Suppression of viral infectivity through mutagen-induced lethal defection

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Optimal mutation rates result from the need to maintain an accurate enough level of genetic information while adapting fast to changes in the environment. It is believed that the high mutation rates of RNA viruses, together with their short replication time and large populations, favour their adaptation. However, as described in molecular evolution theories, the mutation rate has an upper limit and when this threshold is crossed, the genetic information is lost, and the population becomes extinct due to genetic melt down. This is known as error catastrophe.

It has been experimentally demonstrated that small increases of mutation rate through the use of mutagens can force the extinction of viral populations. Classical theories on error catastrophe equal fitness to replicative ability. If these theories are applied to viral quasispecies, it is necessary to consider that fitness is not only determined by the replicative ability of the genomes, and that there are a number of phenotypic functions that are also involved in the completion of the viral life cycle. In a normal infection a variable amount of the viruses produced are non-infective. If the amount of defective particles grows beyond a critical fraction, it is reasonable to suppose that a form of error catastrophe where defective mutants exhaust functional resources produced by viable genomes might supervene. To study the effect of increased mutagenesis in the production of non-infective genomes we have carried out several *in-vitro* experiments with lymphocytic choriomeningitis virus (LCMV). The results obtained will be presented at the workshop.