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Innate immunity has an adaptive component, which has been referred to as "memory," "trained," "imprinted" or "adaptive." Plasticity is a hallmark of cells of the monocyte-macrophage lineage. Microbial recognition and cytokines profoundly affect macrophage function causing a range of adaptive responses including activation, priming, or tolerance. These adaptive responses of macrophages include production of humoral fluid-phase pattern recognition molecules such as the prototypic long pentraxin PTX3. These components of humoral innate immunity in turn cooperate with and regulate phagocyte function. Progress has been made in defining the molecular basis underlying the polarized activation of macrophages, including signaling mediators, transcription factors, epigenetic modifications, and the microRNA network. The definition of molecules and mechanisms associated with plasticity and polarized activation of macrophages may provide a basis for innovative diagnostic and therapeutic approaches.