Macrophages are immune cells that function as antigen presenting and phagocytic cells. Recently, macrophage subtypes were identified and their functional polarization was analyzed. M1 polarized macrophages are classically activated by IFN-γ alone or in combination with microbial stimuli (LPS) or cytokines (TNF and GM-CSF). M2 polarized macrophages are alternatively activated by IL-4, IL-10, IL-13, immune complexes, glucocorticoid or vitamin D3. However, the molecular mechanisms that regulate the differentiation and functions of macrophages are unknown. The large Maf transcription factors are cellular homologs of the avian V-maf musculoaponeurotic fibrosarcoma oncogene; there are four members of this family in both humans and mice. MafB and c-Maf have been reported to be expressed in macrophage lineage hematopoietic cells, but the expression profiles of MafB and c-Maf in macrophage subtypes and tissue-resident macrophages have not been well analyzed. First, we analyzed MafB and c-Maf protein expression in tissue macrophages. Lymph node macrophages expressed both MafB and c-Maf, whereas spleen macrophages expressed only MafB and alveolar and kidney macrophages did not express either of the proteins. To elucidate the molecular mechanism underlying the different expression patterns, we cultured wild type bone marrow-derived macrophages under different conditions and investigated the transcription factors expression. IL-10 induced MafB and c-Maf expression compared to macrophages treated with M-CSF alone. Conversely, IL-4 with IL-13 significantly induced MafB expression but not c-Maf expression. GM-CSF did not induce MafB or c-Maf expression. These results indicate that MafB and c-Maf are differentially expressed in tissue-resident macrophages and that the difference is induced by the combinations of different cytokines. Furthermore, MafB is mainly expressed in M2 macrophages and lymph node macrophages but is not expressed by alveolar macrophages, which also do not express c-Maf. This study is the first demonstration of the different expression patterns of MafB and c-Maf and the molecular mechanisms underlying these differences.