Treatment of Rheumatoid Arthritis with Death Receptor 5 Antibody

Application: Treatment of autoimmune disease

Advantages/Benefits:
- Targets active rheumatoid arthritis (RA) synovial cells and inhibits production of matrix metalloproteinases
- Targets activated macrophages
- Completed clinical Phase I trials using humanized DR5 antibodies

Abstract: RA is the most common form of inflammatory arthritis, costs U.S. society more than $80 billion each year and affects more than one in every 200 Americans. Disease modifying anti-rheumatic drugs are the current gold standard treatment for RA. These drugs only slow the progression of RA, rather than relieve inflammation and joint pain. Up to a third of patients do not respond adequately to current therapies and about half stop using treatment within five years. Researchers at The University of Alabama at Birmingham (UAB) have shown that treatment with Death Receptor 5 (DR5) antibodies successfully blocks joint destruction in RA animal models.

Technology Summary: Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) can play an anti-inflammatory role in the development of RA. TRAIL has several receptors, including DR5. Most normal tissues and cells do not express detectable levels of DR5 and are completely resistant to DR5-mediated apoptosis. In contrast, RA synovial cells express high levels of DR5 and are extremely susceptible to DR5-mediated apoptosis. In vivo studies demonstrated that a DR5 antibody is effective in blocking joint destruction induced by RA synovial cells by inhibiting production of matrix metalloproteinases, preventing bone erosion and cartilage destruction. Further studies demonstrated DR5 antibodies preferentially eliminate macrophages, a main contributor of RA, which results in decreased macrophage infiltration, synovial hyperplasia, osteoclast formation, joint destruction, cathepsin activity and inflammatory cytokine expression in the joints.

Developmental Status: Animal studies

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