**THE ROLE OF CALCITONIN GENE-RELATED PEPTIDE IN DISCOGENIC BACK PAIN**

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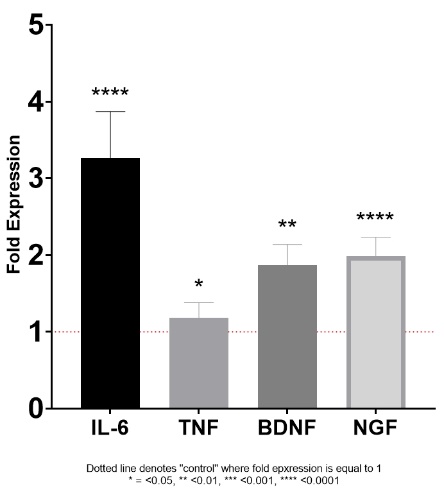
**BACKGROUND:** The prevalence of low back pain secondary to degenerative disc disease cannot be overstated. Recently introduced anti calcitonin gene-related peptide (CGRP) monoclonal antibodies represent an avenue for addressing discogenic back pain by non-operative means.

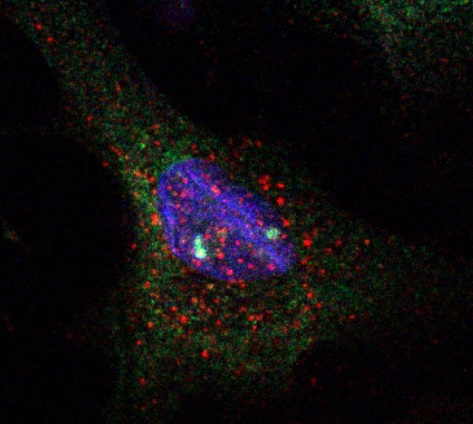
**METHODS:** Six (6) unique human intervertebral disc annulus fibrosus (AF) cell lines were used to study the effects of CGRP and proinflammatory mediators of discogenic pain. Cells were seeded on 3D polystyrene scaffolds to mimic the native disc environment. Treatment groups included CGRP 500nM alone, CGRP + erenumab (ligand blockade), CGRP + galcanezumab (receptor blockade), and control. The mRNA was extracted 3-hours post treatment, and reverse transcribed into cDNA. Quantitative RT-PCR was used to determine relative gene expression of the following: TNF-α, IL-6, BDNF (brain-derived neurotrophic factor), and NGF (nerve growth factor). Immunohistochemical staining was used to qualitatively describe the presence of CLR and RAMP1 (surface receptor proteins that bind CGRP) in AF cells. One-way ANOVA was used to assess the effect size across treatment groups with significance set at p≤0.05.

**RESULTS:** Treatment of AF cells with CGRP led to statistically significant increases in relative fold expression of IL-6 (p<0.0001), TNF-α (p:0.02), BDNF (p<0.01), and NGF (p<0.0001) (Figure 1). Preliminary data samples (n=2) demonstrated approximately 50% reduction in relative fold expression of IL-6 in AF cells pre-treated with either erenumab or galcanezumab before CGRP. There was a similar trend observed for other inflammatory mediators. Figure 2 describes the positive presence of CLR (green)/RAMP1 (red) receptor proteins at the surface of AF cells.

**CONCLUSIONS:** CGRP blockade at the level of the intervertebral disc represents a potential therapeutic pathway to minimize discogenic back pain and related inflammation.

**CONTENT CATEGORY:** basic and translational science

**KEYWORDS:** *low back pain, spine, orthopaedics, CGRP, monoclonal antibodies*



**Figure 1.** Neurogenic Inflammation after CGRP treatment **Figure 2.** Immunohistochemical staining for CLR/RAMP1 in AF Cells