

Biotechnology and Healthcare



Anti-dengue Virus Antibody, Pharmaceutical Composition Comprising The Same, And Uses Thereof

Abstract

Dengue virus (DENV) infection may cause life-threatening dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Although there are several vaccine candidates in clinical trials, including a licensed tetravalent dengue vaccine which was developed by the company Sanofi Pasteur, therapeutic drugs are still highly desirable to cure acute dengue disease before the popularization of the dengue vaccine. DENV nonstructural protein 1 (NS1) has been introduced to act as a viral toxin which can enhance vascular permeability and disturb coagulation systems. However, autoantibodies elicited from molecular mimicry of NS1 to host proteins hinder the development of NS1-based antibody drugs. We identified a promising anti-NS1 monoclonal antibody (mAb) 33D2 that can recognize four serotypes of DENV NS1. In addition to restricting DENV spreading via complement-dependent cytolysis of infected cells, mAb 33D2 can neutralize infectious viral particles directly as well as *in vitro*. Due to the broad-spectrum protection, this mAb 33D2 can be a promising candidate for anti-viral therapy.

Benefits

1. Compared to full-length NS1-induced anti-NS1 polyclonal antibodies, mAb 33D2 can recognize four serotype DENV NS1 but would not cross-react to host proteins such as platelets, endothelial cells, and thrombin/prothrombin.
2. In addition to complement-dependent cytolysis (CDC), mAb 33D2 can also reduce infectious viral particles in complement independent manner.
3. mAb 33D2 can block NS1-induced endothelial permeability.
4. Broad spectrum against four serotypes of DENV infection.
5. No Antibody-dependent enhancement (ADE) effect in this anti-NS1 antibody

Possible Applications

- Medical Industries
- Dengue virus emergency treatment

Keywords

DENV, DHF, DSS, anti-viral therapy, NS1

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Analyze the cross reactivity of parental anti-NS1 mAbs by human tissue array.
Evaluate and compare the therapeutic effects of parental anti-NS1 mAbs 2E8 and 33D2 against DENV infection both *in vitro* and *in vivo*.
Third party validation results for murine anti-NS1 mAbs.
Generate humanized anti-NS1 mAbs 2E8 and 33D2.
Analyze the stability and safety of humanized anti-NS1 mAbs.
Re-evaluate the efficacy, minimum effective dose, and therapeutic mechanism of humanized anti-NS1 mAbs against DENV infection both *in vitro* and *in vivo*.
Establish the pharmacologic characteristics and preclinical information of humanized anti-NS1 mAb candidates.

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	h2E8	h33D2
<i>In vitro</i>		
Affinity (Biacore)	☑	☑
NS1 binding ability	☑	☑
CDC <i>in vitro</i>	☑	☑
ADCC <i>in vitro</i>	☑	☑
Permeability <i>in vitro</i>	☑	☑
<i>In vivo</i>		
Attenuation of prolonged bleeding time in mice	☑	☑
Attenuation of skin hemorrhage in mice	☑	☑
Safety (Cross reaction to human tissues)	☑	☑
Stability (T _{1/2} , day)	☑	☑