

## White (W, Kit) Locus

### Research Applications

Pigmentation  
Anemia  
Deafness  
Brain Development  
Mast Cells  
T Cells  
Reproductive Cells  
Neural Crest Development  
Cell Surface Receptor/Ligand Interactions  
Cell Migration Patterns

### Characteristics of the *Kit* Locus

Mice mutant at this locus have defects affecting pigmentation, development of red blood cells and reproductive cells, inner ear and mast cells, T-cell precursors and hippocampal learning. Homozygotes of most alleles are lethal. The *Kit* (*c-kit*) proto-oncogene encodes a tyrosine kinase family receptor whose function is required for the survival and/or migration of melanoblasts.

The *Kit* ligand, produced by the *Kitl* locus in cells of the substrate in which the melanoblast/melanocyte resides, must bind with and activate the *Kit* receptor on the surface of the melanoblast/melanocyte. In response to binding, *Kit* in pigment cells activates downstream signal transduction molecules such as MAPK, PI3 kinase, JAK/STAT and Src family members and may transiently stimulate transcriptional activity of MITF. If either *kit* or *Kit* ligand is defective, the result is white spotting, or failure of survival of the pigment cell. This same interaction accounts for the pleiotropic effects that result from mutation at either locus. Binding of *kit* and *Kit* ligand is necessary for the development of red blood cells, mast cells, reproductive cells and other specific developmental events.

It is interesting to note phenotypic differences between mice heterozygous for *kit* mutants and those heterozygous for *Kit*-ligand mutants. The former phenotypes reflect failure of migration of the pigment cells, while the latter demonstrate an overall partial failure of survival.

The extent of white spotting of mice heterozygous for *Kit* mutants may be reduced as much as 95% in mice that are pheomelanic. Extent and location of white spotting in mice mutant at the *Kit* locus is also strongly influenced by the modifying genes that are yet to be described and by strain background. In this collection of mice the identical allelic origin is expressed in five different degrees of severity, depending upon the congenic background, and within the congenic mice upon two (or more) discrete modifying genes that have been maintained by selection. These mice could be used to ID at least three modifying genes that determine the severity of the pigmentation defect; once identified, these might be useful markers for prenatal determination of severity of the serious pleiotropic effects that are associated with mutation at *Kit*.