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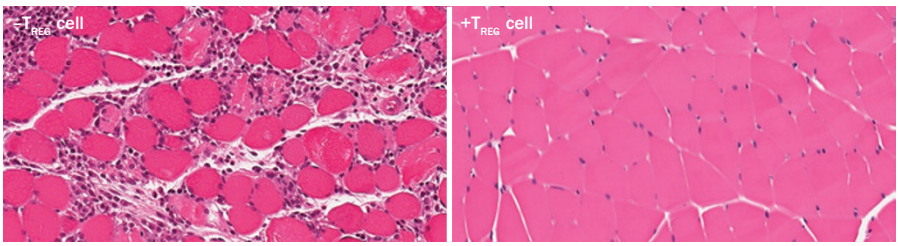
INFLAMMATORY MYOPATHIES

T_{REG}-cell deficiency and abnormal muscle antigen exposure important to the development of myositis

Novel insights into the pathogenesis of myositis have come from the demonstration of a crucial role for regulatory T (T_{REG})-cell deficiency and abnormal exposure to muscle antigens (myosin in particular) in the development of muscle inflammation in experimental models. "Aberrant exposure of muscle antigens is sufficient to induce myositis in the absence of T_{REG} cells," says author Wael Jarjour. "In this regard, we identify myosin to be at least one protein capable of eliciting this response," he explains.

Idiopathic inflammatory myopathies are characterized by chronic inflammation in muscle. Deciphering the underlying pathophysiology of this feature of the disease could enable the development of more specific and effective targeted therapies. To this end, the investigators developed mouse models in which aberrant muscle antigen exposure induced myositis (upon adoptive transfer of lymph node cells from T_{REG}-cell-deficient mice to prime an autoimmune response); additionally, a genetic abnormality in membrane resealing (synaptotagmin VII or SytVII mutant) was combined with a genetic defect causing T_{REG}-cell deficiency (Foxp3 mutant) in mice and the effects on induction of myositis were assessed.



Aberrant antigen exposure induces robust inflammation in muscle tissue (left) in a mouse model of myositis, which is resolved with T_{REG} cell supplementation (right). Magnification ×200; stain, haemotoxylin and eosin. Courtesy of W. Jarjour.

Foxp3-deficient lymph node cells co-transferred with myosin or muscle homogenate induced robust inflammation in skeletal muscle. Furthermore, severe myositis occurred upon transfer of lymph node cells from Foxp3–SytVII double mutant mice. Strikingly, myositis was suppressed when these lymph node cells were co-transferred with T_{REG} cells.

"The identification of myosin as an autoantigen in myositis makes it a potential target for induction of tolerance as a therapeutic approach," notes Jarjour, who hopes that their mouse model could be used to test new drugs for myositis.

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Original article Young, N. A. *et al.* Aberrant muscle antigen exposure is sufficient to cause myositis in a regulatory T cell-deficient milieu. *Arthritis Rheum.* doi:10.1002/art.38184