infusion in our rat model, using powerful anti-inflammatory but non-toxic drugs is to begin soon.

Abstract A15

Proteoglycans as a double-edged sword in multiple sclerosis: Implications for future approaches to immunomodulatory therapy

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Proteoglycans are components of the extracellular matrix that have been identified as barriers to endogenous remyelination. Surfen (bis 2-methyl, 4-amino, 6-quinolyl amide) is a small molecule proteoglycan antagonist. We have previously reported that surfen reduces T cell proliferation in vivo and in vitro while also decreasing the production of chemotactic and pro-inflammatory factors produced by macrophages. Here we extend these studies to clinically relevant mouse models of chronic neuroinflammation (experimental autoimmune encephalomyelitis; EAE) and focal demyelination (lysolecithin). In the EAE model, surfen treated mice displayed a reduced disease severity that was associated with decreased percentages of CD4+CD45+ T cells and CD11b/F480 myeloid populations in the spinal cord. The chemokines RANTES, CCL2, and CCL3 were reduced in the spinal cords of surfen treated mice, resembling previous in vitro macrophage results and implicating a chemotactic mechanism that reduces cell infiltration. By contrast, when surfen was administered into a developing brain lesion using the lysolecithin model of demyelination it produced significantly larger lesions. The opposing effects of surfen observed in EAE and the lysolecithin model suggests that distinct proteoglycan families influence inflammation and remyelination differently depending on the stage of repair.

Abstract A16

Biopsy pathology in a large cohort of juvenile dermatomyositis is heterogeneous and, for the most part, independent of autoantibody phenotype

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Background: Juvenile dermatomyositis has come to encompass several subtypes based on an emerging correlation between autoantibodies and clinical presentation. We hypothesised that myopathological findings may align with clinico-serological subtypes, potentially indicating differences in pathogenesis.

Methods: We studied a large cohort of 101 muscle biopsies from JDM patients in the UK JDM Cohort and Biomarker Study using the international JDM score tool and performing histological analysis of dominant fiber pathology. Autoantibody data were available for the majority of patients and were correlated with histological findings.

Results: Major autoantibody groups in our cohort were anti-TIF1γ (18/101), -NXP2 (15/101), -MDA5 (11/101), -Mi2 (5/101), and -PmScl (6/101). JDM biopsy severity scores varied within antibody groups except for MDA5 with consistently low, and Mi2 with consistently high scores. Dominant fiber pathology was grouped under 8 descriptive labels (minimal change (24/101), diffuse endomysial macrophage infiltrates (40/101), perifascicular atrophy (22/101), macrophage rich necrosis (6/101), scattered necrosis (2/101), clustered necrosis (2/101), inflammatory fiber invasion (2/101), chronic myopathic change (1/101)). All major autoantibody groups showed a mix of fiber pathologies with the exception of MDA5, which consisted predominantly of minimal change biopsies.

Conclusion: JDM patients demonstrate a range of muscle biopsy findings in our cohort with perfascicular atrophy represented in only about one third of biopsies. Dominant fiber pathology or severity scores do not clearly predict autoantibody groups. Heterogeneity of muscle histology in JDM is not fully understood but may indicate differences in activation of inflammatory signaling pathways in muscle between patients.

Abstract A17

Myopathology of Isolated Congenital Ptosis

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Isolated congenital ptosis is incomplete retraction of the upper palpebrae since birth, usually bilateral, and not associated with external ophthalmoplegia, facial weakness or other neurological deficits, neuromuscular disease (myasthenia; congenital myopathies), systemic metabolic disease (mitochondrial cytopathy; organic acidurias) or structural lesions of the eyelid (plexiform neurofibroma; haemangioma; Meibomian or epithelial cysts; abscess). It may occur as a Mendelian trait, especially if the parents are consanguinous, or a genetic defect may not be evident from family history. Treatment is surgical resection of palpebral tissue from the conjunctival side of the eyelid.

We performed pathological examination of such resections in 28 infants and children, including immunocytochemical markers for smooth and striated slow and fast muscle myosin. Results showed structural lesions in 3; agenesis or hypoplasia of the striated levator palpebrae muscle with preservation of the smooth Müller muscle in 23, selective agenesis of Müller muscle in 1 case, and no evident lesions in 1 patient. Mild subconjunctival

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