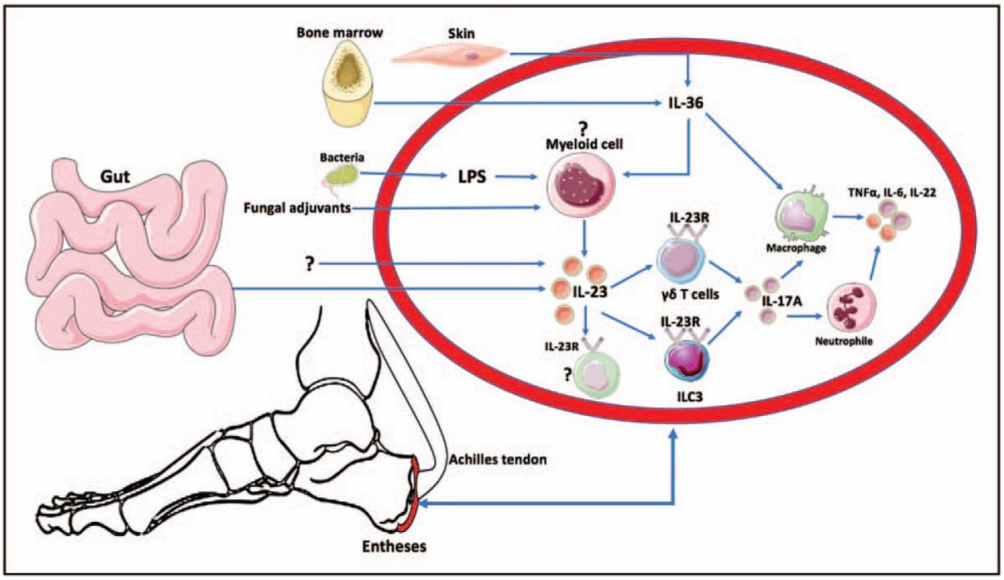
**Figure 2: Diagram showing the signalling pathway of TGF- β in bone.** *After TGF-β production and storage in the ECM, it is activated by bone resorption. The active growth factor then binds to its receptors to initiate the Smad signalling pathways as well as a Smad independent pathway. The end effects include boosting proliferation and differentiation (Wu et al, 2016).*

Meanwhile, good progress has also been made in understanding the genetics and mechanisms behind spondyloarthropathies like AS. Firstly, the most prevalent gene observed in spondyloarthropathies is the human leukocyte antigen B27 gene (HLA-B27), which was the focus of a lot of earlier studies on AS. Around 90% of AS patients (from different ethnic groups) have the HLA-B27 gene that encodes for this class I antigen. Yet, it is important to note that not all individuals with this gene develop AS, possibly due to the impact of other molecular mechanisms or some environmental factors (Chen *et al.*, 2017).

In terms of osteophyte formation and osteoporosis, it was found that high interleukin concentrations, decreased IGF-1 and high tissue necrosing factor alpha (TNF-alpha) all play important roles in the pathogenesis of AS (Lange *et al.*, 2000). Emphasis has been given to IL-17 and IL-23 possibly being the main inflammatory mediators of enthesitis. IL-17 has even shown involvement in both cartilage and bone degradation (Chabaud *et al.*, 2001).



However, Felson & Neogi hypothesised that ossification could instead be connected to imbalanced pyrophosphate levels from a PC-1 deficiency/mutation. They also pointed out how a mutation of the ANK gene has produced similar effects by altering PC-1 expression (Felson & Neogi, 2004).



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