Research directions at Cold Spring Harbor Laboratory Cold Spring Harbor Laboratory follow an ever-changing landscape that is influenced by the intellect of our scientists, by the evolution of scientific problems that can be addressed by current or newly developed technologies, and by a dynamic institutional view that promotes collaborative research and a focus on specific problems that are of collective interest.

future, assachusetts nstitute of echnology , president Susan Hoc field. heir collaborations soon generated insights into the development and organi ation of the mammalian nervous system. ut, alas, these forays into the emerging field of what the CSHL Symposium called — olecular eurobiology were not sustained because the Laboratory lac ed year-round space for neuroscience e perimentation. t was a missed opportunity, but one decisively addressed by im atson and an ad hoc committee of the oard of rustees. n , they set the Laboratory on a course that would result in a full and lasting commitment to neuroscience and in the construction of a ma or state-of-the-art laboratory. amed for rnold and abel ec man, it would enable CSHL to initiate year-round neuroscience research in the Laboratory s centennial year, .

he current era of neuroscience investigation at Cold Spring Harbor dates from this time, over years ago. n early focus on the molecular basis of learning and memory led, in time, to studies pertaining to neural dysfunction in people to memory loss and, separately, to neurofibromatosis , an inherited illness in which tumors form in nerve tissue. hese studies, initially focusing on the fruit fly *Drosophila*, enabled our new neuroscientists to include a genetic approach to under-

olfactory receptors to the brains olfactory corte , where decisions are made based on processed signals. Some decisions, it is believed, are innate, whereas others, such as these, are forged in response to e - perience or environmental cues. ony ador, who heads our Swart Center for Computational eu-

their life span. Whether stem cells that have been expended can be enticed to revert to their former identity and be recruited back into the stem cell pool is a question that Enikolopov's team is now pursuing. Hiro Furukawa's research concerns another aspect of nerve cell biology, that of proteins that lie on the surface of individual nerve cells. He studies the structure of the immense multiunit protein that forms NMDARs (*N*-methyl-D-aspartate receptors) that control the strength of connections between neurons and thereby have a central role in learning and memory. Membrane receptors, the place where neurotransmitter molecules "dock" with nerve cells, are at the "front end" of cell-signaling networks and are of great interest as targets for drug discovery in diseases such as Alzheimer's and in cognitive disorders such as autism and depression. This year, Hiro's team discovered and mapped a new regulatory site in a class of NMDARs, progress that now opens the way to the development of a potentially new class of drugs to modulate the receptor.

igler pursued an inspired hunch that some common genetic disorders such as autism and schi ophrenia might be traceable to C s that occurred spontaneously, that is, not present in either parent of an affected individual. n subse uent wor , this hypothesis was confirmed for both disorders. n autism especially, it became clear that spontaneous C s accounted for a large fraction of cases. ith generous support from the Simons oundation, a large sample of families with an autistic child was assembled. nalysis of the genomes of the affected child compared with that of the parents and sometimes an unaffected sibling enabled the identification of hundreds of regions in the human genome associated with autism. he surprising fact that we all have C s, coupled with the igler labs invention of the technological means to identify them across the genome, was a ma or step along the path toward understanding the cause of the disorder and toward the eventual use of chromosome engineering to create a mouse model of autism.

i e igler continues to e plore the genetics of neuro-psychiatric disorders in humans. He and collaborators have also made a ma or contribution to describing the role of both spontaneous and inherited C s in schi ophrenia. nother of our senior scientists, . Richard cCombie, shares this interest in the human genetics of brain disorders. ic heads the Laboratorys Stanley nstitute for Cognitive enomics and is se uencing patients with schi ophrenia, bipolar disorder, and depression. he collaboration between igler and cCombie has enabled the genetic analysis of autism to proceed to identifying rare single-gene mutations.

he three paths of research in neuroscience human genetics, connectivity, and the study of cognition are rapidly converging. urthermore, the Laboratorys recent investment in building a uanti-