

## ○18. Vitamin K requirement of two VKORC1 resistant Norway rat (*Rattus norvegicus*) strains common in Belgium: Y139F and L120Q

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Vitamin K is an essential co-factor in the activation of several coagulation factors and plays an important role in blood coagulation. Resistance against anticoagulant rodenticides is based on a single nucleotide polymorphism in the VKORC1 gene. A pleiotropic effect of rodenticide resistance is an increased need for vitamin K. Therefore we tested homozygous resistant rats (Y139F, L120Q) for their vitamin K requirement by feeding six males and six females of each strain with a vitamin K deficient diet (Altromin) for two weeks, yet coprophagy was not prevented. Then on days 0,3,5,7,10 and 14 of the experiment prothrombin time (PT) was measured and expressed as international normalized ratio (INR). Rats with an INR>5 were considered responders. Three L120Q-males showed a slightly increased PT (INR>2) on day 0, while five L120Q-males reached an INR>5 (1/day3, 2/day5, 1/day10 and 1/day14). Within the group of the L120Q-females two rats responded to the treatment respectively on day 10 and 14, and one rat died on day 7 without bleeding signs. One Y139F-male showed an INR>5 on day 7 and two Y139F-females died on day 10 with signs of severe anaemia and so considered as responders. None of the Y139F-females reached an INR>5. According to this preliminary study the L120Q-strain is more sensitive to vitamin K deprivation than the Y139F-strain. Although both strains showed a prolonged clotting time compared to warfarin susceptible strains, it remains unclear as to what degree vitamin K deficiency occurs in the field and could affect the relative fitness of resistant rats.

## ○19. Target Resistance to VKA – Part I – An overview about the catalytic mechanism of VKORC1 enzyme

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The VKORC1 gene has been described in 2004 by the groups of Oldenburg and Stafford. Since then, many mutations have been described and linked to resistance to VKAs either in humans or in rodents. In rodents, the involvement of a target resistance, i.e. due to mutations of the VKORC1 gene seems to be extremely frequent in the western part of Europe. Nevertheless, a lot of aspects concerning the VKORC1 enzyme remain quite unknown. The mechanism of action of this enzyme remains quite unclear, and the interaction with VKAs is not understood. The different aspects of this enzyme will be presented and discussed.