β-galactoside binding protein inhibits B cell growth and induces cell apoptosis.

JOHN J. MURPHY, TANYA STEVANIN, DIANA S. SCHOENDORF, VALERIE WELLS* and LIVIO MALLUCCI*

Infection and Immunity Research Group and *Cell Cycle Regulation Laboratory, Division of Life Sciences, King's College London, Campden Hill Road, London W8 7AH, U.K.

β-galactoside binding protein (βGBP) is a novel physiological regulator of the cell cycle secreted by mouse embryo fibroblasts (MEFs) [1]. Addition of βGBP to MEFs has been shown to induce cell cycle arrest. βGBP is a monomeric protein of 134 amino acids long. βGBP’s cytostatic effect is independent of its carbohydrate-binding activity and it operates by binding to high affinity receptors on target cells with a Kd of \(10^{-11}\) M [1].

The effects of βGBP on growth and viability of a range of human B cell lines as well as on the activation of primary tonsillar human B cells has been investigated in the present study. βGBP, in a dose-dependent manner, inhibited growth of JM1 (pre-B), Ramos (Burkitt lymphoma), Raji (Burkitt lymphoma) and Daudi (Burkitt lymphoma) B cell lines. Maximal growth inhibition was achieved with concentrations of between 40 ng/ml and 400 ng/ml which was similar to the concentrations required for growth inhibition of MEFs [1]. Growth inhibition was evident 24h after exposure to βGBP and growth arrested cells were larger than untreated cells, perhaps reflecting a block in a late stage of the cell cycle (late S or G2) and/or induced differentiation as has been observed for IL-6 [3,4]. βGBP treated cells remained viable for up to three days after treatment and then underwent apoptosis.

Figure 1 shows viability of Ramos B cells over a five day time course in the presence and absence of βGBP (400 ng/ml). After day three, there was significantly more cell death in βGBP treated cultures. Acridine orange staining [2] showed nuclear condensation in βGBP treated cultures consistent with apoptosis. βGBP also inhibited \(^{3}H\)-thymidine incorporation in primary human tonsillar B cells activated by each of the following treatments: 1) F(ab')2 anti-μ (3 μg/ml) and anti-CD40 (G28-5, 1 μg/ml), 2) anti-μ and IL-4 (500 units/ml), 3) anti-CD40 and IL-4, 4) anti-μ, anti-CD40 and IL-4. Again a dose-response relationship was evident and βGBP (400 ng/ml) inhibited \(^{3}H\)-thymidine uptake by between 45–60% in response to cell stimulation with all four treatments.

The use of neutralising antibodies to βGBP has shown that this protein has a physiological role in controlling cell cycle progression of MEFs [1]. As a first step to exploring the possibility that this protein may play a similar role in human B cells, the expression of βGBP mRNA in B cell lines and primary B cells representing different stages of B cell development has been studied by Northern Blot analysis. No detectable βGBP mRNA was found by this analysis in REH (acute lymphocytic leukaemia), JM1, Ramos, Raji or B chronic lymphocytic leukaemia cells all of which represent immature B cells. On the other hand, βGBP mRNA expression was found in Daudi, human tonsil B cells, RPMI 8866 (mature B) and RPMI 8226 (myeloma) cells. βGBP therefore appears to be expressed mainly by mature and terminally differentiated B cells and not at early stages of B cell development, suggesting that this protein may have a physiological role in cell cycle regulation/apoptosis in mature B cells.

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