Dendritic cells (DCs) are professional antigen-presenting cells that comprise several subsets with distinct phenotypes and functions, including inflammatory DCs that appear during inflammation. By analyzing human inflammatory fluids (arthritic synovial fluid and tumor ascites), we have identified the human equivalent of inflammatory DCs.

In order to identify potential inflammatory DCs in humans, we analyzed myeloid cell populations in two different inflammatory microenvironments: the synovial fluid of rheumatoid arthritis patients and inflammatory tumor ascites from breast and ovarian cancer patients. In both series of samples, we detected cells expressing markers commonly found on antigen presenting cells (i.e., CD11c and MHC Class II molecules). These cells could be divided into two main populations: CD16+BDCA1− cells, which exhibited features typical of macrophages (i.e., a vacuolar morphology and poor T-cell stimulatory functions) and CD16−BDCA1+ cells, which displayed characteristics typical of DCs (i.e., a dendritic morphology and robust T-cell stimulatory capacities) (Fig. 1A). This population of DCs expressed surface molecules commonly considered as macrophage markers, like CD14 and the mannose receptor (CD206).

To address whether these DCs represented a distinct DC subset or an activated form of conventional DCs, we used Affymetrix microarrays and we compared the transcriptional profiles of DCs and macrophages purified from 5 inflammatory ascites to those of CD14+ and CD16+ cell monocytic populations and BDCA1+ DCs purified from the blood of four healthy individuals. This transcriptomic analysis revealed that inflammatory DCs represent a distinct DC subtype exhibiting molecular features of both conventional DCs and inflammatory macrophages. Interestingly, inflammatory DCs expressed transcription factors involved in DC differentiation, including ZBTB46, which has recently been shown to be specific of the DC lineage in both mice and humans. To investigate whether inflammatory DCs are the in vivo equivalents of monocytic DCs, we designed a two-step strategy. First, we identified gene signatures for human macrophages, BDCA1+ DCs, circulating CD16+ or CD14+ monocytes, and macrocyte-derived DCs generated in vitro using different publicly available human gene expression data sets. Then, we analyzed the transcriptomic profiles of the 5 cell populations that we had isolated for the expression of these genetic signatures. Gene set enrichment analysis revealed that inflammatory DCs are specifically enriched in the macrocyte-derived DC gene signature and are therefore most likely derived from monocytes rather than from DC precursors.

Finally, we analyzed the functional properties of inflammatory DCs. When cultured with allogeneic naive CD4+ T cells, inflammatory DCs, but not inflammatory macrophages, potently stimulated T17 responses. T17 polarization...
that IL-23 signaling has recently been shown to promote tumor growth, inflammatory DCs could represent viable targets for antitumor immunotherapy.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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Figure 1. Identification of human inflammatory dendritic cells. (A) Human tumor ascites contain two populations of antigen-presenting cells: dendritic cells (DCs) and macrophages. Giemsa/May–Grünwald staining. Bar = 10 μm. (B) Like their murine counterparts, human inflammatory DCs differentiate from monocytes that are recruited by inflammatory microenvironments. These DCs induce TH17 responses, whereas inflammatory macrophages do not.