Sample Abstract

HUMAN GENETICS

Strain-Specific Alleles of *Phox2B* Differentially Modify *Sox10^{Dom}* Aganglionosis

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Dissertation under the direction of Professor E. Michelle Southard-Smith

Hirschsprung disease (HSCR) is characterized by a lack of enteric ganglia in a variable portion of the distal bowel. The complex inheritance pattern of this disorder has led researchers to focus on genetic effects other than the putative disease mutation. Mouse models provide a controlled background for these types of studies. *Sox10* is an essential gene for the development of the enteric nervous system (ENS). *Sox10^{Dom}* mice on a mixed genetic background exhibit the variable aganglionosis seen in HSCR cases. Congenic lines of *Sox10^{Dom}* mice on distinct inbred genetic backgrounds, C57BL/6J (B6) and C3HeB/FeJ (C3Fe), differ in penetrance and extent of aganglionosis. A linkage screen for modifiers of *Sox10^{Dom}* aganglionosis was undertaken in a large B6 X C3Fe F_2 population. Several potential modifier regions were identified, with the most significant located on chromosome five (*Sox10m3*). The most relevant candidate gene in this region was *Phox2B*, an essential factor in autonomic neurogenesis.

Approved _____ Date_____

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