



IL-34 Induces the Differentiation of Human Monocytes into Immunosuppressive Macrophages. Antagonistic Effects of GM-CSF and IFN γ

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Auteur	Foucher, Etienne D. [1], Blanchard, Simon [2], Preisser, Laurence [3], Garo, Erwan [4], Ifrah, Norbert [5], Guardiola, Philippe [6], Delneste, Yves [7], Jeannin, Pascale [8]
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Résumé en anglais	<p>IL-34 is a recently identified cytokine that signals via the M-CSF receptor and promotes monocyte survival. Depending on the environment, monocytes can differentiate into macrophages (Mϕ) or dendritic cells (DC). A wide spectrum of Mϕ and DC subsets, with distinct phenotypes and functions, has been described. To date, the phenotype of monocytes exposed to IL-34 remains unexplored. We report here that IL-34 induces the differentiation of monocytes into CD14^{high} CD163^{high} CD1a[−] Mϕ (IL-34-Mϕ). Upon LPS stimulation, IL-34-Mϕ exhibit an IL-10^{high} IL-12^{low} M2 profile and express low levels of the costimulatory molecules CD80 and CD86. IL-34-Mϕ exhibit poor T cell costimulatory properties, and have potent immunosuppressive properties (decrease of TCR-stimulated T cell proliferation). For all the parameters analyzed, IL-34-Mϕ are phenotypically and functionally similar to M-CSF-Mϕ. IL-34 appears as efficient as M-CSF in inducing the generation of immunosuppressive Mϕ. Moreover, the generation of IL-34-Mϕ is mediated through the M-CSF receptor, is independent of endogenous M-CSF consumption and is potentiated by IL-6. In an attempt to identify strategies to prevent a deleterious M2 cell accumulation in some pathological situations, we observed that IFNγ and GM-CSF prevent the generation of immunosuppressive Mϕ induced by IL-34. IFNγ also switches established IL-34-Mϕ into immunostimulatory Mϕ. In conclusion, we demonstrate that IL-34 drives the differentiation of monocytes into immunosuppressive M2, in a manner similar to M-CSF, and that IFNγ and GM-CSF prevent this effect.</p>
URL de la notice	http://okina.univ-angers.fr/publications/ua9195 [9]
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Liens

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