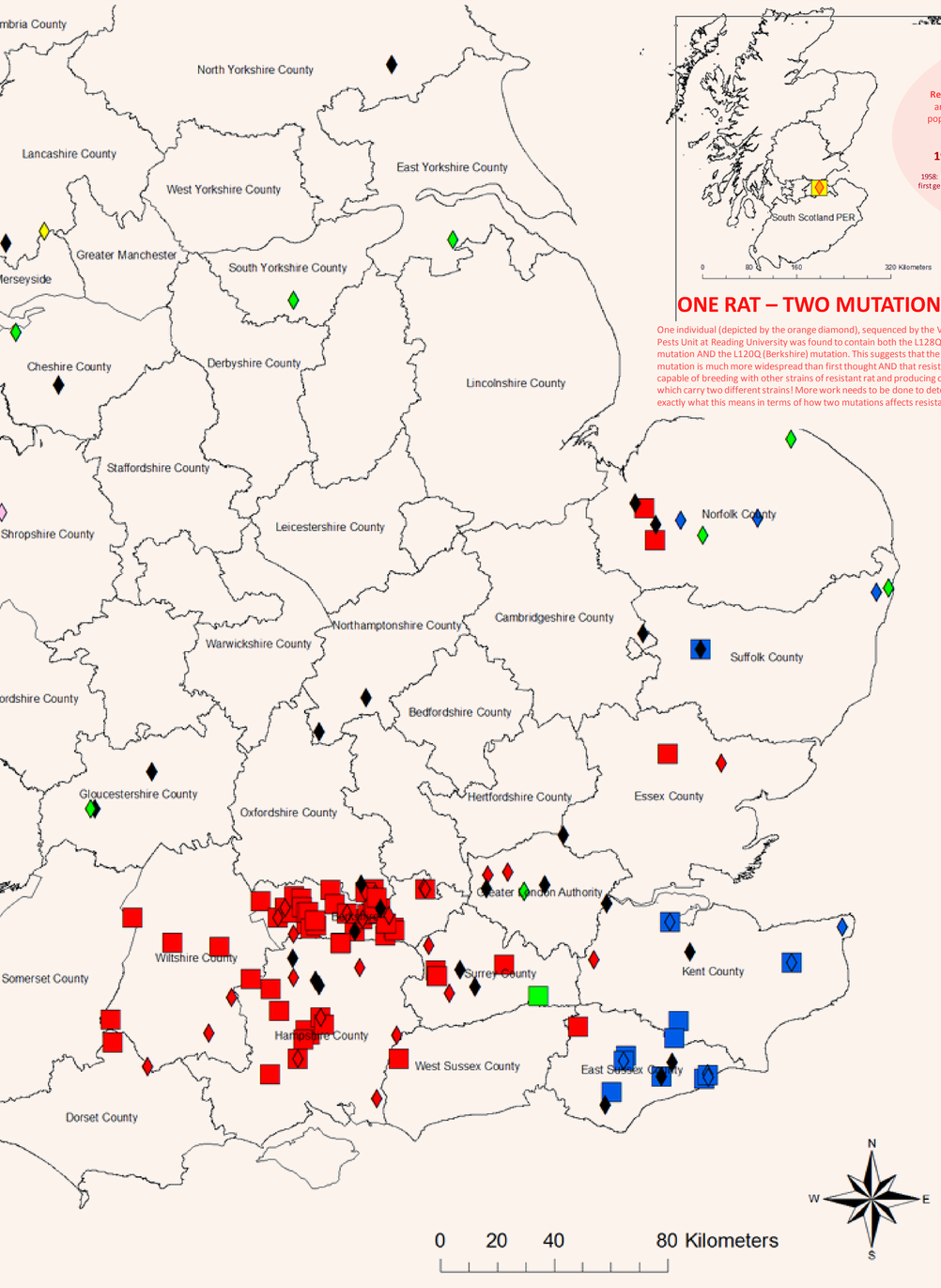
THE BATTLE AGAINST "SUPER RATS"

Norway / Brown Rat

Since the common brown rat colonised the earth it has been battling against our persecutions. And now these highly adaptable pests have mutated into what some have called "Super rats". Through our persistent use of anticoagulants, genetically resistant "super" rats have been selected for and are spreading rapidly around the globe.



Squares refer to homozygous rats (two copies of the resistant gene)

Diamonds refer to heterozygous rats (one copy of the resistant gene)

Susceptible rats (rats which to not possess any resistance strain)

ONE RAT – TWO MUTATIONS

One individual (depicted by the orange diamond), sequenced by the Vertebrate Pests Unit at Reading University was found to contain both the L128Q (Scottish) mutation AND the L120Q (Berkshire) mutation. This suggests that the Berkshire mutation is much more widespread than first thought AND that resistant rats are capable of breeding with other strains of resistant rat and producing offspring which carry two different strains! More work needs to be done to determine exactly what this means in terms of how two mutations affects resistance.

The beginning

1950s

Resistance was first found in the 1950's. It is assumed that these mutations arose from a random mutation event and they were most likely present in populations at low frequency even before the introduction of anticoagulants.

1950 1960 1970 1980 1990 2000 2018

1958: First case of resistance to first generation anticoagulants in UK

Second Generation anticoagulants Bromadiolone & Difenacoum released

Resistance to Bromadiolone & Difenacoum discovered

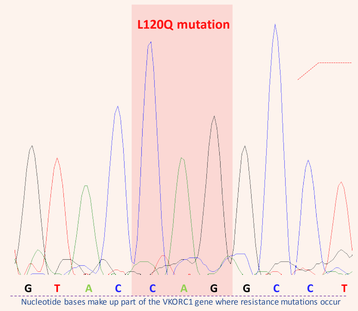
UK's 5 MOST SEVERE MUTATIONS

The development of anticoagulant rodenticides in the early 1950s revolutionised rodent control. By the late 1950s, however, resistance to these compounds was found in some Norway rat and house mouse populations. Consequently, more potent second-generation anticoagulants (Difenacoum and Bromadiolone) were marketed and proved effective. However, within just a few years of their arrival, resistance was identified. Resistance for these compounds has been spreading ever since AND we are still trying to fill in the gaps where we have no resistance data!

	1	2	3	4	5
	L120Q (Berkshire)	Y139C (Gloucester)	Y139F (Kent)	Y139S (Welsh)	L128Q (Scottish)
MAP SYMBOLS	Heterozygous Homozygous	Heterozygous Homozygous	Heterozygous Homozygous	Heterozygous Homozygous	Heterozygous Homozygous
SEVERITY GRADIENT					
RECOMMENDED COMPOUNDS	• Brodifacoum • Flocoumafen • Difethialone	• Brodifacoum • Flocoumafen • Difethialone	• Brodifacoum • Flocoumafen • Difethialone	• Any of the 5 second generation anticoagulants (SGARS) (Note: There is evidence to suggest there is increasing resistance to bromadiolone!)	• Any of the 5 second generation anticoagulants (SGARS)

THE GENETICS

All it takes is one mutation



Nucleotide bases make up part of the VKORC1 gene where resistance mutations occur

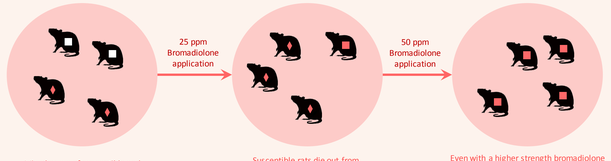
Thanks to early genomic work we are able to identify resistant animals from a simple tissue sample (e.g. a tail cutting). Resistant mutations are known to occur on the VKORC1 gene and will alter the enzymes which are involved in the vitamin k cycle (vital for the coagulation of blood). This in turn inhibits the anticoagulant's mechanism and enables what some have named a "super" rat or mouse to survive. Analysing these genetic sequences involves a chromatogram of the VKORC1 gene (Figure 2). These graphs show the nucleotides that code for the amino acids & proteins which are pivotal in the blood coagulation process. From these graphs we can also figure out the genotype of the individual. A resistance strain exists in two forms: homozygotes and heterozygotes.

This graph is a chromatogram showing part of the genetic sequence of a Norway rat's VKORC1 gene. This individual has the L120Q "Berkshire" resistance. The highlighted sequence of letters "CAG" codes for the glutamine amino acid which means this individual's protein structure is different from that of susceptible rats. All it takes is for one letter (base) to change to cause resistance

Don't use the wrong poison! Using Bromadiolone and Difenacoum against populations with the most severe mutations, (namely L120Q, Y139C & Y139F) can help increase resistance in a population and allow it to spread. If bromadiolone, for example, was used against a population of rats containing L120Q individuals, then any susceptible rats would quickly die out, leaving only resistant rats. These surviving resistant rats will be able to breed quicker, as there is less competition, and eventually this will result in a completely resistant population where homozygous individuals have a selective advantage based on their higher levels of resistance. Furthermore applying higher strength bromadiolone would only make the problem worse. This is because individuals with the highest resistance levels will survive and pass this ability onto the next generation of rats.

Susceptible Heterozygous Homozygous

STOP SPREADING RESISTANCE



Mixed group of susceptible and L120Q resistant rats

Susceptible rats die out from consuming the poison but L120Q rats survive and breed

Even with a higher strength bromadiolone application resistant rats with the highest resistance levels will have a selective advantage which could result in a completely homozygous resistant group

HOMOZYGOUS & HETROZYGOUS RESISTANCE

Homozygous

Heterozygous

A resistance strain exists in two forms: homozygotes and heterozygotes. Heterozygous animals possess one copy of the resistance gene whereas homozygous animals posses two copies.

Homozygous is the most severe form because these animals generally have a higher tolerance to anticoagulants and will always produce resistant offspring. Restrictions on the use of certain anticoagulants has meant that homozygous resistance has been able to increase in frequency and spread. This is because using ineffective anticoagulants kills off the susceptible animals and favours rats with the highest resistance levels which will then reproduce and pass on their genes to the next generation. So it is important that pest control operators are aware of the type of resistant population they are trying to control in order to avoid using ineffective rodenticides and needlessly risking these toxicants entering the environment.

Permanent Baiting - Change to Policy

HSE are not authorising certain products for permanent baiting! These include:

All brodifacoum, flocoumafen & difethialone products

What does this mean in terms of baiting resistant populations?

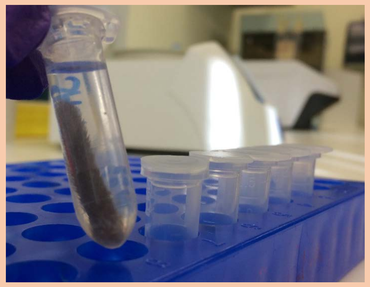
There can be exceptions where justified. If there is a constant risk of reinvasion, for example, and the above products are proving efficacious, then continued use could be accepted.

The likely cause of a failed treatment has to be determined. Where there is no observed decline in rodent activity after 35 days of treatment with continued bait take it is likely that there are resistant rodents.

Further proof of a resistance problem would also help justify the use of these excluded products...

So getting your rat tails tested for resistance is now more important than ever!

SEND IN YOUR TAILS FOR RESISTANCE TESTING – FREE of CHARGE



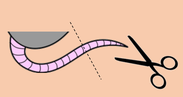
Rat tail clippings being tested at Reading University's laboratories

HAVING TROUBLE CONTROLLING AN INFESTATION?

FREE resistance testing and specialist advise is on hand from the University of Reading's Vertebrate Pests Unit funded by the Rodenticide Resistance Action Group (RRAC).

To know the most effective anticoagulant product to use you must first know if your rat/mouse population carries resistance and what type of mutation they possess. The only way to know this for certain is to have part of your rodent population genetically screened.

All you'd need to do is to put a tail of a rat or mouse into a clean plastic zip-lock bag and post it in an envelope, along with the postcode of where the tail came from. Site postcodes are treated as highly confidential and are not published in any form. Contact the Vertebrate Pests Unit for more information.



1. **CUT** 2-3cm tail tip

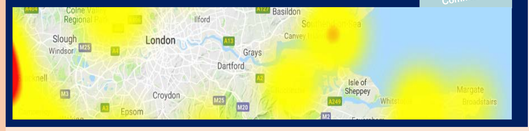
2. **BAG** in sealable bag

3. **POST** within 24hours

You can check if you're near resistance by going to RRAC's interactive map online:

http://guide.rrac.info/resistance-maps/united-kingdom/

RRAC Rodenticide Resistance Action Committee



Contact the Vertebrate Pests Unit Officers for more information about how you can get involved with the resistance project:

Email: e.e.coan@reading.ac.uk (Emily Coan)

Telephone: 0118 378 8329

VPU Vertebrate Pests Unit