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2006 Northeast Regional Meeting of the Society for Developmental Biology

April 28th-30th

ABSTRACT FORM

Deadline: April 3, 2006

Type your abstract in the space below (6.5 x 4.5 inches). Please use 12 pt Times or Times New Roman font. The first lines should read: **Title** (bold), Authors, Department, Institution, Address. Please indicate the presenting author with an *. Skip a line between the header and the body of abstract.

Spina Bifida and Neural Tube Development: Exploring the Role of Neural Tube Closure in the Mouse Mutant *Splotch-delayed*. N Vranich*, M Shah, A Caprariello, J Millonig. Department of Neuroscience & Cell Biology, Center for Advanced Biotechnology & Medicine, UMDNJ-Graduate School of Biomedical Sciences, UMDNJ-RWJMS, Piscataway, NJ 08854. Spina bifida, a failure in neural tube closure, occurs 1:1000 live births. Autopsy studies on spina bifida-affected fetuses have revealed a consistent "overgrowth" phenotype, where there is an excess of tissue in the area of the lesion. In the mouse, the spontaneous mutation *Splotch*^{d}, results in spina bifida. We are analyzing *Sp*^{d} animals at E12.5 with regard to the overgrowth phenotype seen in humans, to address whether such overgrowth affects neurogenesis. Immuno-histochemistry using markers for the dorsal ventricular (Pax7) and mantle (NeuN) zones demonstrates that there is an increase in both dorsal (264%, p=0.0001) and ventral (337%, p=0.0002) ventricular zone areas (VZA) and dorsal and ventral mantle zone areas (MZA) in *Sp*^{d} in the spina bifida region. Specific neuronal populations have also displayed a statistically significant increase in spina-bifida sections (dorsal dl3 Isl1+ cells, 207% increase, p=0.0002; ventral Isl1+ motor neurons, 235% increase, p=0.0002). The number of cells in S-phase was determined by BrdU-labeling, and a 165% increase in the number of BrdU+ cells was observed in spina bifida sections ($p<0.0001$). Analyses at E10.5 have not identified similar phenotypes, suggesting that the effects occur between E10.5 and E12.5. Importantly, anterior *Sp*^{d} sections, that do not display spina bifida, do not exhibit these overgrowth phenotypes, indicating that the defects are coincident with failure to close the neural tube. Furthermore, Folic Acid supplementation experiments demonstrate that closure of the neural tube in *Sp*^{d} is sufficient to rescue these defects at E12.5. In sum, these studies indicate that neural tube closure is likely to regulate neurogenesis during spinal cord development.

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The Society for Neuroscience 34th Annual Meeting, San Diego, California, October 27, 2004.

Analysis of Neural Tube Overgrowth in Spina Bifida Using the Splotch-Delayed Mouse Mutant.

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Spina bifida is characterized by the failure of the posterior neural tube to close, and occurs 1 in 1000 live births. Autopsy studies on spina bifida-affected fetuses have revealed a consistent "overgrowth" phenotype, where there is an excess of tissue in the area of the lesion. In the mouse, a spontaneous mutation in the *Pax3*gene, *Splotch*^{d}, often results in spina bifida. We are analyzing *Sp*^{d} animals at E12.5 with regard to the overgrowth phenotype seen in humans, to address whether such overgrowth affects specific neuronal populations at specific times in development. Immunohistochemistry using markers for the dorsal ventricular (Pax7) and mantle (NeuN) zones demonstrates that there is an increase in both the dorsal (248%, p=0.0001) and ventral (316%, p=0.0002) ventricular zone areas (VZA) and the dorsal and ventral mantle zone areas (MZA) in *Sp*$^{d\ -/-}$ in the spina bifida region. Cell counts of specific neuronal populations have also demonstrated a statistically significant increase in spina-bifida sections (dorsal dI3 Isl1^{+} cells, 173% increase, p=0.0003; ventral Isl1^{+} motor neurons, 235% increase, p<0.0001). When the number of cells in S-phase was determined by BrdU labeling, a 165% increase in the number of BrdU^{+} cells was observed in spina bifida affected sections (p<0.0001). Identical experiments at E10.5 have not identified similar phenotypes, suggesting that the effects occur between E10.5 and E12.5. These results suggest that these overgrowth phenotypes are caused by an increase in the number of cells entering S-phase, which in turn likely leads to an increase in the total MZA. Importantly, anterior *Sp*$^{d\ -/-}$ sections, that do not display spina bifida, do not exhibit these overgrowth phenotypes, indicating that the defects are coincident with failure to close the neural tube. In sum, these studies indicate that neural tube closure is likely to regulate neurogenesis during spinal cord development.

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Society for Developmental Biology 65th Annual Meeting, Ann Arbor, Michigan, June 17-18, 2006.

Spina bifida and neural tube development: The role of neural tube closure in the mouse mutant Splotch-d.

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Spina bifida, a failure in neural tube closure, occurs 1:1000 live births. Autopsies of spina bifida-affected fetuses have revealed a consistent "overgrowth" phenotype, that is an excess of tissue in the area of the lesion. In mouse, a spontaneous mutation Splotch^{d}, results in spina bifida. We are analyzing Sp^{d} mice at E12.5 with respect to the overgrowth phenotype seen in humans, to address whether neurogenesis is affected. Immunohistology using markers for the dorsal ventricular (Pax7) and mantle (NeuN) zones demonstrates an increase in both dorsal (264%, $p=0.0001$) and ventral (337%, $p=0.0002$) ventricular (VZA) and mantle zone areas (MZA) in the spina bifida region. Specific neuronal populations display an increase in size in spina-bifida sections (dorsal dI3 Isl1+ cells, 207% increase, $p=0.0002$; ventral Isl1+ motor neurons, 235% increase, $p=0.0002$). The number of cells in S-phase was determined by BrdU-labeling, and an 165% increase was observed in spina bifida sections ($p<0.0001$). Analyses at E10.5 have not identified similar phenotypes, suggesting that the effects occur between E10.5 and E12.5. Anterior Sp^{d} sections, that do not display spina bifida, do not exhibit these overgrowth phenotypes, indicating that the defects are coincident with failure to close the neural tube. Folic Acid supplement studies demonstrate that closing the neural tube in Sp^{d} is sufficient to rescue these defects. In sum, these studies indicate that neural tube closure is likely to regulate neurogenesis during spinal cord development.