Throughout most of scientific history, spinal cord injury and paralysis have been considered severe and irreversible conditions. As far back as ancient Egypt, physicians recognized that spinal damage was untreatable. Even as our understanding of neurons and their function deepened over the years, the belief persisted that nerves in the central nervous system (brain and spinal cord) simply could not re-grow once injured, unlike nerves in the peripheral nervous system (i.e. outside the brain and spinal cord).

This dogma was overturned in the early 1980s when experiments in rats showed that many types of central nervous system neurons could re-grow their axons under certain laboratory conditions. Researchers now turned their attention towards pinning down the factors that keep axons from re-growing in the living body. In the late 1980s, they discovered the first of these roadblocks: powerful regeneration-blocking proteins produced by the oligodendrocytes, the cells that create the protective myelin sheath that wraps the nerves of the central nervous system. This discovery injected new life into a field that had been dismissed as hopeless, and ushered in a new era of research into all aspects of spinal cord biology.

Throughout the 1990s, many breakthroughs were made that paved the way for today's innovative research.

**Promoting axon growth**

**Enhancing compensatory growth of uninjured neurons**

**Preventing scar formation**

**Replacing lost cells: stem cells and artificial scaffolds**

**Redesigning rehabilitation**

**Exploring the genetic frontier**

**Promoting axon growth**

**1990s:** Scientists began to treat animal neurons with substances that either promoted axon growth directly or blocked the growth-suppressing molecules. Not only were these strategies successful for rebuilding individual injured neurons, but they also led to a partial recovery of overall spinal cord function.

**Today:** Simply re-growing the physical structure of a damaged axon is not enough to restore neuron function; the growing axon also has to end up in an area of the spinal cord that will nourish and support its function. Many regions of the adult spinal cord contain chemical signals that block a re-growing axon and tell it to retreat. Scientists are now working on modifying this environment to make it more hospitable to growing neurons.

**Enhancing compensatory growth of uninjured axons**

**1990s:** Scientists began to notice that treatments designed to repair damaged axons also helped healthy surrounding neurons to grow and support the recovering cells.

**Today:** Researchers are working on tailoring this process to rebuild damaged neuronal networks, particularly in patients with incomplete spinal cord injuries who still have uninjured nerves that could potentially be coaxed into taking over the function of the damaged ones.
**Preventing scar formation**

**1990s**: Scar tissue at the site of the spinal cord injury acts as both a physical and a chemical roadblock to repair. In the 1990s, researchers pinpointed some of the growth-blocking molecular signals that scar tissue gives off and started looking for ways to overcome those inhibitory messengers.

**Today**: Researchers are testing enzymes that interfere with these blocking molecules and successfully allow nerves to cross scar tissue in laboratory studies.

**Replacing lost cells: stem cells and artificial scaffolds**

**1990s**: Since axons need a solid base on which to grow, they are unable to span the physical gap that often spreads as a "ripple effect" immediately after spinal cord injury. In the 1990s, researchers began to test materials that could possibly be used to help neurons cross these breaks. They found that the best results were obtained by transplanting certain supporting cells, known as Schwann cells and olfactory ensheathing glia. Scientists also began transplanting stem cells in an attempt to rebuild damaged neural circuitry in a more global way. They hoped that the undifferentiated cells could migrate to where they were needed and change into the missing cell types.

**Today**: Scientists are working on improving the success of transplantation for both stem cells and specialized cells. They have found that the most promising stem cells to use for neural repair in the spinal cord are neural progenitor cells that are already committed to becoming part of the central nervous system. Investigators are also developing synthetic polymer scaffolds as a gap-spanning alternative to living cells. These scaffolds would not only provide a physical support for growing cells, but could also be combined with growth-promoting molecules to help the neurons along.

**Redesigning rehabilitation**

**1990s**: The importance of physical therapy in spinal cord injury rehabilitation was underlined by animal and human studies that showed that vigorous, repetitive and structured stepping routines could help the lower spinal cord below the area of the injury to actually "learn" how to control movement without input from the brain. Scientists also found that these exercises heightened the body's production of molecular signals that support axon growth and neuron survival.

**Today**: These vigorous exercise routines are becoming a standard part of rehabilitation regimens. Scientists are also working to understand the molecular changes that happen during and after exercise, so that they can design more effective exercise programs and even combine these routines with other types of treatment.

**Exploring the genetic frontier**

**1990s**: Scientists began to study the molecular basis of how the brain and spinal cord form, using the embryonic rat as a model.

**Today**: Armed with powerful new tools such as microarray analysis and molecular data from the mouse and human genome projects, researchers are dissecting the functions of specific biological molecules, both during embryonic nervous system development and after a spinal cord injury.