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TWEAK and its receptor FGF inducible molecule 14 Fn14 members of the TNF TNFR superfamily have emerged as a prominent molecular axis regulating tissue responses Generally leukocyte derived TWEAK signals through Fn14 which is highly induced in injured and diseased tissues on the surface of parenchymal stromal and progenitor cells thereby orchestrating a host of tissue shaping responses including inflammation angiogenesis cell proliferation or death and the regulation of progenitor cells Compelling preclinical results indicate that whereas transient TWEAK Fn14 activation promotes productive tissue responses after acute injury excessive or persistent TWEAK Fn14 activation drives pathological tissue responses leading to progressive damage and degeneration in target organs of injury autoimmune and inflammatory diseases and cancer Given that the highly inducible pattern of Fn14 expression is well conserved between mouse and man the role of TWEAK Fn14 in human disease is an area of intense investigation Recent findings have also begun to shed light on how the TWEAK Fn14 pathway fits into the immune network interplaying with other well established pathways including TNF α IL 17 IL 13 and TGF β in regulating tissue responses The noncanonical nuclear factor κ B NF B pathway plays a role in immunity and disease pathologies and appears to be activated by only a subset of TNF TNFR superfamily members Of the various signaling pathways downstream of TWEAK Fn14 particular attention has been placed on the noncanonical NF B pathway given that given that TWEAK induces acute activation of canonical NF B but prolonged activation of noncanonical pathway Thus dovetailing of the TWEAK Fn14 axis with noncanonical NF B pathway activation may be a key mechanism underlying tissue responses Also of great interest is a deeper understanding of where when and how tissue responses are regulated by other TNF TNFR superfamily members that can signal through noncanonical NF B This Research Topic issue will cover 1 TWEAK Fn14 pathway biology role in tissue responses injury and disease pathogenesis 2 Role of noncanonical NF κ B signaling cascade in tissue responses 3 Translational studies of relevance of TWEAK Fn14 and noncanonical NF κ B in human disease 4 Other TNF superfamily members signaling through noncanonical NF κ B in the regulation of tissue responses 5 Reviews and Perspectives on the above

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