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RATTUS RATTUS AND *RATTUS NORVEGICUS* VITAMIN K 2,3-EPOXIDE REDUCTASE SINGLE NUCLEOTIDE POLYMORPHISMS IN SPAIN

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Abstract Rodents are considered one of the animal pests with the greatest impact on agricultural production and public health. Anticoagulant rodenticides (ARs), used as one of the most effective ways to control rodent populations worldwide. ARs inhibit the vitamin K 2,3-epoxide reductase (VKORC1) enzyme causing animal death due to internal haemorrhages. Resistances to ARs are mainly associated with mutations or single nucleotide polymorphisms (SNPs) in the *vkorc1* gene. Strategies based on an Integrated Pest Management (IPM) try to implement an effective reduction in the use of pesticides decreasing the likelihood of the appearance of pesticide resistance. The information on this subject is scarce in Spain. Pest control operators in coordination with the National Association of Environmental Sanitation Companies (ANECPLA) previously identified the sites with low AR efficacy. We designed a kit with the material for the collection of samples and a questionnaire for location and treatment identification. We received samples of stools and tails from brown rat (*Rattus norvegicus*) and black rat (*Rattus rattus*) collected from 12 Spanish Autonomous Communities. We sequenced the *vkorc1* exon 3 genomic DNA and identified genotypic *vkorc1* variations. The corresponding amino acid changes at the VKORC1 protein depended on the rodent specie. Computational analysis of binding predictions establish that the brown rat mutation predicted a high reduction of the binding affinity of chlorophacinone and brodifacoum. Instead, the black rat mutations slightly reduced bromadiolone AR binding. These results suggest that rodent mutations found in Spanish populations may be one of the causes of the increased resistance. Pest control management should increase accuracy by follow resistance evolution for long time monitoring of the genetics of rodent populations.

Key words: Rodents, Spanish vkorc1 mutants, Anticoagulant rodenticides, Binding predictions