

## **TNF-alpha in an experimental model of myositis: Bilateral involvement in response to unilateral muscle overuse**

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By the use of a new experimental model affecting the triceps surae muscle of rabbits, leading to marked muscle overuse, the process of myositis can be followed. Interestingly, the model leads to muscle affection, including myositis, not only in the experimental side but also in the homologous non-experimental side. TNF-alpha expression becomes detectable in the cells of the inflammatory infiltrates both ipsilaterally and contralaterally. TNF-alpha expression is also seen bilaterally in necrotic muscle fibers and blood vessel walls. The process is accompanied by expression of TNF receptors in the inflammatory process and, unexpectedly, in nerve fascicles. In parallel studies we have noted that marked muscle structural changes take place, and that there is an affection of the nerve fascicles bilaterally. In parallel studies we have also noted that there is an upregulation of the substance P-ergic system bilaterally by the use of this model and that the glutamatergic system is involved in the inflammatory process. Parts of our studies are published, others are in progress. The studies show that unilateral marked muscle overuse leads to pronounced muscle affection including myositis bilaterally. Cross-over effects via the nervous system are likely to occur, similarly as the situation in arthritic processes. The studies furthermore show that TNF-alpha is markedly involved in the myositis process and that effects of TNF-alpha via TNF receptors occur for the muscle tissue itself, but also for the inflammatory infiltrates and, most interestingly, the innervation. The TNF-system is involved bilaterally in this process, i.e. also in the homologous non-experimental muscle.

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