Improving Skin Repair

miR-29 has been implicated in skin repair. Using human skin samples, cultured cells, and a cutaneous wound healing mouse model, Robinson and Thiagarajan et al (Am J Pathol 2024, 195–208) studied the effect of inhibiting miR-29 on epidermal regeneration. Inhibition of miR-29 promoted angiogenesis both in vivo and in vitro and increased maturation of provisional granulation tissue in vivo. miR-29 target mRNA laminin C2 may facilitate these processes. Inhibition of miR-29 or up-regulation of laminin C2 may improve skin repair.

Understanding Pediatric Asthma

The effect of the neuropeptide Substance P (SP) on macrophage phenotype in pediatric asthma is unclear. Using a mouse model, cultured cells, and pediatric asthmatic patient samples, Li et al (Am J Pathol 2024, 238–252) studied this effect. Asthmatic children had an increased level of SP and a higher proportion of M2 macrophages in their bronchoalveolar lavage fluid. SP promoted M2 macrophage polarization by up-regulating STAT6 and sustained allergic inflammation in pediatric asthma by increasing STAT6-dependent transcription activation of lymphocyte cytosolic protein 2 (LCP2). Modulation of SP, STAT6, and/or LCP2 may prove beneficial to pediatric asthmatic patients.

Linking Microbiome and Muscle Pathophysiology

Gut microbiota affects skeletal muscle. Using mdx and control mouse models, Jollet et al (Am J Pathol 2024, 264–279) studied the link between the microbiome and muscle pathophysiology with age. In addition to changes in gene expression, mdx mice showed decreased gut microbiota diversity for specific genotypes, slowed gut peristalsis, and increased intestinal porosity compared to control mice with age. The gut microbiome affects muscle pathophysiology, and hence should be considered in management of muscular dystrophies.

Mitigating Intervertebral Disc Degeneration

The transcription factor FOXO3 has been implicated in intervertebral disc degeneration (IDD); however, the underlying mechanisms are unclear. Using nucleus pulposus (NP) tissue samples from patients undergoing surgery for lumbar disc herniation, mouse cultured NP cells, and a novel mouse model, Hao and Zhu et al (Am J Pathol 2024, 280–295) studied these mechanisms. Foxo3 knockout mice were generated. Foxo3 deficiency in mice impaired intervertebral disc (IVD) maturation and homeostasis in postnatal mice and caused extracellular matrix degradation of the IVD. FOXO3 delayed IDD development via activating HOTTIP transcription, reducing the binding of miR-615-3p to COL2A1, and up-regulating COL2A1. FOXO3 may be targeted to manage IDD.

Studying Macrophage Depletion in Temporomandibular Joint Osteoarthritis

The role of macrophage depletion in temporomandibular joint osteoarthritis (TMJOA) is unclear. Using a mouse model of TMJOA, Hu and Li et al (Am J Pathol 2024, 296–306) studied this role. Macrophages facilitated the progression of TMJOA. Macrophage depletion in TMJOA synoviocytes promoted synovitis, cartilage damage, and condylar destruction, and resulted in the up-regulation of pro-inflammatory cytokines. Macrophage depletion in TMJOA synoviocytes may promote synovitis and cartilage destruction in TMJOA.