Research Project Details	
Title	Investigations of Mechanisms and Treatment in Post-Traumatic Joint Contractures (aka: PrEvention of Post-Traumatic ContRactures with Ketotifen – PERK)
Investigator(s)	Dr. Kevin Hildebrand, University of Calgary
Funding Period	December 2013 – March 2018
Budget	$119,228 (total from all funding periods)
Issue/Rationale	Post-traumatic joint contractures, or loss of motion after injury, are a debilitating condition following elbow trauma. Limited elbow motion interferes with feeding, dressing, grooming and reaching, which markedly reduces quality of life and job performance. Our research estimates that 12,000 elbow injuries per year occur nationally with 12 percent eventually requiring surgical release of the contracture. Our laboratory research on post-traumatic joint contractures over the last 16 years has implicated a myofibroblast-mast cell-neuropeptide axis of fibrosis in the joint capsule, the critical structure limiting joint motion. We have demonstrated in a rabbit model of post-traumatic contractures that Ketotifen, a mast cell stabilizer that prevents growth factor release, decreased contracture severity by 50 percent concomitant with decreased numbers of myofibroblasts, mast cells, neuropeptide containing nerve fibres and improved measures of fibrosis in the joint capsule. These results are very important because Ketotifen is the first and only agent demonstrated to significantly decrease contracture severity.
Objective(s)	To conduct a randomized, double-blind, placebo-controlled trial in participants with isolated elbow fractures or dislocations to determine if Ketotifen treatment (5 mg oral twice daily for six weeks, commenced within one week of injury) will significantly decrease the frequency and severity of post-traumatic joint contractures in patients with elbow fractures or dislocations, compared to placebo treatment.
Anticipated Results/ Impact	A need has been identified for high quality, well-reported, adequately powered randomized clinical trials (RCT) that evaluate medications for the prevention of post-traumatic joint contractures. Ketotifen has a wide safety profile and is available as an oral preparation. The most common side effects are sedation or weight gain (1 – 2 kg). Overdoses are managed with supportive measures and there are no reported deaths following overdose. Ketotifen has been used in the chronic treatment of asthma for over 40 years in humans. We are now in a position to rapidly translate our new knowledge into therapeutic advances for people at risk for this debilitating condition.
Keywords	Joint contractures, Ketotifen, randomized clinical trial, treatment, return to work