中文題目：Cf-02 與槲皮素共享結構相似性的關節保護作用

英文題目：Arthroprotective Effects of Cf-02 Sharing Structural Similarity with Quercetin

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Background*:* we synthesized hundreds of analogues based on the structure of small-molecule inhibitors (SMIs) that were previously identified in our laboratory with the aim of identifying potent yet safe compounds for arthritis therapeutics. One of the analogues was shown to share structural similarity with quercetin, a potent anti-inflammatory flavonoid present in many different fruits and vegetables. We investigated the immunomodulatory effects of this compound, namely 6-(2,4-difluorophenyl)-3-(3-(trifluoromethyl)phenyl)-2H-benzo[e][1,3]oxazine-2,4(3H)-dione (Cf-02), in a side-by-side comparison with quercetin.

Method*:* Chondrocytes were isolated from pig joints or the joints of patients with osteoarthritis that had undergone total knee replacement surgery. Several measures were used to assess the immunomodulatory potency of these compounds in tumor necrosis factor (TNF-α)-stimulated chondrocytes. Characterization included the protein and mRNA levels of molecules associated with arthritis pathogenesis as well as the inducible nitric oxide synthase (iNOS)–nitric oxide (NO) system and matrix metalloproteinases (MMPs) in cultured chondrocytes and proteoglycan, and aggrecan degradation in cartilage explants. We also examined the activation of several important transcription factors, including nuclear factor-kappaB (NF-κB), interferon regulatory factor-1 (IRF-1), signal transducer and activator of transcription-3 (STAT-3), and activator protein-1 (AP-1).

Result: Our overall results indicate that the immunomodulatory potency of Cf-02 is fifty-fold more efficient than that of quercetin without any indication of cytotoxicity. When tested in vivo using the induced edema method, Cf-02 was shown to suppress inflammation and cartilage damage.

Conclusion: The proposed method shows considerable promise for the identification of candidate disease-modifying immunomodulatory drugs and leads compounds for arthritis therapeutics.