# Chemokine-like Factor Expression in the Idiopathic Inflammatory Myopathies

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# Introduction

**Idiopathic inflammatory myopathies are the most common forms of acquired myopathies that includes-**

- **Polymyositis (PM),**
- **Dermatomyositis(DM)**
- **Inclusion body myositis**

## The suggested diagnostic features include

- Symmetrical proximal muscle weakness
- Elevation of serum skeletal muscle enzymes
- Specific electromyographic triad
- Characteristic muscle biopsy abnormalities
- Typical skin rash of DM

**In the pathogenesis of inflammatory myopathies, the following signaling molecules governingthe leukocyte activation and migration have been elucidated**

- Intercellular adhesion molecule
- Vascular cell adhesion molecule
- Veukocyte function-associated antigen
- Very late activated antigen
- Tumor necrosis factor-$\alpha$ (TNF-$\alpha$)
- Interferon-$\gamma$ (IFN-$\gamma$)
- Transforming growth factor-$\beta$ (TGF-$\beta$)

Recently, a novel cytokine, chemokine-like factor (CKLF) containing CC motif has been identified and characterized.

CKLFs, has a role in regulation of human skeletal muscle during myogenesis

Thus, in present study we evaluated the expression of chemokine-like factor (CKLF) in biopsied muscle fibers

- Inflammatory myopathies
- Non-inflammatory myopathies
- Neurologically diseased patients

# Materials and methods

- **Clinical materials**

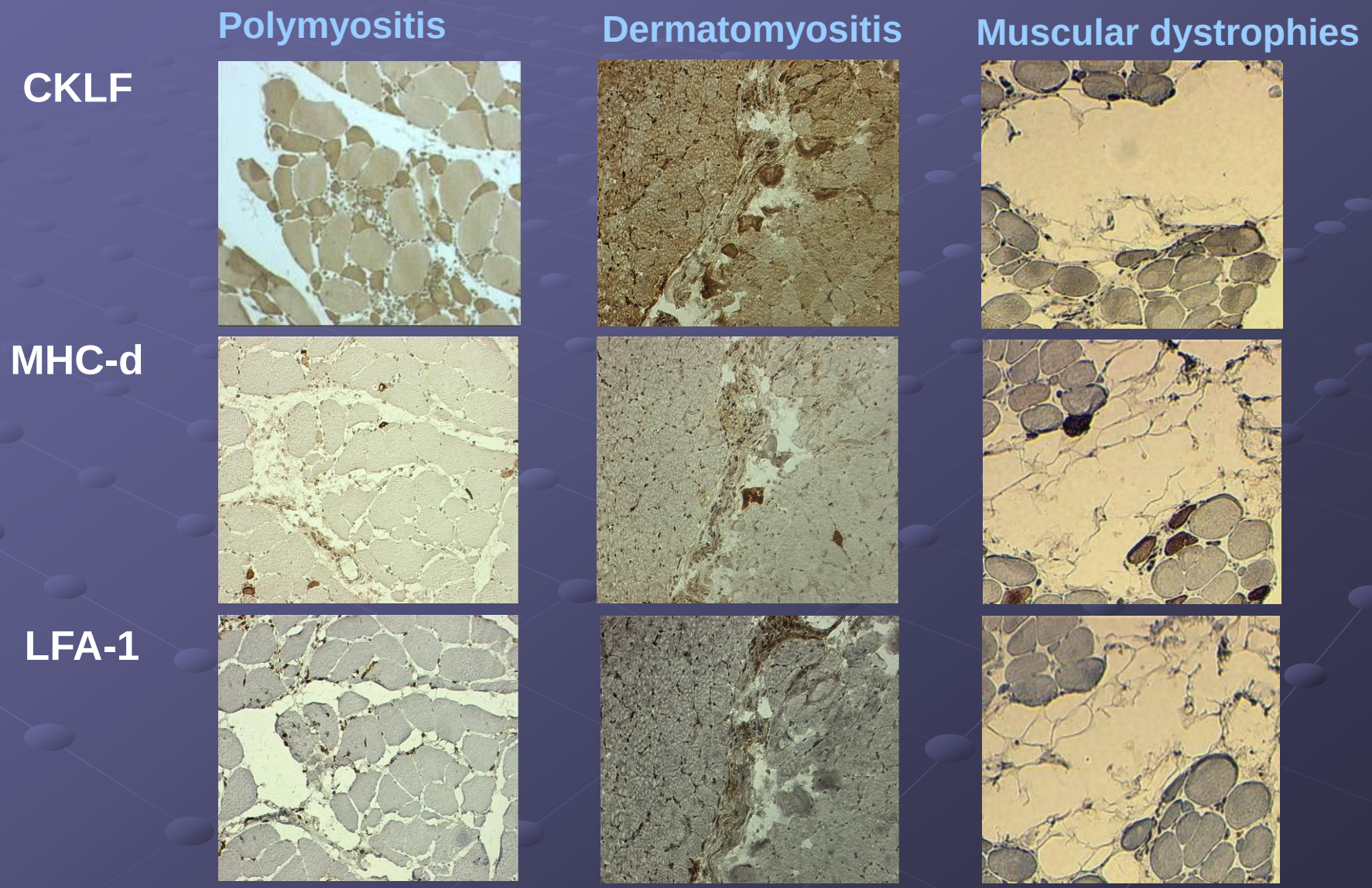
  **Four groups of patients were studied**

  - **The first group (n= 15) with polymyositis,**
  - **second group (n=5) with dermatomyositis**
  - **Third group (n= 15) muscular dystrophies**
  - **Fourth group (n=9) neurological diseased patients**

- **Immunohistochemistry of biopsied muscles**
- **Muscle cell culture**
- **Reverse Transcription Polymerase Chain Reaction (RT-PCR)**
- **Western blot analysis**

# Results

- Immunohistochemistry of biopsied muscle fibers

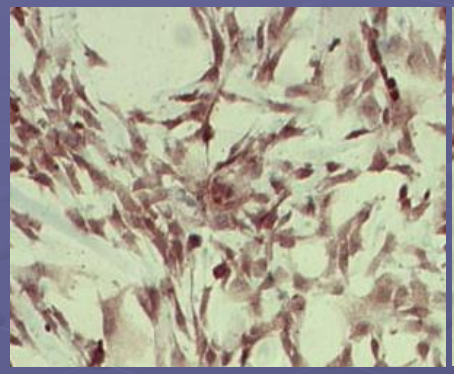
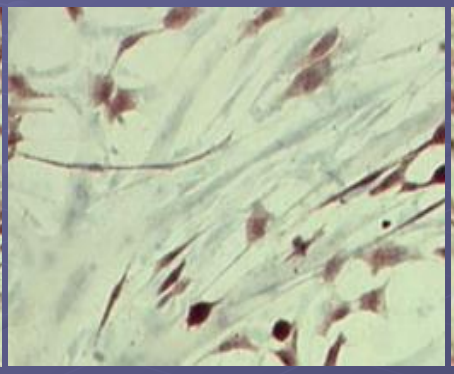
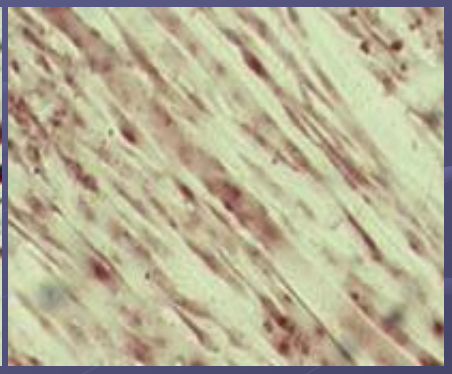


- CKLF immunoreactivities were remarkably detected in the inflammatory myopathies patients (14 PM and 4 DM), but not in the biopsies of non-inflammatory myopathies (n=15) and neurologically diseased patients (n=9)

- CKLF was mainly detected in small diameter (usually less than 5 μm) muscle fibers

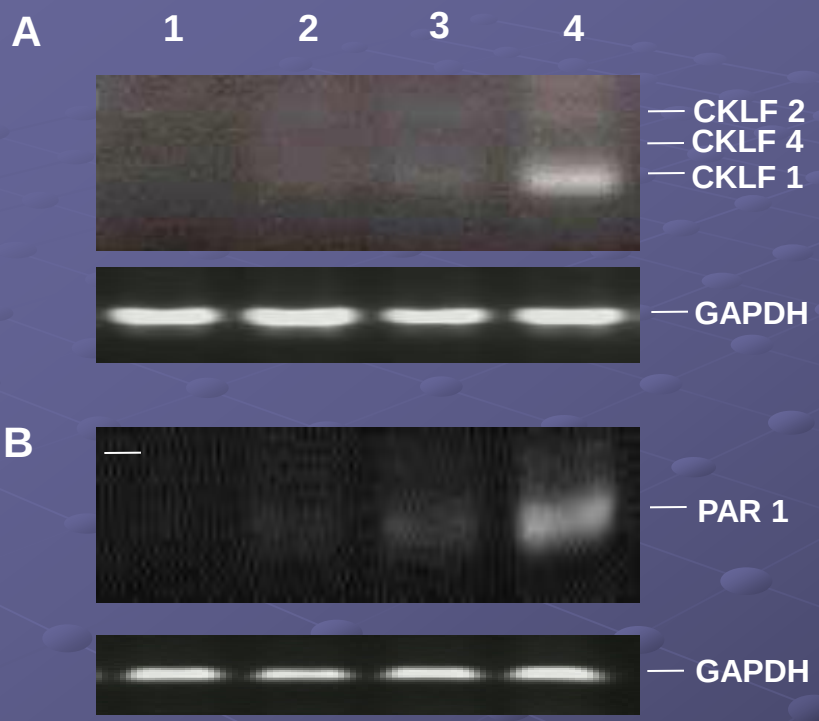
- CKLF-positive muscle fibers was more than that of MHC-d-positive muscle fibers

## Expression of CKLF in muscle cell culture

| | Myoblasts | Myotubes | Myotubes with thrombin |
|---|---|---|---|
| CKLF |  |  |  |

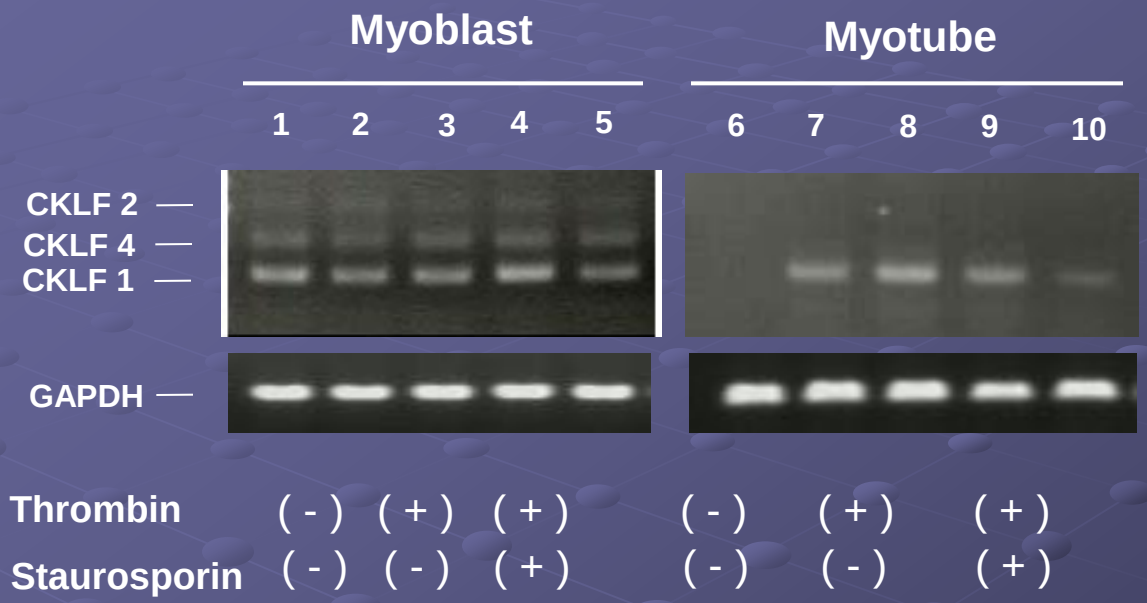
- Initially the myoblasts in muscle cell culture showed positive immunoreactivity for CKLF
- Immunoreactivities were abolished differentiated multinucleated myotubes
- Treatment with thrombin obtained immunoreactivity for CKLF

# Expression CKLFs and PARs in myotubes by RT-PCR



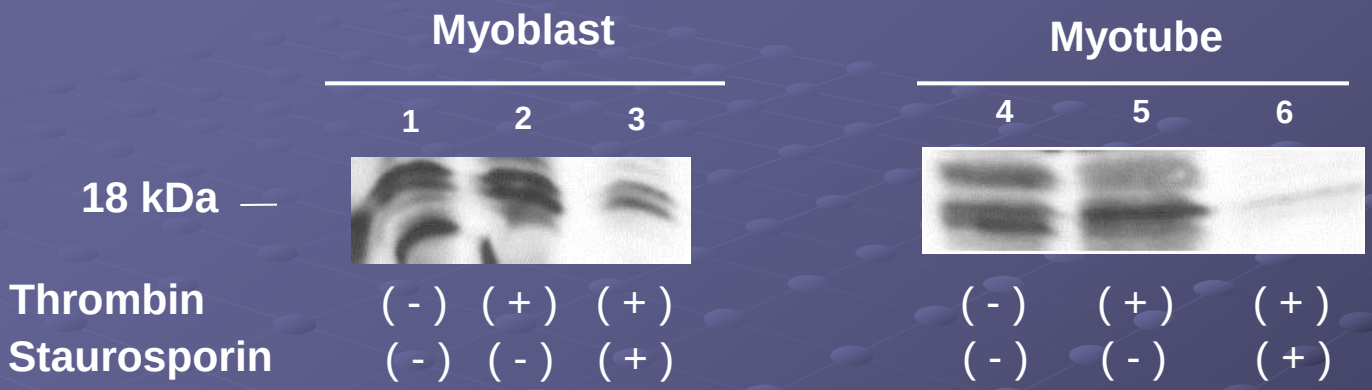

- Thrombin treatment increased CKLF-1, CKLF-4 and CKLF-2 and PAR-1expressions dose-dependently.

# Up-regulation of CKLF gene expression mediated by PKC activation




- In myoblasts, mRNA of CKLF was expressed constitutively
- In myotubes, mRNA of CKLF is inducible and PKC-dependent

## Effect of protein kinase inhibitor on thrombin-induced CKLF up-regulation by Western blot analysis




- In myoblasts and myotubes , control and thrombin treatment showed a clear band below 18 kDa, staurosporine treatment reduced that expression

## Discussion

- CKLF was remarkably expressed in the muscles from DM and PM as compared with non-inflammatory myopathies and neurologically diseased patients

- CKLF might be used as a marker for muscle regeneration in inflammatory myopathies.

- There may be a role of CKLF to chemoattract lymphocytes at the site of inflammation and regenerating muscle fibers

- Thrombin might play a major role for CKLF expression in the regenerating muscle fibers in inflammatory myopathies.

- CKLF was expressed constitutively in myoblats, but was inducible by thrombin in myotubes

- our study provides a new insight of thrombin involvement in the immunopathogenesis of inflammatory myopathies and the expressed CKLF can be used as a novel marker for regenerating muscle fibers during muscle inflammation.

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