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## Technical Brief: Modification of the cellular response as a new target for managing osteoarthritis.

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Osteoarthritis (OA) research has primarily focused on the inhibition of particular enzymes, mainly cyclo-oxygenase, as targets for developing anti-inflammatory therapeutics for OA. Although many of these agents have potent activity, their use may have untoward side effects associated with constitutive cyclo-oxygenase inhibition. Recently, research has described another approach to controlling inflammation based on leukocyte and neutrophil inhibition<sup>1,5</sup>. It is well known that neutrophils are a predominant cellular response to bacterial infections and release a number of pro-inflammatory substances signaling arachidonic acid metabolism by cyclo-oxygenase and lipoxygenase. In addition, neutrophils release a number of lysosomal substances such as elastase and collagenase contributing to tissue destruction. The release of such mediators also signals the recruitment of more cellular infiltrates and may create an additive response.

It is well documented that neutrophils are associated with rheumatoid arthritis, but their implication in OA has largely gone unnoticed. One theory is that neutrophils play a predominant role in the maintenance of synovitis, and release lysate into the synovial fluid. Recent evidence implicates the neutrophil as a participant in the initiation and maintenance of chronic inflammatory conditions including OA<sup>2,3</sup>.

This information has created an entirely new approach to developing functional products targeted at inhibiting the ability of the neutrophil to transmigrate to the site of injury. Duralactin™ is thought to be a potent inhibitor of neutrophil adherence, migration and participation in the immune response to musculoskeletal conditions including arthritis. A recent study supports the function of Duralactin in dogs<sup>4</sup>.

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