P G Trentin, , T P T Ferreira, A C S Arantes, B T Ciambarella, R S B Cordeiro, R J Flower, M Perretti, M A Martins and P M R Silva (2015). Annexin a1 mimetic peptide controls the inflammatory and fibrotic effects of silica particles in mice. *British Journal of Pharmacology*, v. 172, p. 3058-3071.

BACKGROUND AND PURPOSE:

Endogenous glucocorticoids are pro-resolving mediators, an example of which is the endogenous glucocorticoid-regulated protein annexin A1 (ANXA1). Because silicosis is an occupational lung disease characterized by unabated inflammation and fibrosis, in this study we tested the therapeutic properties of the N-terminal ANXA1-derived peptide annexin 1-(2-26) (Ac2-26) on experimental silicosis.

EXPERIMENTAL APPROACH:

Swiss-Webster mice were administered silica particles intranasally and were subsequently treated with intranasal peptide Ac2-26 (200 μg per mouse) or dexamethasone (25 μg per mouse) for 7 days, starting 6 h post-challenge. Ac2-26 abolished the leukocyte infiltration, collagen deposition, granuloma formation and generation of pro-inflammatory cytokines evoked by silica; these variables were only partially inhibited by dexamethasone.

KEY RESULTS:

A clear exacerbation of the silica-induced pathological changes was observed in ANXA1 knockout mice as compared with their wild-type (WT) littermate controls. Incubation of lung fibroblasts from WT mice with Ac2-26 in vitro reduced IL-13 or TGF-β-induced production of CCL2 (MCP-1) and collagen, but this peptide did not affect the production of CCL2 (MCP-1) by stimulated fibroblasts from formyl peptide receptor type 1 (FPR1) knockout mice. Ac2-26 also inhibited the production of CCL2 (MCP-1) from fibroblasts of FPR2 knockout mice.

CONCLUSIONS AND IMPLICATIONS:

Collectively, our findings reveal novel protective properties of the ANXA1 derived peptide Ac2-26 on the inflammatory and fibrotic responses induced by silica, and suggest that ANXA1 mimetic agents might be a promising strategy as innovative anti-fibrotic approaches for the treatment of silicosis.