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IN BRIEF

CANCER

Minimizing metastasis

There is a lack of therapeutic approaches that block metastasis, primarily due to the complexity of the process. In a metastatic prostate cancer cell line, Frankowski et al. carry out a high-content screen using reduction of the perinuclear compartment (a complex subnuclear body formed almost exclusively in cancer cells and associated with metastasis) as a phenotypic biomarker to identify anti-metastatic compounds. Optimization of a screening hit identified metarrestin, which disrupts the nucleolar structure and inhibits RNA polymerase I transcription. In mouse cancer xenograft models, intraperitoneal metarrestin treatment suppressed metastasis and increased survival.

ORIGINAL ARTICLE Frankowski, K. et al. Metarrestin, a perinucleolar compartment inhibitor, effectively suppresses metastasis. *Sci. Transl Med.* **10**, eaap8307 (2018)

INFECTIOUS DISEASE

Alphavirus receptor identified

The host factors required for entry of arthritogenic alphaviruses, such as Chikungunya virus (CHIKV), remain poorly characterized. Using a genome-wide CRISPR–Cas9-based screen in mice, Zhang et al. identified the host cell adhesion molecule MXRA8 as a mediator of CHIKV entry. Further studies in mouse and human cell lines revealed MXRA8 to be required for infection by multiple other arthritogenic alphaviruses. Mechanistically, MXRA8 bound directly to CHIKV particles, which enhanced virus attachment and internalization into cells. Injection of mice with anti-MXRA8 blocking antibodies reduced CHIKV and O'nyong nyong virus titres and decreased foot swelling.

ORIGINAL ARTICLE Zhang, R. et al. Mxra8 is a receptor for multiple arthritogenic alphaviruses. *Nature* **557**, 570–574 (2018)

AUTOIMMUNE DISEASE

Aryl hydrocarbon receptor suppresses inflammation

The aryl hydrocarbon receptor (AHR) plays a key role in modulating the immune response and has been linked to several autoimmune diseases. Rothhammer et al. now report that the AHR limits microglial pro-inflammatory transcriptional responses in the experimental autoimmune encephalomyelitis (EAE) mouse model of multiple sclerosis (MS). By regulating microglial production of TGFα and VEGF-B (which ameliorate or worsen disease respectively), the AHR modulates astrocyte pathogenic inflammatory activities. TGFα and VEGF-B similarly controlled inflammatory activity of primary human astrocytes and were detected in microglia in human MS lesions. Interestingly, dietary tryptophan metabolites — which are produced by the intestinal flora and are agonists of AHR — modulated TGFα and VEGF-B production and controlled microglia–astrocyte interactions, ameliorating CNS inflammation in EAE mice. Meanwhile, Shinde et al. focus on the role of AHR in efferocytosis and immune tolerance, as defects in these processes causes systemic autoimmunity in mice. In vitro and in mice, efferocytosis triggered the activation of macrophage AHR, which induced the immunoregulatory cytokine IL-10, leading to downstream immunosuppression. AHR blockade in mouse systemic lupus erythematosus (SLE) increased serum levels of pro-inflammatory cytokines and autoantibodies, whereas treatment with an AHR agonist decreased autoantibody levels and disease. Furthermore, ageing mice with a myeloid cell-specific AHR deficiency developed spontaneous systemic autoimmunity. Notably, peripheral blood mononuclear cells from patients with SLE exhibited an AHR transcriptional signature.

ORIGINAL ARTICLES Rothhammer, V. et al. Microglial control of astrocytes in response to microbial metabolites. *Nature* **557**, 724–728 (2018) | Shinde, R. et al. Apoptotic cell–induced AhR activity is required for immunological tolerance and suppression of systemic lupus erythematosus in mice and humans. *Nat. Immunol.* **19**, 571–582 (2018)