DR6 Agonistic Antibody for SLE Therapy

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Technology description

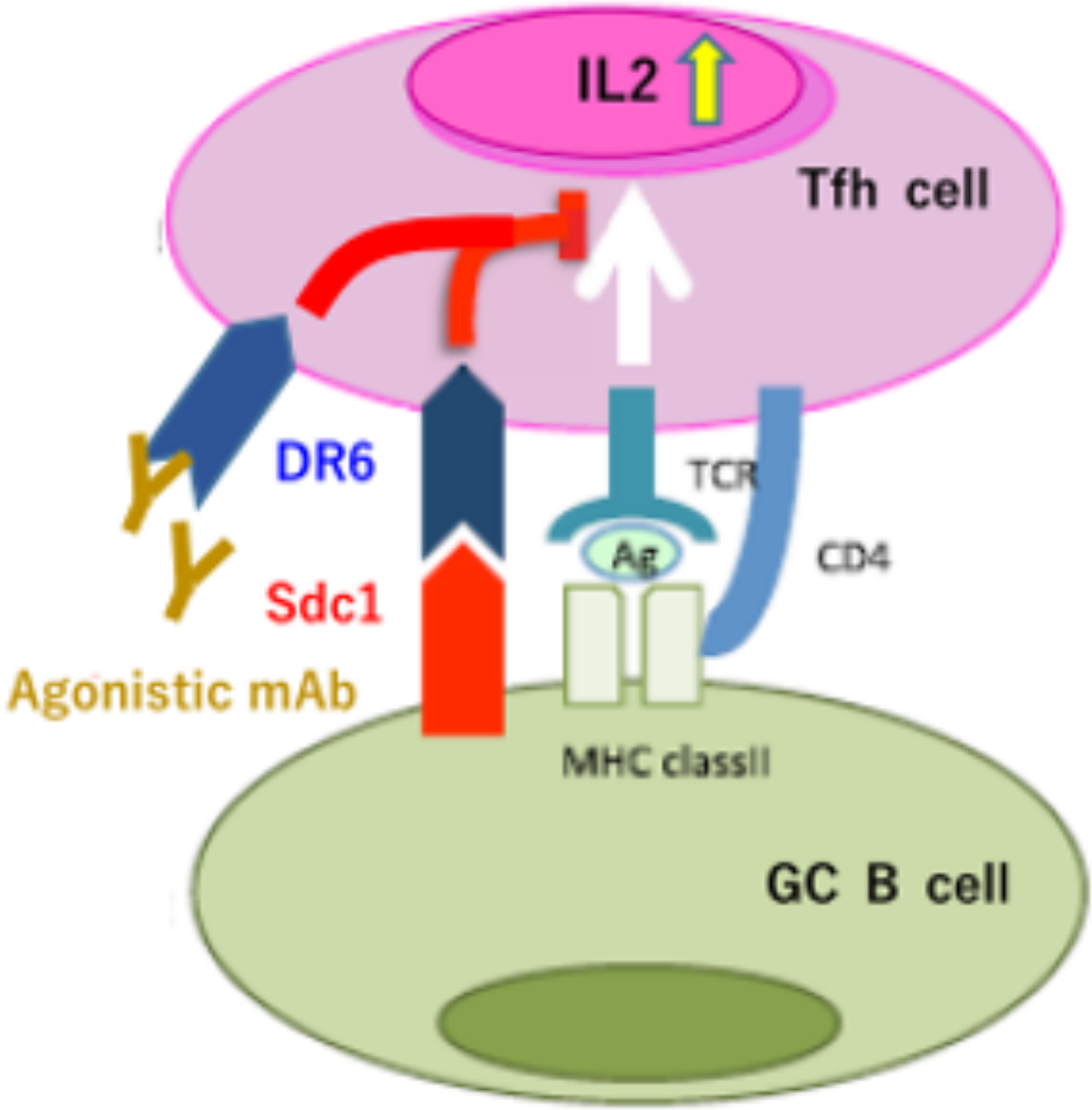
DR6 mAb promotes Sdc1-DR6 dependent immunosuppressive pathway in autoreactive T cells

Advantage and Core Benefit

We newly identified Sdc1 as a DR6 specific ligand inducing immunosuppressive effect in autoreactive Tfh cells expanding in autoimmune diseases.
DR6 is a promising target to control immune-response in autoimmune diseases and we already obtained DR6 specific agonistic monoclonal antibodies.

Background and Technology

Death receptor 6 (DR6 / TNFRSF21 / CD358), a tumor necrosis factor (TNF) receptor superfamily member, is type I transmembrane receptor, possesses four extracellular cysteine-rich motifs and a cytoplasmic death domain. DR6 is known as an orphan immunoregulator associated with T cell function in immunological diseases, including experimental autoimmune encephalomyelitis (EAE), asthma, acute graft versus host disease and systemic lupus erythematosus (SLE).
Syndecan-1 (Sdc1) is a glycosylated type-I transmembrane protein. Several studies suggest that Sdc1 has a suppressive function on the progression of immunological disease models such as EAE, nephritis and lung inflammation. In addition, it is reported that there is correlation between the amount of Sdc1 shed into peripheral blood and disease severity in SLE patients.
Here, we show DR6 expression on follicular helper T (Tfh) cells that are highly expanded in lupus-like disease model and identify Sdc1 as a specific ligand for DR6, and revealed an interaction between Sdc1 and DR6 resulting in immunosuppressive functions. Importantly, Sdc1 is expressed specifically on autoreactive germinal centre (GC) B cells that are critical for maintenance of Tfh cells. DR6 specific agonistic mAb delays disease progression in lupus-prone mice.
As additional potent application, DR6 can be a target for immuno-cancer therapy by using DR6 antagonistic mAb. We already have DR6 antagonistic mAbs.



Publication

Fujikura D et al., Nature Communications (2017) 3;8:13957.

Institution

Tech Manage Corp

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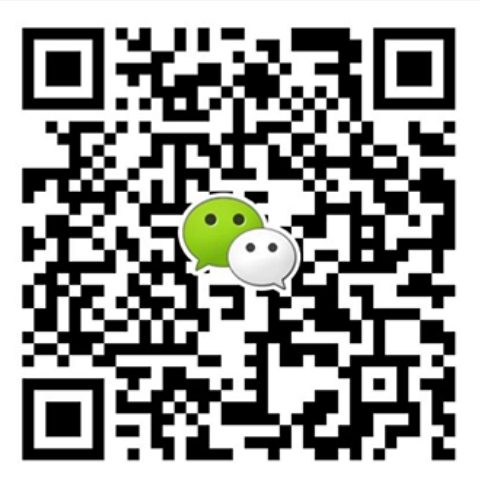

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