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[**Mouse Nkrp1-Clr gene cluster sequence and expression analyses reveal conservation of tissue-specific MHC-independent immunosurveillance.**](http://www.ncbi.nlm.nih.gov/pubmed/23226525)

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**Source**

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**Abstract**

The Nkrp1 (Klrb1)-Clr (Clec2) genes encode a receptor-ligand system utilized by NK cells as an MHC-independent immunosurveillance strategy for innate immune responses. The related Ly49 family of MHC-I receptors displays extreme allelic polymorphism and haplotype plasticity. In contrast, previous BAC-mapping and aCGH studies in the mouse suggest the neighboring and related Nkrp1-Clr cluster is evolutionarily stable. To definitively compare the relative evolutionary rate of Nkrp1-Clr vs. Ly49 gene clusters, the Nkrp1-Clr gene clusters from two Ly49 haplotype-disparate inbred mouse strains, BALB/c and 129S6, were sequenced. Both Nkrp1-Clr gene cluster sequences are highly similar to the C57BL/6 reference sequence, displaying the same gene numbers and order, complete pseudogenes, and gene fragments. The Nkrp1-Clr clusters contain a strikingly dissimilar proportion of repetitive elements compared to the Ly49 clusters, suggesting that certain elements may be partly responsible for the highly disparate Ly49 vs. Nkrp1 evolutionary rate. Focused allelic polymorphisms were found within the Nkrp1b/d (Klrb1b), Nkrp1c (Klrb1c), and Clr-c (Clec2f) genes, suggestive of possible immune selection. Cell-type specific transcription of Nkrp1-Clr genes in a large panel of tissues/organs was determined. Clr-b (Clec2d) and Clr-g (Clec2i) showed wide expression, while other Clr genes showed more tissue-specific expression patterns. In situ hybridization revealed specific expression of various members of the Clr family in leukocytes/hematopoietic cells of immune organs, various tissue-restricted epithelial cells (including intestinal, kidney tubular, lung, and corneal progenitor epithelial cells), as well as myocytes. In summary, the Nkrp1-Clr gene cluster appears to evolve more slowly relative to the related Ly49 cluster, and likely regulates innate immunosurveillance in a tissue-specific manner.