PhD studentship 1: Structural pain modification in models of osteoarthritis (OA).

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**Background**
The link between OA joint pathology and pain experience is complex and incompletely understood. Disease modifying treatments, aiming to reduce joint damage, have met with limited success in reducing OA symptoms. This may indicate that some measures of joint damage do not address aspects of joint pathology that contribute to pain. We have proposed that 2 aspects of OA structural joint pathology are key to the pain experience in knee OA; (1) neoinnervation of structures within the joint that in the normal state contain no nerves, and (2) permeabilisation of the osteochondral junction, thereby exposing subchondral nerves to excitatory and sensitising factors in the synovial fluid. This project will use interventions in models of knee OA, with clinical validation where feasible, to explore the potential of modifying nerve growth and osteochondral permeabilisation as a sustained analgesic approach in OA.

**Methods**
Neoinnervation at the osteochondral junction and meniscus will be quantified by immunohistochemistry. Osteochondral permeability will be measured by morphology and conductance. Pain behaviour will be measured as differential weight bearing and distal allodynia. Effects of interventions on structural parameters and pain behaviour will be measured for inhibitors of nerve growth factor, and of articular cartilage degradation. Effects on pain behaviour will be distinguished between those due to structural modification and short term analgesic effects according to their associations with structural change and persistence after treatment withdrawal, and by comparison with centrally acting analgesic agents. Possible confounding by inflammation will be addressed by observational and histological measures of inflammation, and by control experiments using anti-inflammatory treatments.

The project will interact with other research within the Arthritis Research UK Pain Centre, and may be modified to take advantage of developments in pain and disease assessment that are expected through these related activities.

**References**