Universitat Autònoma de Barcelona

FACULTAT DE VETERINÀRIA

EVOLUTION OF MYXOMA VIRUS AND RABBIT RESISTANCE

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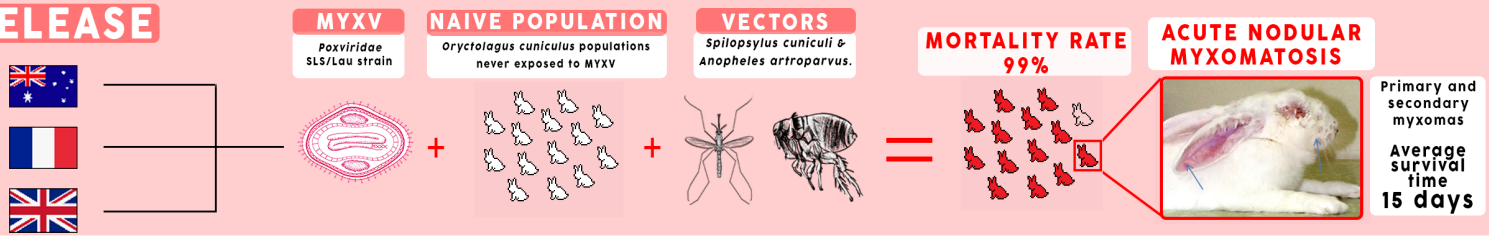
OBJECTIVES

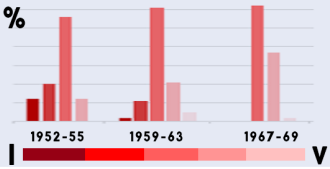
1. Describe the myxomatosis virus and the interaction with its host (*Oryctolagus cuniculus*).
2. Characterization of myxomatosis strains and evolution of virulence.
3. Discover the genetic mechanisms responsible for viral attenuation, rabbit resistance and the appearance of highly virulent strains
4. To describe how does the genome of the pathogen and its host adapts and evolve to survive.

RELEASE



SURVIVAL MECHANISMS TO MYXV

ATTENUATION

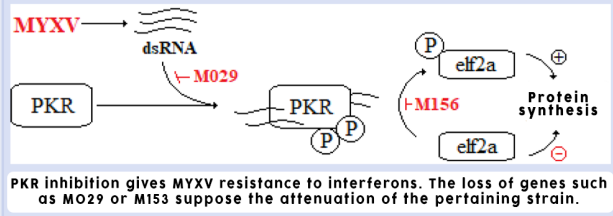


normal *aa* chain → Virulence protein

$1 \cdot 10^{-8}$ subs/site/year (INDEL type)

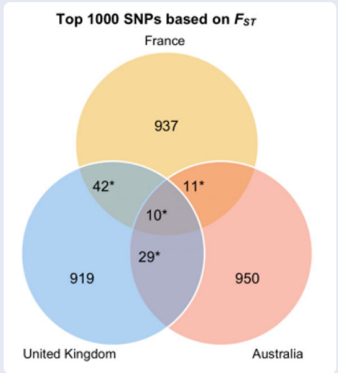
Type of mutations affecting virulence genes and protein function.

- Frameshift
- STOP-gain
- Readthrough



PKR inhibition gives MYXV resistance to interferons. The loss of genes such as M029 or M153 suppose the attenuation of the pertaining strain.

RESISTANCE



STANDING VARIATION

MHC-I loci | CD96 | IFN-α21A | MFDS1

Genetic variants present before the exposure to MYXV that have been selected in the three rabbit populations.

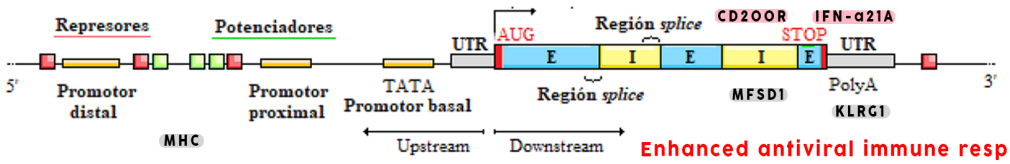
SPECIFIC VARIATION

CD200R | KLRG1

Genetic variants that have evolved independently in each population.

ATTENUATED NODULAR MYXOMATOSIS

Myxomas with spontaneous healing and recovery with a good general condition.



Enhanced antiviral immune response

CHANGE IN PATHOGENESIS

1975-80: Emergence of new hypervirulent strains

AMYXOMATOUS STRAINS

ACUTE COLLAPSE
Massive immunosuppression (10-12d of survival)

PROLONGED SURVIVAL
Blepharoconjunctivitis and pneumonia (25-30d of survival)

CHANGE IN PATHOGENESIS
Possible genetic mechanisms

- KEY MUTATION (M009L)
- MULTIPLE MUTATION
  Phenotypic convergence and compensatory genetic mechanisms
- CHANGES IN PROMOTING REGIONS

CONCLUSIONS

1. In a naive population with vectors, MYXV produces high mortality that is rapidly reduced because virulence decreases.
2. Attenuation of MYXV strains is caused by indel-like mutations affecting virulence genes.
3. The basis of genetic resistance in rabbits is polygenic and is the main mechanism for surviving MYXV. Standing variation allowed resistance to appear quickly, although there have also been changes that have evolved independently.
4. The myxomatosis virus is able to adapt to the resistance of its host by changing the pathogenesis and tropism to counteract the effectiveness of the immune response.