ABSTRACT
The results of our study support the hypothesis that zebrafish Delta proteins, which are expressed by newly specified neurons, promote Notch activity in neighboring precursors. This signaling is necessary to maintain a proliferative precursor population and generate late-born neurons and glia. As argued, Delta-Notch signalling may diversify vertebrate neural cell fates by coordinating cell cycle control and cell specification.

INTRODUCTION
In the last decade, researchers have developed strategies that allow them to study the impact of genetic changes in developmental disorders such as autism. These include gene therapy, which uses the genetic material of individuals with the disorder; gene-editing techniques such as CRISPR-Cas9 and CRISPR-Cas9-Cas9, which use the genetic material of an animal to edit it; and synthetic approaches such as CRISPR-Cas9-Cas9-Cas9, which use the genetic material of a human to edit it.

The aim of this study was to investigate the effects of a novel approach to gene therapy on developmental disorders, zebrafish spinal cord development.

Methods:

Zebrafish spinal cord development was evaluated using two different approaches. The first approach was a single-cell Specification of cells at different times and places is essential for the generation of cellular diversity in the vertebrate nervous system. Different types of neurons and glia develop at characteristic times, and molecular signals that promote formation of different cell types are regulated spatially and temporally. Thus, neural pattern formation requires coordination of signals providing spatial and spatiotemporal information. The process of lateral specification, or lateral inhibition, involves the creation of fine patterns of distinct cell types. This means that while some cells have the potential to adopt a particular fate, others are assigned different fates. For instance, when neurons from the central nervous system were ablated, they were replaced by cells normally fated to give rise to epidermis. Delta and Notch are responsible for the molecular mechanism of lateral inhibition. Evidence suggests that Delta's expression by specific cells triggers Notching in nearby cells, leading to other developmental pathways. The expression of Notch gene is typically associated with undifferentiated cells in the nervous system of vertebrate embryos, while scattered cells within these zones express Delta. However, the expression pattern does not include a soluble subunit called Delta1 in chicks during the S-phase of the cell cycle, suggesting that it is only attainable for newly post-mitotic cells. In frog and zebrafish neural plate, Delta gene expression appears to precede expression or prediscipline of early neuronal markers. Newly-specified neurons may use Notch to signal neighboring precursor cells. This could diversify the development of neural cells by maintaining a pool of precursors that respond to other instructive signals or by promoting alternative developmental pathways. Recently, there have been several reports suggesting that Notch activity may promote the specification of specific cell types, including glial cells. Forced expression of Nac has been shown to promote formation of cells expressing markers of Müller chia (mathrus glabra) in rat and zebrafish retinae (many other cell type-bearers are present at this time), but it appears that not all late-born cell lines expressed by NotCH activity in rats; however, it did not promote cell

proliferation in mice and also promoted radial lucination in human Conversely the inhibition or disruption of Notch signaling leads to the formation of early-born neurons: antisense NotCH RNA or expression of a dominant negative form of Nocturnal Related Protein (NDP-DL) in chick led to excess ganglion cells, while LDPD in zebrafish repressed and expressed CD11b(e) mutant mice also produced less than 10% of the predicted SDLC. In order to understand the role of Notch-mediated cell-cell signaling in vertebrate neural development, we have tested the formation of neural pattern in zebrafish embryonic neurons by ablating single, identified primary motor neurons. We show that without lateral inhibition, the time during which neighboring cells can replace a missing cell is transient, indicating that temporal and spatial cues specifying cell fate are tightly controlled. Furthermore, neural precursor cells in mutant embryonates stop dividing and differentiate as early-born neurons within dlA mutant mice

CONCLUSION
Remarkable conclusions Zebrafish exhibit three notch genes and three delta genes, which are expressed by different sets of proliferative neural precursors and subsets of post-mitotic neurons. These genes also signal to neighboring ledge-expressing precursor proteins in order to regulate primary motor neuron specification. Removal of primarymotor neurons after a few days results in premature termination of cell division and differentiation of these precursor cells as early as before cell body positions, at the expense of later-born neurons and glia. Our hypothesis is that Delta-Notch signaling mechanisms coordinate the transition from Promethom