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Confirmation of rat arthritis susceptibility locus

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Genetics, linkage, oil-induced arthritis, rheumatoid arthritis

Context

Incomplete Freund's adjuvant and squalene are arthritogenic oils that can be used to induce arthritis (oil-induced arthritis [OIA] and squalene-induced arthritis [SIA], respectively) in susceptible strains of rats. Both OIA and SIA have been used as experimental models of rheumatoid arthritis (RA). Previous work has identified two genetic susceptibility loci outside the MHC that are linked to OIA. One of these loci, Oia3 on rat chromosome 10, has also been linked to SIA. The aim of the current study was to transfer the genetic region containing the Oia3 locus into a strain of rat usually resistant to SIA to create a congenic strain and to determine whether the transfer of this genetic region conferred susceptibility to SIA.

Significant findings

Rats made congenic for the Oia3 locus had a higher incidence and severity of SIA compared to noncongenic animals, supporting the hypothesis that the Oia3 locus on rat chromosome 10 does, in fact, harbour a gene or genes that confer susceptibility to arthritis. In these animals, the length of the congenic was 10.5 centiMorgans (cM) (16.4-26.9 cM). Three subcongenic strains were created on the resistant background strain, each containing a shorter interval of the Oia3 locus. Two of these subcongenic strains remained susceptible to SIA whereas the third did not, thus narrowing the region containing arthritis-susceptibility gene(s) from a 10.5 cM to a 9.3 cM (23.7-33 cM) region. Differences in susceptibility to arthritis between male and female rats in the remaining two subcongenic strains (congenes of 23.7-33 cM and 4-19 cM) suggest that the region could harbour more than one arthritis-susceptibility gene.

Comments

This study demonstrates that it is possible to confer arthritis susceptibility by transferring a genetic region from rat chromosome 10 from a susceptible to a resistant rat strain. It confirms that the region contains at least one true arthritis-susceptibility gene. Investigation of human genes homologous to those mapping to the Oia3 locus in rats is now indicated to determine whether they play a role in RA susceptibility.

Methods

Intercross, backcross, microsatellite genetic analysis, recombinant strains

Additional information

References

1. Holm BC, Wei Xu H, Jacobsson L, Larsson A, Luthman H, Lorentzen JC: Rats made congenic for Oia3 on chromosome 10 become susceptible to squalene-induced arthritis. *Hum Mol Genet.* 2001, 10: 565-572.