were sacrificed at either 7, 14 or 30 days after the last injection and blood, aorta and heart specimens were harvested. A pathologist (OT), blinded to treatment groups, examined aortic root and adjacent myocardium specimens and assigned a score for the degree of inflammation (0-6).

Results: Seven MCD-CAWS mice died unexpectedly within 24 hours of the first CAWS injection. Autopsies reviewed marked liver sinusoidal dilation in all and patchy necrosis of the liver in 4. Similar, liver findings were seen in 75% of MCD-CAWS after 7 days, but not in other groups. MCD-CAWS mice had higher systemic IL-6 compared to WT-CAWS at both 7 days (208 ± 21 vs 152 ± 12 pg/ml; $p < 0.001$) and 14 days (226 ± 49 vs 169 ± 19 pg/ml; $p = 0.04$), but not at 30 days. By 14 days mice in MCD-CAWS had significantly higher serum INF γ compared to WT-CAWS mice (97 ± 4 vs 87 ± 7 pg/ml, $p = 0.0086$) which remained persistently elevated even at 30 days (103 ± 8 vs 91 ± 4 pg/ml; $p = 0.002$). TNF α was higher in MCD-CAWS compared to WT-CAWS at 7 days (258 ± 8 vs 243 ± 6.5 pg/ml, $p = 0.0016$), 14 days (266 ± 14 vs 239 ± 6 pg/ml, $p < 0.001$) and 30 days (326 ± 52 vs 256 ± 8 pg/ml, $p = 0.002$). The average aortic root inflammatory score was non-significantly higher in the MCD-CAWS group compared to WT-CAWS at both 7 days (1.5 vs 1.3) and 14 days (3.7 vs 2.4).

Conclusion: Mast cell deficiency resulted in higher systemic levels of IL-6, TNF α and INF γ in the CAWS mouse model of Kawasaki's disease. Similarly, mast cell deficiency resulted in more intense inflammation at the root of the aorta in this model. These results support the novel concept that mast cells play a protective role in reducing the initial systemic inflammatory response in Kawasaki's disease.

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THU0507

TYPE I INTERFERON SCORE AND INTERFERON INDUCED MEDIATORS CXCL10 AND NEOPTERIN ARE CORRELATED WITH DISEASE ACTIVITY IN JUVENILE DERMATOMYOSITIS

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Background: Interferons (IFNs) seem to play an important role in the pathogenesis of juvenile dermatomyositis (JDM). Our group previously reported that expression of both type I and type II IFN related genes is increased in muscle biopsies of JDM patients and correlates with histological and clinical features of the disease.

Objectives: The aim of this study was to investigate expression of interferon regulated genes (IRGs), as well as serum levels of two type I and type II IFN induced chemokines (CXCL9, CXCL10) and neopterin in peripheral blood of JDM patients and to assess their correlations with clinical and laboratory findings.

Methods: We collected 189 blood samples from 39 JDM patients at different time points during follow-up. In 11 patients we obtained the first blood sample at time of muscle biopsy. We measured expression of type I IRGs (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1), IFN γ and type II IRGs (CXCL9, CITA, IDO1) by quantitative PCR (qPCR) and calculated a type I and type II IFN score for muscle and blood samples; serum

levels of CXCL9, CXCL10 and neopterin were analyzed by ELISA. Ten healthy subjects were used as controls (HC). At each visit, the following clinical data were recorded: physician's global assessment (PGA) of disease activity VAS (Visual Analogue Scale), cutaneous VAS, Cutaneous Assessment Tool (CAT) activity score, Childhood Myositis Assessment Score (CMAS), serum levels of creatine phosphokinase (CK, IU/l), presence of myositis specific or myositis associated antibodies (MSA/MAA), prednisone (or equivalent) dose (mg/kg/daily), ongoing immunosuppressive medications.

Results: Serum levels of CXCL9 were significantly correlated with muscle expression of IFN γ and type II IFN score. The correlation of CXCL10 levels with muscle type I and type II IFN score was weaker. Muscle expression of CXCL9 and CXCL10 correlated with serum levels of these chemokines. Type I IFN score in blood of JDM patients was increased compared to HC and significantly correlated with PGA, cutaneous VAS, CAT activity score. Serum levels of CXCL9 and CXCL10 were significantly higher in JDM patients compared to HC. MSA positive JDM patients showed higher levels of CXCL9 and CXCL10 compared to MSA negative patients. CXCL10 levels correlated with PGA and CMAS, but not with cutaneous disease activity. CXCL9 showed no significant association with the evaluated clinical features. Neopterin levels significantly correlated with PGA, cutaneous VAS, CAT activity score and CMAS.

Conclusion: Our findings indicate that expression of IRGs, measured as type I IFN score, and serum levels of CXCL10 and neopterin reflect specific features of disease activity in JDM, supporting their role as valuable disease biomarkers.

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CHANGES IN MIR-17-92 CLUSTER EXPRESSION LINK SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS, MONOCYTE-TO-MACROPHAGE DIFFERENTIATION, AND INTERFERON REGULATION

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Background: MicroRNAs (miRNAs) are small noncoding RNAs which post-transcriptionally regulate gene expression. The miR-17-92 cluster is well studied in cancer biology and cellular differentiation; its overexpression has been found to serve a major oncogenic role in the targeting and downregulation of tumor-suppressive pathways, such as PTEN or TGF β . Our previous work identified several members of the cluster – miR-18, miR-19a/b, miR-20a, and miR-92a – with significantly higher levels in monocytes from patients with active Systemic Juvenile Idiopathic Arthritis (SJIA). SJIA is a chronic inflammatory disease of childhood with features of autoinflammation, and innate immune cells including monocytes have important roles in disease pathogenesis. Children with SJIA are at risk for life-threatening complications including Macrophage Activation Syndrome (MAS), an episode of overwhelming inflammation characterized by macrophage proliferation and driven by IFN γ .

Objectives: Characterize the regulation of the miR-17-92 cluster, define key targets, and determine the cluster's role in inflammation and SJIA.