Inhibition of Casein kinase II reduces TGFβ induced fibroblast activation and ameliorates experimental fibrosis

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CK2 (casein kinase II)
- A serine/threonine protein kinase that is ubiquitously distributed in eukaryotes
- A tetrameric complex
- Promotes tumorigenesis. Inhibition of CK2 by pharmacological inhibitors (e.g. TBB) showed in vivo inhibition of proliferation, inflammation and fibrosis leading to improvement in glomerulonephritis
- Upregulate Wnt signaling by inhibiting GSK3β
- Selective inhibitors of CK2 are currently evaluated in clinical trials

Inhibition of CK2 prevents myofibroblast differentiation and collagen release

CK2α and CK2β expression is increased in SSc in a TGFβ dependent manner

Disclosures

O. Distler has consultancy relationships and/or has received research funding from Actelion, Pfizer, Ergonex, BMS, Sanofi-Aventis, United BioSource Corporation, medac, Biovitrum, Novartis, 4D Science and Active Biotech in the area of potential treatments of SSc

J.H.W. Distler has consultancy relationships and/or has received research funding from Actelion, Pfizer, Ergonex, BMS, Celgene, Bayer Pharma, JB Therapeutics, Ansiaphere, Inc, Sanofi-Aventis, Novartis, Array Biopharma and Active Biotech in the area of potential treatments of scleroderma and is stock owner of 4D Science

The other authors declared no disclosures
Experimental fibrosis

Fibrosis

Inflammatory Early stage

Noninflammatory Late stage

CK2α and CK2β are increased in bleomycin-challenged and TBR-induced fibrosis

CK2α and CK2β staining

CK2β staining

CK2α staining

CK2β staining

Inhibition of CK2 prevents bleomycin-induced skin fibrosis

CK2 inhibition ameliorates TBR-induced fibrosis

Summary

• The expression of CK2α and CK2β is increased in SSc patients and in experimental fibrosis
• Pharmacologic inhibition of CK2 by TBB prevents the stimulatory effects of TGFβ on fibroblasts and inhibits JAK2-STAT3 signaling in vitro
• TBB prevents fibrosis in different mouse models of SSc and down-regulates JAK2-STAT3 signaling in vivo

CK2 inhibitors are currently evaluated in clinical trials with first promising results

Targeting CK2 may have translational potential

Acknowledgements

– Jörg Distler
– Colleagues:
  Clara Dees
  Christian Beyer
  Attiya Distler
  Pawel Zerr
  Katrin Zerr
  Ning Yu Lin
  Barbora Šumová
  Rosalbith Kagwiria
  Jinggang Huang
  Tatjana Mallano
  Chin-Hsien Chien