

# GENETICS

## The Ontogeny of Normal mRNA Expression of Genes from the SHFM3 Critical Region in Developing Chicken Limb

SHFM is a congenital limb malformation characterized by a reduction or loss of the central digits of the hand and/or feet and affects one in every 8,500 to 25,000 births, accounting for 8-17% of all limb reduction defects. A tandem duplication of approximately 500 Kb has been determined to be the causative mutation at the SHFM3 locus. Patients that are heterozygous for this duplication have three copies of the genes *BTRC*, *POLL*, and *DPCD* as well as an extra copy of exons 6-9 of *FBXW4*. The SHFM3 critical region also contains the *FGF8* and *SUFU* genes. The aim of this study was to determine if these genes are expressed during normal limb development of the chicken and where. *Poll* was the only gene from the critical region not detected by RT-PCR of RNA from the limbs of stage E3-E13 embryos, and thus was not studied further. *In situ* hybridization of paraffin sections from E6 and E8 limbs showed that *BTRC*, *DPCD*, *FBXW4*, *FGF8*, and *SUFU*, are expressed in the region of the limb where digit formation occurs. Taken together, the data suggests that all of the genes, with the exception of *POLL* play a role in the development and patterning of the limb, and that alteration of the expression of these genes may lead to the SHFM phenotype in patients with the duplication. This could be a result of the overexpression of one or more of these genes, or the duplication removes a gene from the control of a regulatory element.

**TIME:** 10:00 am

**DATE:** November 16, 2009

**LOCATION:** BRC Seminar Room