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Funding Source: USDA

Characterization of polyoxometalate I as an inhibitor of RNA-dependent RNA polymerase of Foot and Mouth Disease virus

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Foot and Mouth Disease (FMD) is a highly contagious disease that affects a variety of domesticated cloven-hoofed animals including cattle, swine, sheep and goats, as well as several wild animal species. FMD outbreaks are currently controlled with mass-extermination of livestock. The financial cost of potential outbreaks would be immense. This disease is caused by foot-and-mouth disease virus (FMDV), a non-enveloped, single-stranded, positive-sense RNA virus. The purpose of our investigation is to identify chemicals that interfere with the replication of FMDV. As part of this effort we have identified a polyoxometalate inhibitor (polyoxometalate I). We have cloned, expressed and purified FMDV RdRp. We use steady-state kinetic experiments and polymerization assays to characterize the inhibitory activity of the polyoxometalate I, determining the precise inhibitory potential and the mechanism of inhibition. Preliminary results show that polyoxometalate I inhibits the FMDV RdRp surprisingly efficiently with an IC50 of 0.5uM. Current experiments are focusing on a detailed kinetic characterization of the mechanism of action for this inhibitor. This research may provide insights that lead to new treatment options to prevent the further spread of FMD to unaffected animals.