

Investigation of the current status of anticoagulant resistance in UK Norway rats by VKORC1 genotyping

Clarke, D.J.¹, Prescott, C.V.²

¹Department of Chemical & Biological Sciences, University of Huddersfield, Huddersfield, HD1 3DH, UK, d.j.clarke@hud.ac.uk

²School of Biological Sciences, University of Reading, Berkshire, RG6 6AS, UK

DOI: 10.5073/jka.2011.432.030

Abstract

Anticoagulant rodenticide resistance in Norway rats was first reported in the 1950s in Scotland (Boyle et al., 1960) and has been recorded in a number of other foci in England and Wales from the 1960s to present. Up until the mid-1990s resistance was monitored in trapped live rats using lethal feeding period (LFP) and blood clotting response (BCR) tests (Myllymaki, 1995). However, in 2004 the identification and sequencing of the vitamin K epoxide reductase (VKORC1) gene that confers resistance in Norway rats and House mice (Rost et al., 2004) made it possible to identify resistant animals in the laboratory using the new molecular DNA sequencing technology. As DNA can be extracted from tissue taken from the tip of the tail of recently killed animals, there is no longer a requirement for trapping and testing live animals. Pilot testing of small numbers of UK rats by Pelz and colleagues in 2005 and 2009 (Pelz et al., 2005; Rost et al., 2009) revealed 5 mutations associated with resistance from samples of frozen tissue archived from wild rats caught in the 1990s and a further 2 mutations from lab strains generated from wild founder animals caught in the 1960s and 1990s. Substantially higher numbers of animals have been genotyped in Belgium, Denmark, France and Germany (Grandemange et al., 2009; Rost et al., 2009). In contrast to France and Germany where spatial mapping of hundreds of resistant animals has occurred using this new technique, in the UK we have a very limited current knowledge of the distribution and prevalence of the different genotypes that cause resistance. Only two areas (Cambridge and Kent) have had more than 2 animals analyzed (Prescott et al., 2011; Rost et al., 2009). This report describes the VKORC1 genotyping of over 150 wild rats in the UK from 2007 to date, from areas close to known resistance foci as well as new locales where resistance has not been reported before. The results reveal a more detailed spatial mapping of resistance mutations in the UK that will contribute to the future management of rat populations in the UK.

Keywords: anticoagulant resistance, DNA sequence, mutations, Norway rat, UK

References

- Boyle CM 1960 Case of apparent resistance of *Rattus norvegicus* Berkenhout to anticoagulant poisons. *Nature* 188: 517
- Grandemange A, Lasseur R, Longin-Sauvageon C, Beniot E, Berney P 2009 Distribution of VKORC1 single nucleotide polymorphism in wild *Rattus norvegicus* in France. *Pest Management Science* 66: 270-276
- Myllymaki A 1995 Anticoagulant resistance in Europe: appraisal of the data from the 1992 Eppo questionnaire. *Pesticide Science* 43: 69-72
- Pelz HJ, Rost S, Hünerberg M, Fregin A, Heiberg AC, Baert K, MacNicoll AD, Prescott CV, Walker AS, Oldenberg J, Müller CR 2005 The genetic basis of resistance to anticoagulants in rodents. *Genetics* 170: 1839-1847
- Prescott CV, Buckle AP, Gibbings JG, Allen NW, Stuart AM 2011 Anticoagulant resistance in Norway rats (*Rattus norvegicus* Berk.) in Kent – a VKORC1 single nucleotide polymorphism, tyrosine139phenylalanine, new to the UK. *International Journal of Pest Management* 57: 61-65
- Rost S, Fregin A, Ivaskевич V, Conzelmann E, Hörtnagel K, Pelz HJ, Lappégard K, Seifreid E, Scharrer I, Tuddenham EGD, Müller CR, Strom TM, Oldenberg J 2004 Mutations in VKORC1 cause warfarin resistance and multiple coagulation factor deficiency type 2. *Nature* 427: 537-540
- Rost S, Pelz HJ, Menzel S, MacNicoll AD, Leon V, Song KJ 2009 Novel mutations in the VKORC1 gene of wild rats and mice- a response to 50 years of selection pressure by warfarin? *BMC Genetics* 10: 4