

**Stony Brook University  
The Graduate School**

Doctoral Defense Announcement

**Abstract**

**A Novel Mouse Model for Human EEC Syndrome**

By

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Human ectrodactyly, ectodermal dysplasia, clefting (EEC) syndrome is a developmental disease characterized by severe congenital defects. The clinical features of EEC are distal limb defects including lobster claw, skin and skin appendage defects, and clefting of the lip or lip and palate. Hallmark features of EEC are incomplete penetrance and variable expressivity, characteristics that have made the causative gene elusive. However, the discovery of p63's involvement in ectodermal development provided *p63* as a candidate gene for human EEC syndrome; it is now known that EEC is caused by heterozygous missense mutations in *p63*. *P63<sup>R279H</sup>* is the most common missense mutation in EEC and corresponds to the *p53<sup>R248</sup>* mutation—one of the most frequently mutated amino acids in human tumors. We have generated an EEC mouse model by knocking in the *p63<sup>R279H</sup>* mutation within exon 7 of the DNA binding domain. Interestingly, our EEC mouse model recapitulates the three main features of human EEC syndrome: 1) limb defects, 2) ectodermal defects, and 3) cleft palate. In addition to the phenotypes that correspond with clinical features of human EEC, *p63<sup>R279HN</sup>/+* male mice have anomalies of the genitalia such as hypospadias. Several of the phenotypes in EEC mice exhibit incomplete penetrance, suggesting that modifier genes affect the severity of EEC-like phenotypes. The EEC mouse model will be invaluable for understanding EEC pathogenesis as well as for determining the role of p63 in normal development.

**Date:** May 22, 2007

**Program:** Genetics

**Time:** 10:00am

**Dissertation Advisor:** Alea A Mills

**Place:** Plimpton Conference Room, Beckman Hall, Cold Spring Harbor Laboratory