

Antibody that Inhibits Wnt Signal Activation Pathway

Background:

Every year, almost 2.5 Million people are bitten by poisonous snakes and about 10 thousand of these people are killed by snake venom. Although it is believed that an antivenin therapy is the best treatment, there are concerns of a global anti-serum shortage and anti-serums against each snake species is needed. Vascular Apoptosis-inducing protein (VAP1), which is in haemorrhagic snake venom, is a member of the ADAM (A Disintegrin And Metalloprotease) proteases family and induces apoptosis specifically in vascular endothelial cells. Elucidation of the target of ADAM proteases by researchers at Nagoya University has enabled the development of a therapeutic drug for multiple snake venom.

Technology Overview:

Although it is known that ADAM family proteases cause the severe bleeding from haemorrhagic snake venom, the detailed mechanism of the haemorrhage is unclear. Researchers at Nagoya University have found that the target of ADAM proteases is a Wnt/ β -catenin signal receptor, LRP5/6 which controls cell differentiation and proliferation. Furthermore, they revealed the mechanism of haemorrhage. They found that ADAM proteases cleave the Wnt/ β -catenin signal receptor on the cell surface to activate the signalling pathway. Therefore, the researchers invented a specific antibody that inhibits the Wnt/ β -catenin signal activation by binding to the ADAM recognition site on LRP5/6. Moreover, this invention is expected to inhibit infiltration-related ADAM protease activities as well, since Wnt/ β -catenin signalling involves vascular permeability or vascular invasion of leukemia and cancer cells.

Further Details:

Seo, T., *et al.*, 'Haemorrhagic snake venom metalloproteases and human ADAMs cleave LRP5/6, which disrupts cell-cell adhesions in vitro and induces haemorrhage in vivo.' FEBS J., 2017 Jun;284(11):1657-1671.

Potential Applications:

- New treatment for a poisonous snake bite by *Trimeresurus flavoviridis* (habu snake) or *Gloydius blomhoffii* (Japanese pit viper)
- Drug candidate for anti-vascular permeability or anti-vascular invasion of leukemia and cancer cells caused by inflammation or cancer.
- Therapeutic drug candidate for ADAM related disease such as arteriosclerosis

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