Targeting enteroviral 2A protease by a 16-mer synthetic peptide: inhibition of 2Apro-induced apoptosis in a stable Tet-on HeLa cell line.


Abstract

Enteroviridae such as coxsackievirus are important infectious agents causing viral heart diseases. Viral protease 2A (2Apro) initiates the virus life cycle, and is an excellent target for developing antiviral drugs. Here, to evaluate the validity of the 2Apro as a proper therapeutic target, and based on the existing information and molecular dynamics, a 16-mer peptide was designed to specifically target the active site of protease 2Apro in order to block the activity of CVB3 2Apro. We showed that the peptide could compete with endogenous substrate in a concentration-dependent manner. Further, we established a HeLa cell line that expressed 2Apro. Expression of 2Apro resulted in significant morphological alteration and eventual cell death. Western blot and viability assay showed that the 16-mer peptide (200 microg/ml) could significantly block 2Apro activity and its cytotoxic effect. Future modification of the 16-mer peptide can improve its affinity for 2Apro and therefore develop effective antiviral drug.