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# Differential Expression of a Glycoprotein (p15E-RT) of Retroviral Origin in Patients Suffering from Various Hematological Disorders

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## A. Introduction

Sequences coding for human endogenous reverse transcriptases (RT) were recently identified in normal human DNA with the use of cDNA clones shown to be homologous to MuLV enzyme [1–3]. The expression of some of these endogenous retrovirus genes was also shown at the RNA level [4]. Earlier molecules with enzymatic properties of RT had been identified in the tissues of some leukemic patients [5–7]. We previously reported the presence of antibodies recognizing specific type C virus RT associated with the membrane of some hematopoetic cells, principally in leukemic patients, but also in some normal individuals [8, 9]. More recently, we purified a protein of 74 kilodaltons containing retroviral RT and p15E determinants [10]. This protein was purified to homogeneity and a specific radioimmunoassay was developed, allowing us to quantitate the level of this protein in the plasma of patients in various hematologic situations [11]. The level of the protein appeared elevated in hematologic situations where a stimulation of hematopoietic tissues was happening or was needed.

## B. Results

A glycoprotein of 74 kilodaltons was purified to homogeneity from the plasma of a CML patient with the use of newly developed monoclonal antibodies. A similar protein was also partially purified from the plasma of a normal individual. This protein was analyzed immunologically with a battery of antibodies (hyperimmune and monoclonals) and was shown to contain RT and p15E antigenic determinants of retroviruses (Table 1).

By specific radioimmunoassay, the level of this protein was measured in normal individuals (25.5 μg/ml) and in various hematologic situations (Table 2). We could not correlate the level of the protein with the white blood cell count (WBC). Some leukemic patients with high WBC had a high level of antigen (patients with CML-BC, myeloproliferative syndromes, and acute leukemias) while others in bone marrow depletion harbored a high level of antigen (patients with aplastic anemia and congenital neutropenia). On the contrary, some patients who had undergone an intensive course of chemotherapy had a low level of antigen in their plasma. Follow-up studies of patients receiving chemotherapy are under way.

## C. Discussion

The level of the 74 kilodaltons glycoprotein that we purified which contained RT and p15E of retroviruses, was measured in various patients. A high level (> 50 μg per milliliter plasma) appeared to correlate with a necessity of enhancement of hematopoietic cell proliferation or with an actual stimulation of cell proliferation. High levels of

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**Table 1.** Summary of the antibody results against the 74 kilodaltons glycoprotein

| Source of antibodies | 74 kilodaltons glycoprotein | |
|---|---|---|
| | Poly-G purified | Poly-G + Immuno-affinity purified |
| Normal sera: Rabbit, goat, mouse, cat, gibbon, human | – / – / – / – / – / – | – / – / – / – / – / – |
| Goat anti-SiSVp30, SiSVgp70 | + / – | – / – |
| Goat anti-HTLVp24 | – | – |
| Rabbit anti-MuLVp30, MuLVgp70 | – / – | – / – |
| Rabbit anti-FeLVp15E, anti-FeLVp15 | + / – | + / – |
| Rabbit anti-RT of MuLV, BaEV, RD114, SiSV | + / – / – / – | + / – / – / – |
| Cat anti-FeLV RT | – | – |
| Gibbon anti-GaLV RT | – | – |
| Human anti-HLA (BW17, BW4,A2) | – / – / – | – / – / – |
| Rabbit anti-human $\alpha_1$-glycoprotein | – | – |
| Rabbit anti-human albumin | – | – |
| Monoclonal antibodies: | | |
| Mouse anti-MuLVp 15E | + | + |
| Mouse anti-MuLVgp70 | – | – |
| Rat anti-MuLVp15 | – | – |
| Rat anti-MuLVp30 | – | – |
| Mouse anti-BaEVgp70 | – | – |
| Mouse anti-BaEVp15 | – | – |
| Mouse anti-HTLVp19 | – | – |
| Newly developed mouse anti-74 kilodalton glycoprotein | + | + |

**Table 2.** Plasma level of 74 kilodaltons glycoprotein in different hematologic situations

| Clinical diagnosis | Cases | Age (years) | WBC/µl | Glycoprotein (µg/ml) (extreme values) |
|---|---|---|---|---|
| Normal individuals | 10 | 22–52 | 5 000– 13 000 | 10– 37 |
| Cord blood | 10 | | | 8– 30 |
| CML-BC | 5 | 37–77 | 25 000–150 000 | 51–350 |
| Myeloproliferative syndromes | 3 | 55–61 | 11 000– 78 000 | 96–234 |
| Myelofibrose | 1 | 66 | 50 000 | 20 |
| Acute leukemia | 3 | 20–75 | 17 000–250 000 | 50–100 |
| Aplastic anemia | 3 | 11–60 | ~2 000 | 90–100 |
| Congenital neutropenia | 1 | 16 | Low | 125 |
| Myeloma | 1 | 60 | 3 400 | 90 |
| ALL (post allogeneic bone marrow transplantation) | 1 | 16 | 2 500 | 350 |
| Post chemotherapy | | | | |
| CML-BC | 2 | 25–59 | 4 000– 8 000 | 2–3 |
| AML | 1 | 44 | 3 600 | 4 |
| ALL | 1 | 6 | 5 600 | 4 |

antigen were also recorded in patients with bone marrow aplasia as well as in patients in leukemia with high leukocyte counts. We tentatively explained the presence of this 74 kilodaltons glycoprotein as being a growth factor, maybe in an unprocessed form. This protein will be tested in vitro for different growth stimulation properties.

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