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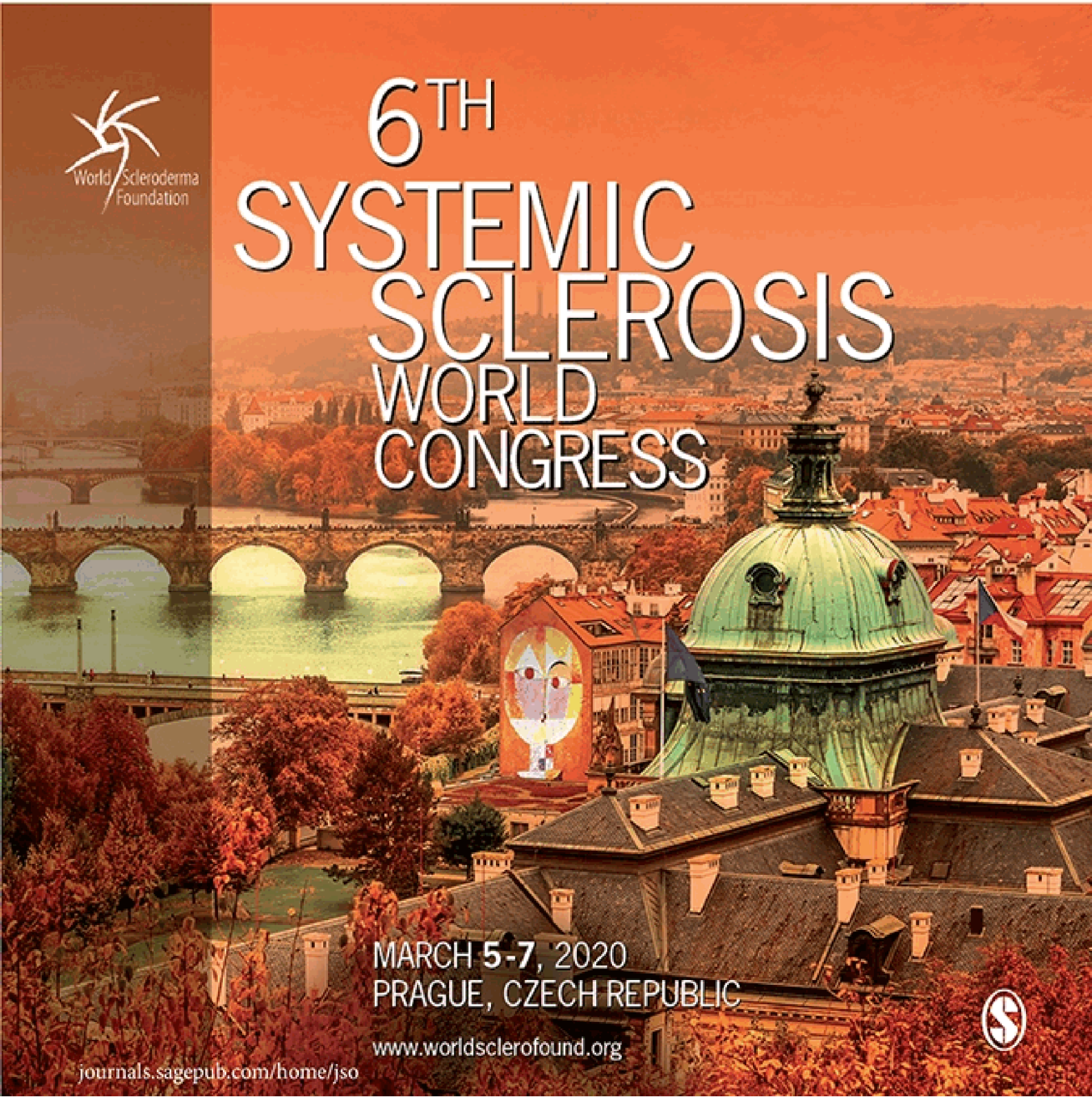

Conclusions: In conclusion, our findings support the potential use of NLR and PLR as inflammatory markers in activity and/or severity in patients with SSc.

1.Absenger G. et al. Br J Cancer 2013; 109:395
2. Valentini G. et al. Ann Rheum Dids 2001; 60:592

P.026

THE INTERCONNECTIONS BETWEEN ACTIVITIES OF THE OXIDATIVE-RELATED ENZYMES AND DISEASE ACTIVITY IN SYSTEMIC SCLEROSIS

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Introduction: Systemic sclerosis (SSc) is a chronic autoimmune disorder that is intimately associated with vascular damage and therefore with chronic perfusion/reperfusion and oxidative organ injury. Mesenchymal cell activation in SSc is now also considered to be mediated primarily through oxidative burst. Regulation of oxidative stress by specific enzymes including several purine metabolism enzymes is likely to play an important role in SSc progression. The objective is to characterize interrelationships among circulating xanthine oxidase (XO), xanthine dehydrogenase (XDH), superoxide dismutase (SOD) activities and SSc activity.

Material and Methods: 51 patients with verified SSc and 30 healthy controls were enrolled in the study. The diagnosis was verified using ACR/EULAR 2013 criteria. We assessed SSc activity in compliance with the original activity scale that is commonly used in Russia [Guseva, 1993] and by the 2001 European Scleroderma Study Group Activity Index. XO (EC 1.17.3.2), XDH (EC 1.17.1.4) and SOD (EC 1.15.1.1) plasma activities were measured by means of the spectrophotometric techniques [Dubinina, 1983; Karpova, 2006]. Results are expressed as mean±SD. The Mann-Whitney U test and Spearman's correlation coefficient were used for statistical analysis.

Results: Mean age of patients was 42.8±1.3 years, mean SSc duration was 7.9±0.7 years. Mean enzymatic activities in normal controls were 3.43±0.56 nmol/ml×min (for XO), 5.19±0.71 nmol/ml×min (for XDH), and 5.40±1.03 U (for SOD). The respective enzymatic activities in SSc group were 3.91±0.62 nmol/ml×min, 7.10±0.71 nmol/ml×min, and 7.10±2.19 U. All these mean activities were significantly higher in SSc patients comparing to healthy individuals ($p<0.001$). XO and XDH activities positively correlated with SSc activity ($r=0.499$, $p<0.001$; $r=0.741$, $p<0.001$, respectively). The opposite but weaker trend was observed for SOD activity and SSc disease activity ($r=-0.190$, $p=0.188$).

Conclusions: A close relationship between prooxidant/antioxidant enzymes and some of the key SSc pathogenetic mechanisms, especially vascular disease and fibroblast activation, is widely accepted. Overall increase of oxidative stress in patients with higher disease activity, as well as depletion of antioxidant capacity can be also linked with disturbance of purine metabolism through XO and XDH modulation. Pathogenetic influence of this imbalance can also be mediated through initial phase of neutrophil extracellular traps (NETs) formation, an eventual source of nucleoprotein containing autoepitopes.

P.027

THE ROLES OF PLATELET-DERIVED GROWTH FACTOR RECEPTOR (PDGFR) INHIBITOR IN SKIN FIBROBLASTS AND IN MICE MODEL OF SYSTEMIC SCLEROSIS

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Introduction: Systemic sclerosis (SSc) is an acquired autoimmune disorder that typically results in fibrosis of the skin and internal organs. Activated fibroblasts are the key effector cells in SSc responsible for the production of collagen and the development of fibrosis. In this study, we examined the role of crenolanib, an inhibitor of PDGFR signaling, in cultured skin fibroblasts and evaluated its antifibrotic effect in the angiotensin II (Ang II)-induced mice skin fibrosis.

Material and Methods: Healthy control (HC) and SSc dermal fibroblasts were cultured in the presence of crenolanib, TGF-β, PDGF ligands or CCN2. Cell proliferation was measured using the Incucyte® system. Skin biopsy samples collected from 15 healthy controls and 33 dcSSc patients were included in the microarray analysis. Ang II was administered by subcutaneous osmotic pumps in mice.

Results: Crenolanib effectively inhibited proliferation of SSc and HC fibroblasts, and attenuated basal and TGF-β-induced expression of CCN2 and periostin. In contrast to HC fibroblasts, SSc fibroblasts proliferated in response to PDGFAA, while a combination of PDGFAA and CCN2 was required to produce a similar response in HC fibroblasts. PDGFRα mRNA correlated with CCN2 and other fibrotic markers in the skin of SSc. In mice challenged with Ang II, PDGFRα-positive cells were increased in the skin. These PDGFRα-positive cells co-localized with PDGFRβ, procollagen and periostin. Treatment with