Correlation between interferon sensitivity of reovirus isolates and ability to discriminate between normal and Ras-transformed cells

The oncolytic virus must be able to efficiently destroy cancer cells without causing pathology, but normal cells can resist its replication. Comparing with normal cells, cancer cells have an impaired antiviral response that sensitizes them to oncolytic viruses (2). One such virus is reovirus, a benign, naturally occurring virus that can effect tumor regression in animal models. Reoviruses exhibit a propensity to replicate in transformed cells (3). It is currently believed that the interferon-inducible RNA-dependent protein kinase (PKR), an intracellular host-cell resistance factor that is inhibited by an activated Ras-dependent pathway in transformed cells, is responsible for this discrimination. In this study, it was observed that most isolates can bypass resistance mechanisms of parental cells at high m.o.i., and that there is a correlation between the ability to discriminate between transformed and parental cells, and interferon sensitivity. The interferon-hypersensitive mutant virus was more dependent on Ras activation than any other viral isolate. Altogether, this suggests that optimal reovirus isolates could be selected to attack tumour cells depending on the nature of the alterations in interferon-inducible pathways found in these cells (1).

Reference: