In Vivo Induction of HLA-DR on Human Neutrophils in Patients Treated With Interferon-γ

To the Editor:

Mudzinski et al. have reported HLA-DR expression on circulating human neutrophils in two patients after subcutaneous administration of granulocyte-macrophage colony-stimulating factor (GM-CSF). This data would be in line with in vitro findings of an induction of HLA-DR on mature human neutrophils by GM-CSF. Nevertheless, in vivo indirect effects of GM-CSF on myeloid progenitor cell proliferation and neutrophil maturation leading to the appearance of HLA-DR positive neutrophils cannot be excluded, as discussed by the authors. One of the most potent inducers of major histocompatibility complex (MHC) class II on many types of cells is interferon-γ (IFN-γ). This has also been shown for mature neutrophils in vitro. To determine if IFN-γ has a similar effect in vivo, we measured MHC class II expression on blood neutrophils obtained from four patients with metastatic hypernephroma before and after two weeks of treatment with IFN-γ (Imukin; Bender + Co GesmbH, Vienna, Austria), 100 µg subcutaneously three times per week. Peripheral blood (PB) polymorphonuclear neutrophils (PMN) were discriminated by their characteristic forward/sideward scatter in whole blood lysis flow cytometry.

Before treatment no expression of HLA-DR, -DP, or -DQ could be detected on PB PMN. After treatment with IFN-γ neutrophils stained positive for HLA-DR from 22% to 38%, but remained negative for HLA-DP, -DQ. To confirm HLA-DR expression on neutrophils, CD16/HLA-DR double staining was performed. Neutrophils were discriminated as CD16<sup>hi</sup> and CD16<sup>lo</sup>/HLA-DR<sup>+</sup> cells were isolated by means of flow cytometry cell sorting and cytocentrifuged onto slides. Histochemical staining confirmed that more than 98% of sorted cells were mature neutrophils. Enhanced expression of HLA-DR on mature neutrophils under IFN-γ treatment could be because of indirect or direct mechanisms. The occurrence of HLA-DR<sup>+</sup> neutrophils as a result of enhanced myelopoiesis can be excluded in our patients because administration of IFN-γ resulted in a significant reduction of absolute PB neutrophil counts without any change in the ratio of band to segmented neutrophil forms. Furthermore, blasts or other immature myeloid forms were absent in the blood smears. This also suggests that the IFN-γ effects are not mediated via the induction of colony stimulating factors (GM-CSF, interleukin-3), which have been shown to induce HLA-DR expression on mature neutrophils in vitro. Therefore, a direct effect of IFN-γ on HLA-DR induction in neutrophils in vivo has to be suggested.

Polymorphonuclear neutrophils have long been regarded as terminally differentiated cells with their primary function as effectors in nonspecific immune reactions. The demonstration that expression of MHC class II antigens on neutrophils can be induced by IFN-γ and GM-CSF in vitro and in vivo leads to a new view of the role of PMN in specific immune responses.

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REFERENCES
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