Casing the joint

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Current research provides a novel model for rheumatoid arthritis research. The related report by LaBranche et al, "Characterization of the KRN cell transfer model of rheumatoid arthritis (KRN-CTM), a chronic yet synchronized version of the K/BxN mouse," appears in the September 2010 issue of The *American Journal of Pathology*.

Nearly 1% of the population is affected by rheumatoid arthritis, and women are affected three to five times more often then men. Although the course of disease varies greatly, daily living activities are impaired in most affected individuals and after 5 years approximately 33% of sufferers are no longer able to work.

Rheumatoid arthritis is characterized by chronic inflammation of the distal joints and is mediated in part by emigration and activation of immune cells. The restrictions of present animal models, which either mimic chronic disease or a synchronized version of early disease (but not both), have hampered scientific understanding of the specific roles immune cells and their mediators play in disease initiation and maintenance. In this regard, Dr. Paul Allen and colleagues at the Washington University in St. Louis School of Medicine, in collaboration with Dr. Timothy LaBranche and colleagues at Pfizer Global Research & Development developed and characterized a chronic yet synchronized animal model of rheumatoid arthritis (KRN-CTM). Disease in these animals developed with a uniform onset of 7 days post-initiation and was maintained chronically (through Day 42). These mice revealed a time course of rheumatoid arthritis characteristics including edema, immune cell infiltration, cartilage damage and osteoclast-mediated bone

resorption.

According to Dr. LaBranche, "the main benefit of the KRN-CTM is its utility, which adds significant logistical and platform advantages to study T cell targets since the model is T cell-dependent and engages both early and late stages of innate and adaptive immune responses (a drawback of the antibody-dependent K/BxN serum transfer model). In addition, by polarizing T helper (Th) cells and/or knocking down genes prior to transfer, the KRN-CTM may enable investigators to ask how specific Th subsets and/or specific T cell genes contribute to disease. Lastly, incidence, onset, and severity of disease are highly synchronized without requiring adjuvant. The KRN-CTM presents a novel opportunity for investigators to study specific pathways and mechanisms involved in both the early and chronic phases of disease, thereby enabling the validation of targets and biopharmaceuticals for rheumatoid arthritis patients."

In future studies Dr.'s Allen and LaBranche aim to demonstrate the utility of the KRN-CTM, illustrating the roles Th subsets and particular genes have in both the model and people.

More information: LaBranche TP, Hickman-Brecks CL, Meyer DM, Storer CE, Jesson MI, Shevlin KM, Happa FA, Barve RA, Weiss DJ, Minnerly JC, Racz JL, Allen PM: Characterization of the KRN cell transfer model of rheumatoid arthritis (KRN-CTM), a chronic yet synchronized version of the K/BxN mouse. Am J Pathol 2010, 177: 1388-1396

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