# Abstract

Phagocytes of an early embryo represent a mixture of myeloid lineages that differ from adult macrophages phenotypically, biochemically and by their origin. Recent studies suggested that there are at least three waves of macrophages populating the early embryo: a maternally-derived one and two waves of extraembryonic, YS-derived origin. In addition, the occurence of early embryonic phagocytes of undetermined origin in developing anterior head mesoderm in evolutionary distinct species is well documented. This origin-related heterogeneity among early embryonic phagocyte subpopulations coupled with the lack of specific markers makes it difficult to distinguish them phenotypically and study their potentially distinct physiological roles in early development.

The aim of this study is to identify and characterize a set of novel markers suitable for identification of embryonic phagocytes. Here, using qRT-PCR approach, we have established the kinetics of expression of Toll like receptors (TLRs) and their TIR-domain containing adaptors during early embryogenesis (E7.5-E12.5) and demonstrate that their major cellular source are indeed phagocytes. Using whole-mount embryo immunohistochemistry we also show that negative regulator of TLR signaling Sigirr is expressed during very early stages of mouse development. Approximately 0.7-1% of cells in E10.5 embryo are of macrophage phenotype characterized by surface coexpression of TLR2, TLR4, CD45, CD14, CD11b and F4/80 antigens. Using reciprocal matings between the wild type and transgenic mice ubiquitously expressing EGFP, in combination with TLR2 staining, we provide evidence that the early occuring, maternally-derived phagocytes are replaced by those of embryonic origin. The microarray analysis of $CD11b^{+}$ $TLR2^{+}$ cells isolated from E10.5 embryos has revealed upregulated expression of a set of genes which could be used for phenotypic characterization of these cells. These results are first to describe the regulated expression of TLRs and other immune-related molecules during mammalian embryogenesis and demonstrate the potential of TLRs to serve as markers for early embryonic phagocytes.



# Key words

Embryonic phagocytes, Toll-like receptors, TIR-domain adaptors, phagocyte’s markers.