A microRNA in the excretory-secretory products of helminth parasites induces dedifferentiation in epithelial cells within gastrointestinal organoids

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Infection with helminth parasites is a major health and economic problem in humans and livestock. Helminths can modulate host immune responses, mainly via release of excretory-secretory (ES) products, including proteins and microRNAs (miRNAs). The impact of parasite miRNAs on host gene expression and immune outcome remains unclear. Nematodes infecting the gastrointestinal (GI) tract are closely associated with host epithelial cells that initiate a type 2 response and are responsible for the 'weep and sweep' response to expel GI nematodes. In this study, we detail the effect of a pan GI-nematode-secreted miRNA on host epithelial cells using GI organoids. We show that this secreted parasite miRNA can suppress the effects of the type 2 cytokine IL-13, resulting in reduced expansion of tuft and mucous-secreting cells. Bioinformatic and organoid studies indicate that the parasite miRNA regulates host transcription factors, stimulating GI cell proliferation and suppressing differentiation and, at the same time, promoting tissue regeneration following IL-13 stimulation. Our data advance understanding of the intricate crosstalk between host and parasite and identify novel functions of a parasite miRNA with potential therapeutic benefits in the repair of GI tissue caused by infection or immune-mediated damage.