Abstract

Human osteoclast-associated receptor (hOSCAR) is a member of the leukocyte receptor cluster (LRC) of an unknown ligand. hOSCAR has been reported to be expressed in several mononuclear cells (MNC) of myeloid origin and plays a role in modulating innate and adaptive immune response. We identified an alternative spliced isoform of hOSCAR that we named 3D10. Sequence analysis showed that 3D10 is one of a group of hOSCAR with a non-spliced intron resulting in larger transcripts and soluble proteins lacking a trans-membrane domain. Comparisons were made in tissue distribution between the two groups using specific PCR primers and rabbit polyclonal anti-hOSCAR and anti-soluble hOSCAR antibodies. Both groups were found to be differentially expressed in peripheral blood leukocytes and in a wide variety of tissues. They were also found to be expressed in all MNC and neutrophils. The membrane-bound isoforms were down-regulated more than the soluble isoforms following stimulation in MNC with the mitogens PWM, Con A and PHA. Studies using THP-1 cells showed that the soluble isoforms are up-regulated by both PMA and LPS, and that they are secreted and may act as decoy receptors. Performing yeast two hybrid screening of macrophage cDNA library identified potential binding partners that might include hOSCAR ligand and cytoplasmic modulators. Screening mouse tissues with anti-soluble hOSCAR Ab suggests the existence of the soluble group of mOSCAR. Finally, although 3D10 has been found to be secreted, over-expressed intra-cellular 3D10 inhibits NF-κB in a TNF-α-independent pathway.