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Título artículo: Identification of a novel Myxoma C7-like host range factor that enabled a species leap from rabbits to hares

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Resumen: Myxoma virus (MYXV) is naturally found in rabbit Sylvilagus species and is known to cause lethal myxomatosis in European rabbits (*Oryctolagus cuniculus*). In 2019, an MYXV strain (MYXV strain Toledo [MYXV-Tol]) causing myxomatosis-like dis-ease in Iberian hares (*Lepus granatensis*) was identified. MYXV-Tol acquired are combinant region of;2.8 kb harboring several new genes, including a novel host range gene (M159) that we show to be an orthologous member of the vaccinia virusC7 host range family. Here, to test whether M159 alone has enabled MYXV to alter its host range to Iberian hares, several recombinant viruses were generated, including an MYXV-TolDM159 (knockout) strain. While MYXV-Tol underwent fully productive infection in hare HN-R cells, neither the wild-type MYXV-Lau strain (lackingM159) nor vMyxTol-DM159 (deleted for M159) was able to infect and replicate, showing that the ability of MYXV-Tol to infect these cells and replicate depends on the presence ofM159. Similar to other C7L family members, M159was shown to be expressed as an early/late gene but was translocated into the nucleus at later time points, indicating that further studies are needed to elucidate its role in the nucleus. Finally, in rabbit cells, the M159 protein did not contribute to increased replication but was able to upregulate the replication levels of MYXV in non-permissive and semi-permissive human cancer cells, suggesting that the M159-targeted pathway is conserved across mammalian species. Altogether, these observations demonstrate that the M159 protein plays a critical role in determining the host specificity of MYXV-Tol in hare and human cells by imparting new host range functions.

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