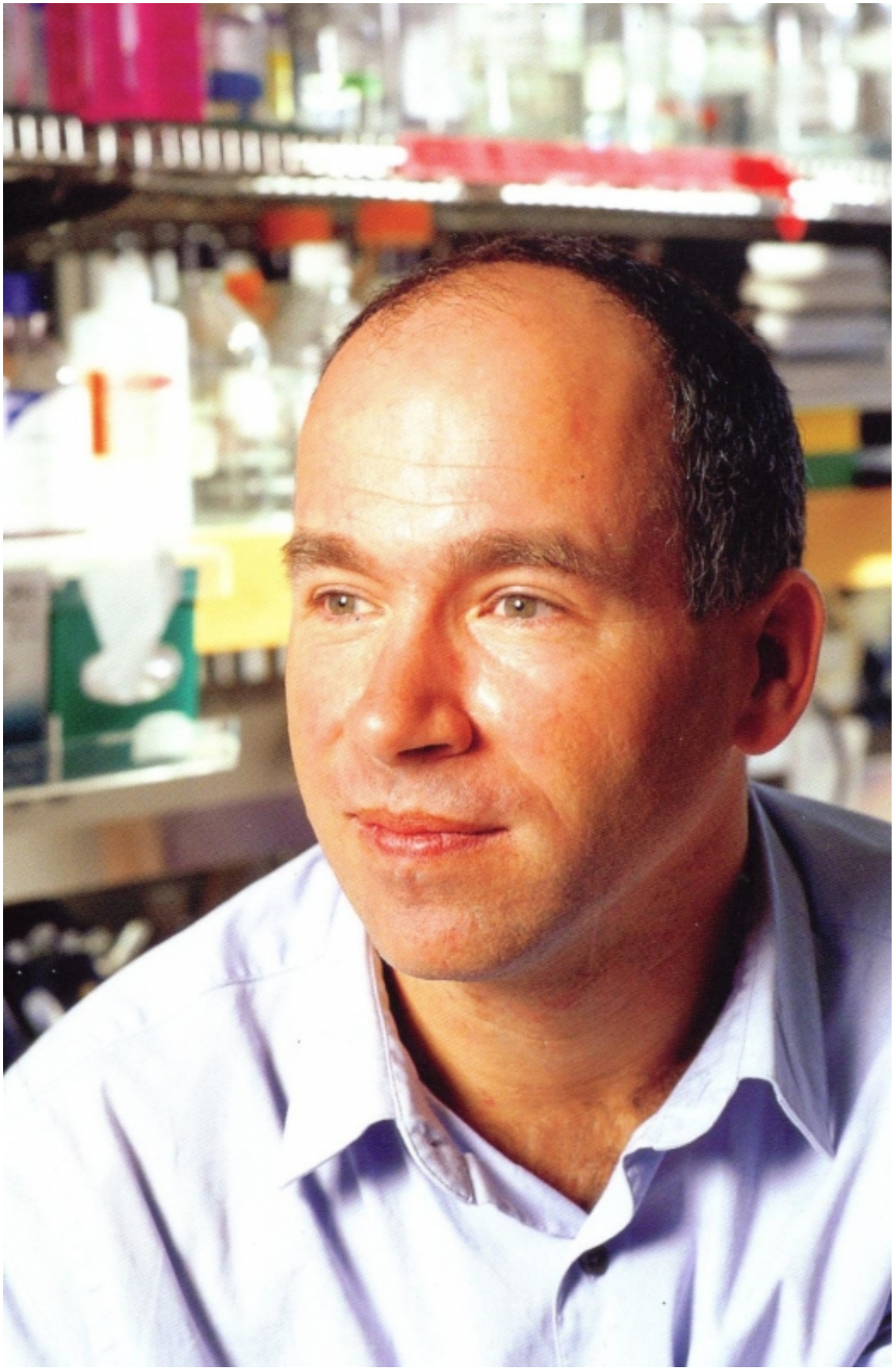

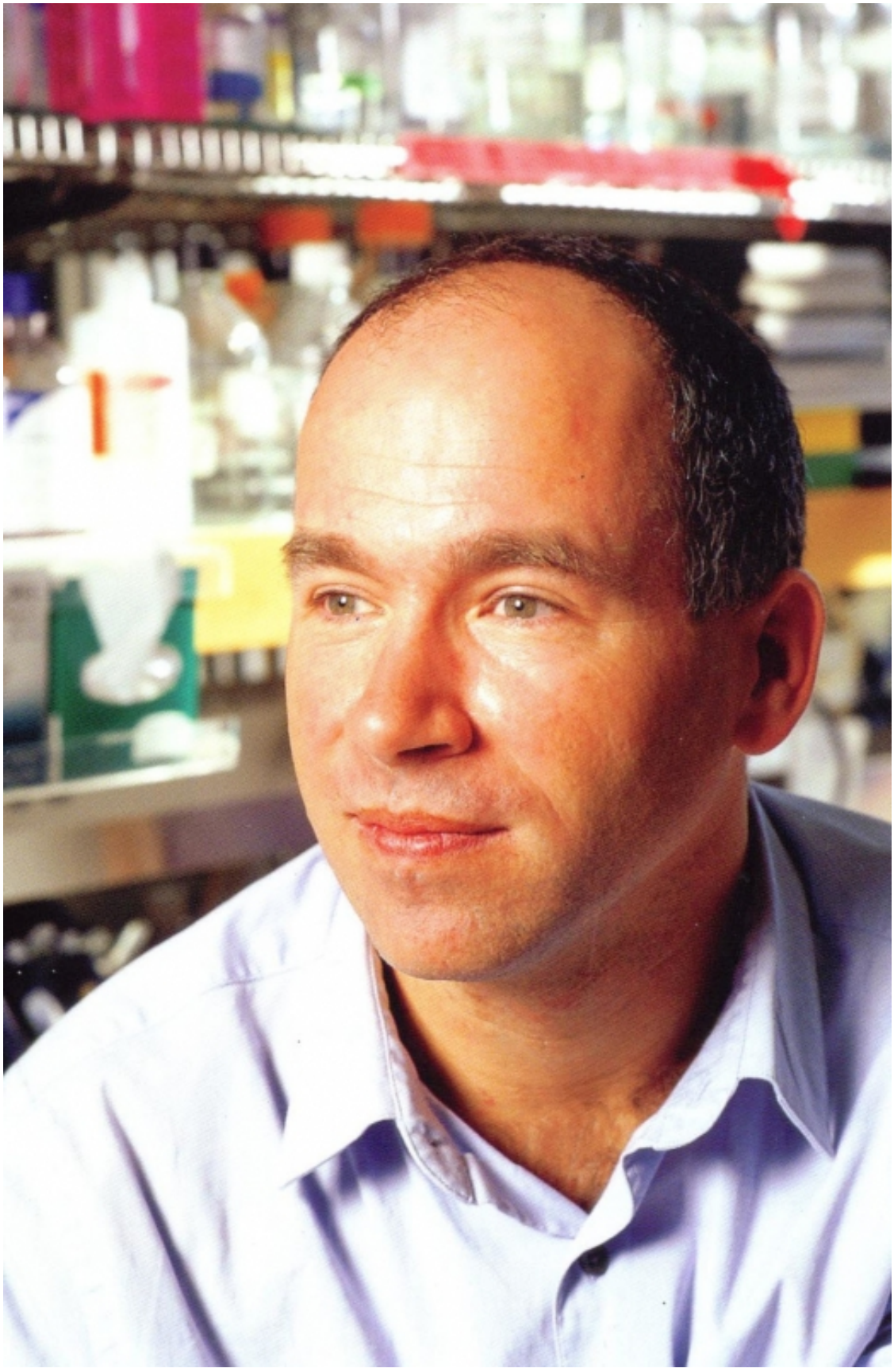

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In May 2002, on an isolated hilltop in Delphi overlooking the Aegean Sea, several dozen scientists convened to discuss how the cerebral cortex, the brain's outer layer, develops.

It was there, at the site of the legendary Greek oracle, that Gordon Fishell reached a turning point in his career.

Fishell, then 42, had been studying how the developmental environment in a mouse embryo influences how stem cells turn into different types of interneurons ? the intriguing cells that dampen electrical signaling in the brain[1]. But he needed help understanding the next step: measuring the activity of fully developed interneurons.

He found his answer in conference organizer **Arnold Kriegstein**, then a Columbia University physiologist renowned for his brain-cell recording techniques. Soon after the Delphi meeting, on a much noisier island five thousand miles west, the two scientists began what Fishell now calls the "taxi cab collaboration."

Downtown at his **New York University lab**, Fishell transplanted different kinds of interneurons, tagged with fluorescent green molecular markers, into mouse embryos. Once the transplanted mice were born, he transported them uptown by taxi to Kriegstein's Columbia lab.

"As you might imagine, the taxi bills were killing us," Fishell ? 'Gord' to his friends ? jokes in his tidy office overlooking the East River. "So eventually we moved it all down here."

Along with answering fundamental questions about mammalian brain organization, watching interneurons' "handshake" with other brain cells is the key to understanding autism, Fishell says. "When you look at the 30-odd genes that are linked to autism, a remarkable number of them turn up in interneurons," he says.

This summer, the Simons Foundation gave Fishell a **SFARI pilot grant** to explore how disruption of five of these genes in mice might lead to brain and behavioral abnormalities similar to those seen in individuals with autism.

"Gord is one of the most creative scientists I know," says Kriegstein, who now heads the Program in Developmental and Stem Cell Biology at the University of California, San Francisco. "He's among a small handful of people who are applying the latest molecular and genetic technologies to the problems of cortical development."

Complex circuits