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EXPERIMENTAL ARTHRITIS

OUTCOME OF BTK BLOCKADE IN MICE

The Bruton tyrosine kinase (Btk) inhibitor PCI-32765—currently in clinical development as a potential treatment for B-cell lymphomas—shows therapeutic promise in mouse models of inflammatory arthritis, according to a paper now published in *Arthritis Research & Therapy*.

The research was conducted by Betty Chang and colleagues at Pharmacyclics Inc., a company that is actively involved in the commercialization of Btk inhibitors. First, the team assessed the *in vivo* effects of PCI-32765 in animal models of arthritis, and then they investigated how the drug might work.

The researchers showed that PCI-32765 reduced disease severity in mice with established collagen-induced arthritis (CIA) in a dose-dependent manner, resulting in reduced inflammation, reduced pannus formation, and less cartilage destruction and bone resorption than seen in mice given control treatment. Similar results were obtained in collagen antibody-induced arthritis (CAIA): disease development was blocked in a dose-dependent manner in mice receiving PCI-32765 for 14 days after administration of the anti-collagen antibodies; control mice developed clinically advanced disease in the same period.

In both the CIA and CAIA models, PCI-32765 treatment resulted in reduced numbers of inflammatory cells (monocytes, macrophages and lymphocytes) and their cytokine and hemokine products in the synovial fluid of treated mice in comparison with control mice. Furthermore, the authors showed *in vitro* that, in addition to blocking B-cell proliferation downstream of the B-cell receptor, PCI-32765 also inhibited the production of proinflammatory mediators by monocytes and mast cells following Fcγ receptor stimulation.

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Original article Chang, B. Y. *et al.* The Bruton tyrosine kinase inhibitor PCI-32765 ameliorates autoimmune arthritis by inhibition of multiple effector cells. *Arthritis Res. Ther.* **13**, R115 (2011)