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Rheumatoid Arthritis (RA) specific therapy with disease-specific monoclonal antibodies

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CD44 and RHAMM (CD168) are migration-supporting molecules in cancer and inflammatory cells, including synovial fluid cells from RA patients. In addition, CD44 is a transmitter of apoptotic signals. Exploring the human rheumatoid arthritis disease, we have discovered a CD44 variant (designated CD44vRA), that is generated by alternative splicing, and exclusively expressed on joint inflammatory cells of the RA patients. Monoclonal antibodies (mAbs) directed against human CD44vRA (anti-CD44vRA mAbs) bind exclusively to joint inflammatory cells of RA patients and kill them by apoptosis ,whereas peripheral blood leukocytes derived from the same patient remained undamaged when treated with the same antibodies. Anti-CD44vRA mAb injected at the onset of collagen-induced arthritis of DBA/1 mice markedly reduces the joint inflammation, indicating cross-reactivity between the mouse arthritic CD44 and human CD44vRA. We have shown earlier that RHAMM can compensate for CD44 in supporting *in vitro* cell migration and *in vivo* joint inflammation, when CD44 is genetically deleted (e.g., by CD44 Knock out). Hence, Injection of anti-RHAMM antibodies at the onset of CIA can also reduce the joint inflammation, but only when CD44 is genetically deleted. The clinical feasibility of anti-CD44vRA and anti-RHAMM mAbs is now under investigations in preclinical studies and part of available conclusions will be discussed.

Biography

David Naor completed his Ph.D. studies in the Hebrew University of Jerusalem and holds research positions, as post doc or visiting professor, in UC Berkley, UCLA and Imperial College, London. At present he is a professor of Immunology in the Faculty of Medicine, the Hebrew University. He published 150 articles, including publications in leading journal such as *Nature, PNAS, J Exp Med, J clin Invest* and *J Immunol*. He received award from Johnson & Johnson, in recognition of outstanding research toward the advances of science and technology in health care.

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