ENU Mouse Mutagenesis: Generation of Mouse Mutants with Aberrant Plasma IgE Levels

Background: The ENU Mouse Mutagenesis Project aims at a large-scale, systematic production of mouse mutants using the alkylating agent ethyl-nitrosourea (ENU). Offspring of mutagenized mice are subjected to a multiparameter screen to detect alterations in various phenotypes with the ultimate goal of identifying novel genes relevant for the expression of the phenotype. Using this approach, we have analyzed plasma IgE concentrations to identify mouse mutants with aberrant plasma IgE levels. Methods and Results: ENU-mutagenized male C3HeB/FeJ were mated to wild-type females to produce F1 offspring. F1 animals were analyzed for alterations in their plasma IgE concentrations that showed a dominant mode of inheritance, or bred further to screen for recessive phenotypes. Plasma IgE concentrations were determined by ELISA and a normal range for plasma IgE was established using C3HeB/FeJ wild-type animals. So far we have tested 6568 F1 animals. Repeated testing confirmed a stable aberrant IgE phenotype in 124 animals. To confirm the genetic basis of the observed phenotype, these mice were subjected to confirmation crossing. Currently we have established 9 independent mutant mouse lines (3 with high plasma IgE and 6 with plasma IgE below detection limit) that have been genetically confirmed and additional 24 variant mouse lines are currently undergoing confirmation testing.
Conclusion: ENU mouse mutagenesis allowed us to generate and identify mouse mutants with aberrant plasma IgE levels, which may be used to characterize novel genes involved in IgE regulation and may serve as animal models for IgE-mediated diseases.

Stichworte: IgE; Mutants; mouse; Mutagenesis

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