A NOVEL ANTITHROMBOTIC VACCINE AGAINST S100A9 WITHOUT RISKS OF BLEEDING IN ISCHEMIC STROKE IN MICE

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Introduction

Background

Long-term treatment with antiplatelet agents is important for secondary stroke prevention in patients with non-cardioembolic stroke. However,...

- Poor medication adherence
- Increased risk of bleeding
  - Intracranial hemorrhage
  - Gastrointestinal bleeding

Development of long-acting antiplatelet therapy w/o risk of bleeding

S100A9, a key molecule accelerating thrombus formation after vascular injury

Hypothesis

Neutralization of S100A9 with peptide vaccine could inhibit thrombus formation for a long duration without increasing risk of bleeding

Aims

- S100A9 peptide vaccine could produce adequate neutralizing antibodies to inhibit thrombus formation in ischemic stroke model without affecting hemostasis?
- How long the acquired antibody against S100A9 is kept in blood?
- There was no adverse immune response, such as cytotoxic T cell response?

Results

Antibody against S100A9 was successfully produced

Summary

- The epitope-based vaccine against C-terminus of S100A9 could successfully produce neutralizing antibody against S100A9 and prolong the occlusion time in a dose dependent manner.
- S100A9 vaccine had no influences on tail bleeding time nor hemostatic parameters.
- The produced antibody was kept to be expressed in blood at least up to two months. Boost immunization was effective.
- S100A9 vaccine did not induce adverse autoimmune responses.

Conclusions

Peptide vaccine targeting the C-terminus of S100A9 significantly suppressed thrombus formation after vascular injury in middle cerebral artery without affecting hemostatic parameters nor causing adverse autoimmune responses.

Although further studies on safety issues and clinically available adjuvant are needed, this new antithrombotic vaccine might be a novel strategy to prevent recurrent strokes.