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Dengue virus (DENV) infection is a mosquito-borne disease causing a spectrum of clinical symptoms ranging from mild febrile illness to dengue fever to more severe systemic disorders such as dengue hemorrhagic fever and dengue shock syndrome (1). DENV infection has emerged as a public health problem worldwide with over 2.5 billion people (>40%) of the world population at risk and with an annual rate of 50–100 million people in more than 100 endemic countries infected with DENV (2). DENV belongs to the Flavivirus genus and Flaviviridae family comprising four antigenically distinct serotypes, DENV1–4. DENV infection normally generates low immunogenic cross-protection; thus, the infected persons can be infected later with different DENV serotypes. Intriguingly, subsequent infection with different DENV serotypes may cause more severe disease because non-neutralizing antibodies from earlier DENV infections augment the severity of later infection via the binding of the virus–antibody complex to Fc receptor-bearing cells. This enhances DENV entry into host cells, a mechanism termed the antibody-dependent enhancement phenomenon (3). This mechanism increases the challenge for the development of a safe and effective vaccine to provide protective immunity against all four DENV serotypes. Currently, DENV vaccine candidates are at the clinical trial stage (4,5). Although the development and availability of a DENV vaccine should provide effective DENV protection, an anti-DENV agent for therapeutic use in patients with active DENV infection is urgently required. It was previously reported that the levels of circulating DENV load in infected patients correlated with disease outcome and that low levels of viremia in DENV-infected individuals were associated with a mild form of DENV fever (6–9).

Peptides are natural molecules used by many living organisms to defend themselves from viral, bacterial, fungal, and parasitic infections (10). Peptides possess several characteristics suitable for the development of antiviral agents. First, they are generally safer or less toxic when used as drugs compared with synthetic compounds (11). Second, they are structurally and biochemically diverse, which allows for a rationale design to specific target proteins of interest and to elicit therapeutic responses (12). Third, there is an example of an approved peptide inhibitor, enfuvirtide, against human immunodeficiency virus (13),
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Mimicking-Peptide Inhibitor Against Dengue

Figure 1: MLH40 peptide and its inhibitory effect on DENV infection in Vero cells.
Figure 2: Half maximal inhibitory concentration (IC50) values of MLH40 peptide against four DENV serotypes. DENV1 (A), DENV2 (B), DENV3 (C), and DENV4 (D) were treated with MLH40 peptide.
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**Figure 3:** Binding of MLH40 peptide to DENV. **Figure 4:** Effects of MLH40 peptide on time of addition and DENV2 infections. The inhibitory effect of 50 nM-MLH40 was tested to inhibit approximately 400 FFU of DENV2 based on the time of addition.
Figure 5: Inhibitory effects of MLH40 peptide on DENV2 in different cell types. DENV2 was treated with MLH40 before infection of Vero, A549, and Huh7 cells.
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Figure 6: Molecular docking and proposed mechanism of MLH40 peptide interactions with DENV E protein.