**Introduction:** Giant Cell Tumour of Bone (GCTB) is tumour that contains numerous scattered osteoclast-like giant cells and a mononuclear cell component of fibroblast/osteoblast-like spindle-shaped cells and macrophages. The cellular mechanisms underlying the accumulation of osteoclast-like giant cells in these tumours is not clear. The canonical pathway of osteoclast formation involves differentiation of mononuclear (macrophage-like) precursors into osteoclasts in the presence of receptor activator of nuclear factor kappa B ligand (RANKL) and macrophage-colony stimulating factor (M-CSF). Abundant RANKL and M-CSF-producing cells have been noted in GCTB.1,2 Other growth factors are known to be present in abundance in GCTB, notably vascular endothelial growth factor (VEGF), and hepatocyte growth factor (HGF). In this study we determined whether these and other growth factors might play a role in M-CSF independent osteoclast formation in GCTB.

**Materials and Methods:** The (CD14-positive) monocyte/macrophage-like fraction of peripheral blood mononuclear cells (PBMCs) was isolated and cultured on coverslips and dentine slices in the presence of RANKL +/- M-CSF, VEGF or HGF. Osteoclast formation was assessed by noting the formation of multinucleated cells which expressed osteoclast-specific markers including tartrate-resistant acid phosphatase (TRAP), vitonectin receptor (VNR), F-actin rings and formation of resorption lacunae on dentine slices.

**Results:** It was found that numerous TRAP+/VNR+/F-actin ring-forming multinucleated cells capable of lacunar resorption formed in PBMC cultures where HGF and VEGF was substituted for M-CSF. The presence of these growth factors and their receptors was noted immuno-histochemically in GCTB specimens. Two other growth factors, FLT3 and placental like growth factor (PIGF) were also able to substitute for M-CSF to support osteoclast formation. The addition of these growth factors to GCTB cultures did not increase osteoclast resorption, indicating that these factors operate mainly by stimulating osteoclast formation.

**Discussion:** Our findings indicate that VEGF and HGF can substitute for M-CSF to support osteoclastogenesis and that they may play a role in the extensive osteoclast formation that occurs in GCTB. These factors may provide a therapeutic target to inhibit the extensive osteoclast formation and osteolysis that is associated with these tumours.

**References:**