Genetic factors relevant to inflammation and carcinogenesis in the mouse.

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Two non-isogenic mouse lines were selected on the basis of high (AIRmax) or low (AIRmin) acute inflammatory response (AIR) to polyacrilamide beads (Biogel). The genetic analysis of the bi-directional selective process revealed that about 11 *Quantitative Trait Loci* (*QTL*), with additive effect, account for the phenotypic divergence between AIRmax and AIRmin mice. AIRmax mice were found resistant and AIRmin susceptible to lung tumorigenesis induced by ip injection of urethane or by repeated epicutaneous applications of DMBA or by ip injections of DMH. In urethane-treated mice tumor incidence, multiplicity and malignant transformation into adenocarcinomas reached 100% incidence in AIRmin but only <5% in AIRmax mice. AIRmin are also more susceptible than AIRmax to two-step skin carcinogenesis induced by DMBA and TPA. A significant inverse correlation ($p<0.001$) was observed between the intensity of local AIR to Biogel and the multiplicity and size of urethane induced lung tumors, or of skin tumors after DMBA/TPA, in two independent linkage assays in F2 intercross populations, suggesting that at least some of the AIR *QTL* should contain tumor modifier genes. AIRmax and AIRmin mouse lines present extreme and opposite phenotypes and are genetically heterogeneous, providing a high resolution power for linkage disequilibrium (LD) mapping of inflammation modifier genes. By this method we have identified a 452-kb region, containing 5 genes in linkage located at the distal region of chromosome 6 (*Pas1 locus*), which was found involved in lung carcinogenesis and in AIR regulation. The identification of functional polymorphisms in genes relevant to the variations in the inflammatory response, could be predictive of an altered risk to neoplasic diseases. The selected AIRmax and AIRmin mouse lines which largely differ in the degree of inflammatory response and in the susceptibility to chemical carcinogenesis provide a model to explore the genetic link between both traits.