MYOSITIS

Gene expression profiles in muscle differ in myositis subtypes

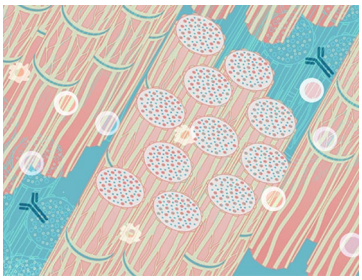
The results of a new study suggest that subtypes of the idiopathic inflammatory myopathies can be distinguished on the basis of their unique gene expression patterns in muscle biopsy specimens. Moreover, these patterns also identified pathological processes that are highly relevant in each subtype.

In the study, the researchers first identified all differentially expressed genes in muscle tissue specimens from 119 patients with inclusion body myositis (IBM) or myositis-specific antibody (MSA)-positive myositis (dermatomyositis, anti-synthetase syndrome or immune-mediated necrotizing myopathy (IMNM)) as well as in 20 specimens from healthy individuals that were used as comparators. They then compared the ability of ten different machine learning models to classify the specimens into each subtype of myositis on the basis of the gene expression data; one model, the linear support vector machine (SVM) model, was able to do so with >90% accuracy.

> “the researchers identified several genes that were overexpressed only in one type of myositis”

The recursive feature elimination technique was then used to determine which genes used by the linear SVM model were most important for differentiating the myositis subtypes. Using this approach, the researchers identified several genes that were overexpressed only in one type of myositis; for example, *CAMK1G*, *EGR4* and *CXCL18* were overexpressed only in anti-synthetase syndrome samples. Other genes were expressed at high levels only in certain MSA-defined myositis subtypes, such as *APOA4* and *MADCAM1*, which were upregulated in anti-HMGCR-positive IMNM and anti-Mi2-positive dermatomyositis samples, respectively.

Consistent with previous observations related to myositis pathogenesis, genes associated with



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interferon signalling were among the top differentially expressed genes in dermatomyositis, and genes related to muscle regeneration were prominently overexpressed in IMNM.

Although the study did not include specimens from patients with polymyositis or MSA-negative patients, and the analysis was restricted to gene expression (and not protein expression), the findings suggest that analysis of the gene expression profiles of myositis subtypes could provide pathologically relevant information.

Sarah Onuora

ORIGINAL ARTICLE Pinal-Fernandez, I. et al. Machine learning algorithms reveal unique gene expression profiles in muscle biopsies from patients with different types of myositis. *Ann. Rheum. Dis.* https://doi.org/10.1136/annrheumdis-2019-216599 (2020)

PAIN

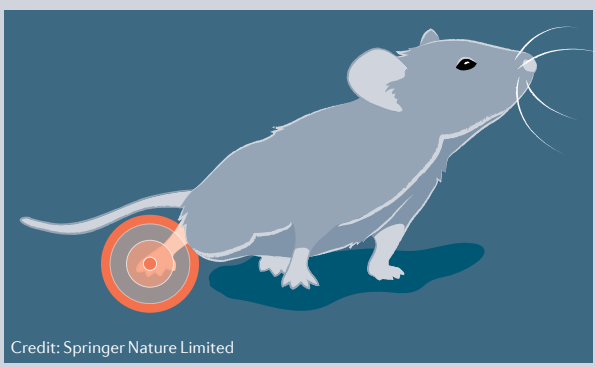
IL-23 promotes arthritic and inflammatory pain

IL-23 is a well-known pro-inflammatory mediator commonly associated with adaptive immune responses, particularly T cell responses, in arthritis; however, the involvement of this cytokine in innate immune responses and pain progression is less clear. A new study published in *Arthritis Research & Therapy* highlights a lymphocyte-independent role for this cytokine in disease and pain progression in mouse models of arthritis.

Previous findings had implicated various cytokines, including TNF, GM-CSF and CCL17, in innate immune-driven arthritis and arthritic pain. Given that inhibiting the p19 subunit of IL-23 could reduce the pain scores of patients with psoriatic arthritis in a clinical trial, the researchers of the new study sought to explore whether IL-23 has a T cell-independent function in arthritis that might be similar to that of, or involve, these other cytokines.

The researchers investigated the role of IL-23 in several models of arthritic pain and inflammatory pain using *Il23p19*$^{-/-}$ mice. In a macrophage-dependent model of monoarticular arthritis induced by intra-articular injection of zymosan, the absence of p19 protected the mice from the development of arthritis and arthritic pain. Similarly, compared with their wild-type counterparts, *Il23p19*$^{-/-}$ mice were protected from the development of inflammatory pain following intraplantar injection of zymosan.

> “IL-23 was … required for the induction of acute pain in various models”



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IL-23 was also required for the induction of acute pain in various models of cytokine-driven inflammatory pain involving systemic injection of either GM-CSF, TNF or CCL17 into mice with a methylated BSA (mBSA) ‘primed’ joint. Notably, intraplantar injection of exogenous IL-23 was sufficient for inducing acute pain in wild-type mice, which also required the presence of TNF, GM-CSF and CCL17.

“Currently, targeting GM-CSF or its receptor seems to be a promising approach in patients with rheumatoid arthritis,” says Kevin Lee, corresponding author on the new study. “Characterizing the possible connection between IL-23 and the GM-CSF–CCL17 pathway could help in understanding the biology of GM-CSF blockade in rheumatoid arthritis and therefore aid in the design of future clinical trials.”

Jessica McHugh

ORIGINAL ARTICLE Lee, K. M.-C. et al. IL-23 in arthritic and inflammatory pain development in mice. *Arthritis Res. Ther.* **22**, 123 (2020)