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HUMAN ANTIBODIES FOR THE TREATMENT OF THROMBOINFLAMMATORY DISEASES

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Value Proposition: *Novel antithromboinflammatory therapeutic that utilizes humanized antibodies to prevent and attenuate thromboinflammatory diseases, including arterial thrombosis, ischemic stroke, and vascular inflammation.*

Technology Description

Researchers at Washington University in St. Louis have developed human anti-protein disulfide isomerase (PDI) antibodies (3H3 and 2C9) that can effectively reduce arterial thrombosis, ischemic stroke, and vascular inflammation. Thromboinflammatory diseases, including myocardial infarction, ischemic stroke, and vasculitis, result in a high number of deaths globally. Underlying these pathologies is increased adhesion activity of platelets and leukocytes. Current anti-thrombotic agents that block a cell signaling molecule, a ligand-cell surface receptor interaction, and coagulation factors reduce the morbidity and mortality associated with thrombotic disease, but they increase the risk of major bleeding. Also, anti-inflammatory therapies that target cytokines, cytokines receptors, or ligand-receptor interaction have been used for inflammatory disease treatment. However, these drugs impair immune responses.

These two antibodies effectively block platelet thrombus formation in mouse models of arterial thrombosis and reduce neutrophil recruitment to microvessels under thromboinflammatory conditions; making treatment for thromboinflammatory conditions safer, reducing the risk for major bleeding and immune responses.

Stage of Research

Tested in mice

Publications

- Cho J. Protein disulfide isomerase in thrombosis and vascular inflammation. J Thromb Haemost. 2013 Dec;11(12):2084-91. doi: 10.1111/jth.12413. PMID: 24118938; PMCID: PMC4076787.

- Hahm E, Li J, Kim K, Huh S, Rogelj S, Cho J. Extracellular protein disulfide isomerase regulates ligand binding activity of αMβ2 integrin and neutrophil recruitment during vascular inflammation. Blood 2013;121:3789-3800 (Plenary Paper) (Commentary in Blood 2013;121:3779-3780) PMCID: PMC3650702

- Kim K, Hahm E, Li J, Holbrook LM, Sasikumar P, Stanley RG, Ushio-Fukai M, Gibbins JM, Cho J.

Platelet protein disulfide isomerase is required for thrombus formation but not for hemostasis in mice. Blood 2013;122:1052-1061 PMCID: PMC3739031

- Li J, Kim K, Jeong SY, Chiu J, Xiong B, Petukhov PA, Dai X, Li X, Andrews RK, Du X, Hogg PJ, Cho J. Platelet protein disulfide isomerase promotes glycoprotein Ibα-mediated platelet-neutrophil interactions under thromboinflammatory conditions. Circulation 2019;139(10):1300-1319 PMCID: PMC6464389

- Jha V, Kumari T, Manickam V, Assar Z, Olson KL, Min JK, Cho J. ERO1-PDI redox signaling in health and diseases. Antioxid Red Signal 2021;35(13):1093-1115 PMCID: PMC8817699

Applications

- Treatment for thromboinflammatory conditions

Key Advantages

- Safer, and unlikely to cause immune responses
- Does not cause prolonged bleeding
- Novel therapeutic for thromboinflammatory conditions

Patents

Patent pending

Related Web Links – Jaehyung Cho Profile; Cho Lab