

Distribution and consequences of VKORC1 polymorphisms in Germany

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Abstract

Derivates of 4-hydroxycoumarin have been used worldwide as rodenticides since the 1950s. These rodenticides inhibit blood clotting by repression of the vitamin K-reductase reaction. Only a few years after the first application of anticoagulant rodenticides resistant Norway rats were detected. Nucleotide polymorphisms within the vitamin K-reductase complex subunit 1 (VKORC1) locus were found to provide the genetic basis for resistance to anticoagulants within Norway rats and other commensal rodents throughout the world (Rost et al., 2004, Pelz et al., 2005). The occurrence of rodents resistant to anticoagulants during the last decades led to increasing difficulties in the control of rodent populations, with consequent associated hygiene problems and possible increased risk of infection of humans and livestock by epizootic and zoonotic pathogens. Therefore, different monitoring programs were conducted in Germany and the consolidated results of these studies are presented here.

Since 2004, samples of Norway rats were screened for the Tyr139Cys polymorphism to define resistance areas in the German Federal States of Lower Saxony, Saxony-Anhalt, Berlin, Schleswig-Holstein, Hamburg and North Rhine-Westphalia. A special monitoring program was implemented in Lower Saxony to obtain more detailed information on the occurrence of resistant rats. Therefore, since 2008, Norway rats obtained as by catch of muskrat trapping, as well as rats caught purposely for the study from rural or urban areas, were investigated for sequence changes in the gene VKORC1. At some sites rat feces were also examined for resistance polymorphisms.

The Tyr139Cys polymorphism, within the VKORC1 locus, was detected by a newly-developed real-time PCR method using minor groove binding probes. In total, about 660 samples from Lower Saxony were investigated. 3.8% of these samples showed a heterozygous Tyr139Cys mutation within the VKOR gene and 4.7% showed an equivalent homozygous mutation.

Sequencing of all samples confirmed the prevalence of Tyr139Cys as the most abundant polymorphism in Germany. However, two further polymorphisms, Ala26Thr (also known from England) and Ser79Phe, were identified in single populations in Saxony-Anhalt and Berlin. The resistance effects of these polymorphisms have yet to be investigated. In the present paper we present the geographical distribution and consequences of the Tyr139Cys polymorphisms in Norway rats in terms of management issues and the risk of outbreaks of zoonotic diseases.

References

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