Inhibition of the Essential Enterovirus VP4 Myristoylation Is a Potential Anti-viral Strategy for Hand, Foot and Mouth Disease

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Background/Objective

As an emerging public health threat, outbreaks of hand, foot and mouth disease (HFMD) has had an apparent increase in both frequency and severity in the recent years, particularly in Asia. The disease can result from infections by a plethora of enteroviruses, with type A enterovirus human enterovirus 71 (HEV71) being one of the most common aetiologic agents isolated during HFMD outbreaks. The N-terminal myristoylation signal (MGXXXS) of viral capsid protein VP4, one of the four viral structural proteins, is an extremely well conserved feature of enteroviruses, highlighting the integral role this co-translational modification plays in enterovirus replication and an anti-viral target worthy of further research. In this study, we sought to evaluate the possibility of targeting VP4 myristoylation in the treatment of HFMD.

Method

Small interfering RNA to human N-myristoyltransferases was used to confirm the importance of myristoylation in the replication of HEV71. Two myristic analogues, 2-hydroxymyristic acid (2OHM) and 4-oxatetradecanoic acid (4O), were used to inhibit myristoylation in infected rhabdomyosarcoma (RD) cells.

Result

We have confirmed myristoylation of VP4 is essential for HEV71 replication. Infected RD cells treated with 2OHM displayed a deficiency in VP0 cleavage into mature proteins VP4 and VP2 while those treated with 4O were found to have reduced viral replication on general.

Conclusion

Myristoylation of VP4 is essential to ensure progeny virus viability and the differential effects displayed by 4O and 2OHM highlights the possibility of further development of myristic acid analogues similar to 2OHM which exhibit lower cellular toxicity while retaining the ability to disrupt viral assembly.