

Hereditary Factors Modify Risk of Bone Tumour Following Radiation Exposure

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Due to the additive interaction of several susceptibility loci a hereditary predisposition for radiation-induced bone tumours (*osteosarcomas*) may develop in mice. In man, this type of tumour is becoming increasingly important as a secondary tumour following childhood radiation therapy. Our search for inherited susceptibility factors in mice shows, that the accidental cosegregation of high-risk alleles from both parental animals results in a significant increase in the individual bone tumour risk in some of their progeny.

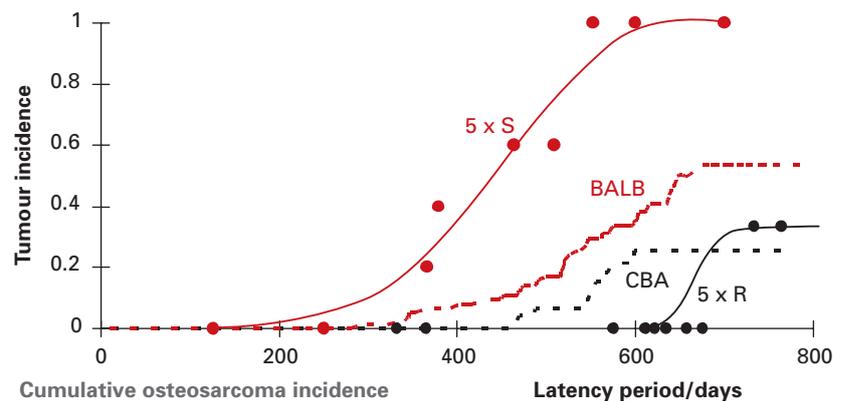
A hereditary influence on the risk of bone tumour development following radiation exposure has only been known for a few rare hereditary diseases which lead to a high frequency of a number of tumours in some families. Due to their severe effects, which often affect very young patients, however,



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Cumulative osteosarcoma incidence following injection with the bone-seeking alpha-emitter thorium227 shows that a combination of susceptibility loci from the parental BALB/c and CBA/CA strains (dotted lines) may occur in the F2 generation (solid lines), which results in a hypersensitive (5 x S) or hyperresistant (5 x R) phenotype in the offspring.

the mutations underlying these so-called familial cancer syndromes are rarely found in the population.

In genetic tests of radiation-induced bone tumours in various mouse strains we could identify chromosome sections which had been unknown, and which only increase the frequency of this type of cancer, when they are combined. In these instances an accidental combination of risk alleles from both parents may result in a hereditary predisposition for these bone tumours, which had not been seen in previous generations.

Translating our findings to the situation in the human population one might expect to find hypersensitive person which, in contrast

to the case of familial cancer syndromes mentioned, are not characterized by the existence of close relatives with early or frequent tumor incidences. Therefore, the examination of a family history may not be very promising. More characteristic indications of a hereditary predisposition, however, would be: Unusually young age of tumour development or patients with multiple tumours.

This work brought us a good deal closer to the aim of determining such a hereditary predisposition by a molecular test, before any clinical symptoms are manifested.

Literature:

- Rosemann, M., Kuosaitė, V., Kremer, M., Favor, J., Quintanilla-Martinez, L., Atkinson, M.J.: Multilocus inheritance determines predisposition to alpha-radiation induced bone tumour-igenesis in mice. *Int. J. Cancer* 118, 2132-2138, 2006.