CK-MB), and reagent C removes CK-MM along with CK-MB1. Total CK-MB is measured by subtracting the residual CK activity found with reagent B from that of reagent A. CK-MB2 is measured by subtracting of the residual CK activity of reagent C from that of reagent A. The CK activities were measured in the ABA-100 (Abbott Diagnostic Division, Abbott Park, IL 60048) with use of a 1:5 proportion of sample to substrate (FastChem; Boehringer Mannheim, Indianapolis, IN 46250).

We obtained 100 EDTA-treated plasma specimens initially submitted for blood count from 41 patients admitted to a metropolitan hospital with suspicion of acute MI and measured their CK-MB and CK-MB2 content. We obtained the following results: CK-MB2 = 0.854CK-MB - 2.0 U/L (r = 0.974).

The presence of EDTA in plasma samples minimized conversion of the tissue-specific isoform to the serum-specific isoform.

These patients were classified into non-MI and MI groups on the basis of mass concentration of CK-MB in serial serum samples as determined by an immunoradiometric assay (IRMA) method (QuiCK-MB; International Immunoassay Laboratories, Inc.) routinely used in this institution. The concentration of CK-MB2 by IMPRES-MB in 36 of the patients judged to be non-MI by IRMA was 1.2 (SD 0.8) U/L. The upper limit of the reference interval for CK-MB2 was set at 3.0 U/L. The concentration of CK-MB2 was 6.4 (SD 5.4) U/L in specimens collected within 4 h of admission of 16 patients subsequently judged to have MI based on serial IRMA CK-MB results. The CK-MB2 concentration was increased in 81.2% of the specimens in the MI group, whereas CK-MB as measured by IRMA was increased in half of the specimens in this same group. The value for CK-MB2 was outside the normal range in 57.1% of the 50 specimens collected after 4 h, compared with 62.2% by IRMA.

The upper limit of the reference interval was 5 U/L for total CK-MB as measured by IMPRES-MB. Samples with <3 U/L of total CK-MB per liter would fall within the reference interval for CK-MB2, even if all the CK-MB was tissue-specific. Samples in the 3-5 U/L range of total CK-MB could indicate MI if the sample shows high percentage of CK-MB2. In some specimens in this group, the percentage of CK-MB2 was 0.42%, 0.8%, and 0.5% for non-MI patients; 0.8%, 0.92%, 0.80%, and 0.91% for MI patients.

The results obtained with IMPRES-MB reagents are similar to those reported by Puleo et al. (1) and suggest that, irrespective of the technique of measurement, CK-MB2 and CK-MB assays are sensitive, rapid, and specific for the diagnosis of MI in <4 h after onset of MI.

Reference

Vipin D. Shah
International Immunoassay Laboratories, Inc.
1900 Wyatt Drive, Suite 14
Santa Clara, CA 95054

β2-Microglobulin and Immune Activation

To the Editor:

β2-Microglobulin (B2M), a 12 800-Da protein, represents the light-chain moiety of the major histocompatibility complex class I antigens. B2M is shed from the cell surface during growth and differentiation of nucleated cells. Concentrations of B2M are increased in serum and urine of patients with diseases associated with increased cell turnover, such as malignancy (1), and in patients with renal dysfunction (2). B2M appears to have particular value in monitoring patients with human immunodeficiency virus (HIV) infection (3, 4).

B2M and neopterin share some characteristics as markers of disease (5). Increased neopterin concentrations were reported in several clinical conditions (6) in which B2M concentrations are increased. Close correlations between B2M and neopterin concentrations in serum were reported.

Most recent investigations deal with HIV-infected patients, Spearman's rank correlation coefficients up to 0.8 being reported (7, 8). Neopterin is released from human monocyte-derived macrophages on stimulation with interferon-γ (9), and cytokines also are capable of inducing B2M release from macrophages in culture (10).

We tested whether interferon-γ can induce release of B2M from a variety of nucleated cells. Human monocyte-derived macrophages, human skin fibroblasts, and tumor cell lines (liver adenocarcinoma SK-HEP-1, glioblastoma U-138-MG, kidney carcinoma A-498, bladder transitional-cell carcinoma T-24), which were proven to express MHC antigens on stimulation with interferon-γ (11), were cultured as described (12). Cells (5 × 10⁵ per milliliter) were incubated with human interferon-γ (Bioferon GmbH, Laupheim, F.R.G.) for 48 h (100 int. units/L), then the supernates were harvested and concentrations of B2M were measured by radioimmunoassay (Pharmacia, Upsala, Sweden).

Most of the cell lines did not spontaneously release detectable amounts of B2M (limit of detection: 0.2 mg/L), except being T-24 bladder cancer cells and human monocyte-derived macrophages. In contrast, all the supernates of cells stimulated by interferon-γ gave a positive result (Table 1). The data show that interferon-γ induces release of B2M from a variety of nucleated cells. Spontaneous release of B2M from proliferating cells could only rarely be detected by the test system used. It remains to be shown whether other cytokines can induce B2M release from cells. We conclude from these preliminary data that increased B2M concentrations in patients probably reflect immune stimulation by inducing endogenous release of interferon-γ and possibly other cytokines. This observation may

<table>
<thead>
<tr>
<th>B2M in supernates, mg/L</th>
<th>No Interferon</th>
<th>Interferon-γ, 100 units/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Macrophages</td>
<td>0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Fibroblasts</td>
<td>nd b</td>
<td>nd</td>
</tr>
<tr>
<td>SK-HEP-1</td>
<td>nd</td>
<td>0.2</td>
</tr>
<tr>
<td>U-138-MG</td>
<td>nd</td>
<td>0.3</td>
</tr>
<tr>
<td>A-498</td>
<td>nd</td>
<td>0.4</td>
</tr>
<tr>
<td>T-24</td>
<td>0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Medium control</td>
<td>nd</td>
<td>nd</td>
</tr>
</tbody>
</table>

* Results of two parallel experiments are shown. b nd, not detectable.
explain the high correlations found between B2M and neopterin. However, only monocyte-derived macrophages release significant amounts of neopterin when stimulated by interferon-γ, and none of the other cell lines tested here released notable amounts of neopterin, although all of them accumulated increased amounts of pterine intracellularly upon stimulation (12). Thus, release of B2M by human cells stimulated with interferon-γ seems to be a more general phenomenon than is the release of neopterin, which is more closely related to activated macrophages.

This work was financially supported by the "Österreichisches Bundesministerium für Wissenschaft und Forschung, Sektion Forschung."

References

Dietmar Fuchs
Arno Haunen
Gilbert Reibnegger
Ernst R. Werner
Gabriele Werner-Felmayer
Helmut Wachter

Institute of Med. Chem. and Biochem.
University of Innsbruck
A 6020 Innsbruck, Austria