The specific induction of *myc* protooncogene expression in normal human B cells is not a sufficient event for acquisition of competence to proliferate

[illegible]

[illegible]

[illegible]

ABSTRACT [illegible] Resting human B cells can be activated to proliferate in the presence of both polyclonal antibodies to immunoglobulin μ-heavy chains and B-cell growth factor (BCGF). This process appears to be temporally controlled in that the initial activation of the B cells and their responsiveness to BCGF [illegible] polyclonal anti-μ-chain antibodies [illegible]. We have used this system to investigate the role of the *myc* gene in the cell cycle of normal human peripheral blood B cells. Our results show that the polyclonal anti-μ chain antibody induced B cell activation is accompanied by a specific induction of *c-myc* gene expression without prompting subsequent entry into the S phase unless BCGF is added. Monoclonal antibodies to either μ chain or the pan-B cell antigen [illegible] also [illegible] transition and activation of c-*myc* gene expression. However, unlike activation with polyclonal anti-μ-chain antibodies, cells stimulated with these monoclonal antibodies do not acquire responsiveness to BCGF. The results imply that additional stimulatory functions must be present to [illegible] the *myc* specific function in order for the B cells to acquire the capacity to proliferate in response to BCGF. These findings are discussed in relation to the origin of B-cell malignancies.

[illegible]

Several lines of evidence strongly suggest that the *myc* [illegible] in the induction pathway to competence for cell proliferation [illegible]. In [illegible] B and T cells, Kelly et al. demonstrated that c-*myc* gene expression could be induced by mitogens prior to DNA synthesis [illegible]

[illegible]

one function of the *myc* protein product may be to promote an acquisition of competence to respond to exogenously added growth factors.

To further study the influence of transcriptionally activated c-*myc* genes upon normal human phenotypes, we utilized the activation pathway of human B cells, purified from peripheral blood, [illegible]. Under certain conditions the stimulation of B cells [illegible] proliferation can be divided into at least two separate steps. First, B cells can be activated initially by [illegible] interaction with T cells or by cross-linking of surface immunoglobulin (sIg) by antigen or anti-Ig (14, 15). This treatment renders the cells responsive to [illegible] well defined [illegible] factors such as the B-cell growth factor (BCGF), an important event possibly involving the [illegible] receptors for these factors (14–16). As shown in this report, the expression [illegible] of the [illegible] Thus, this system provides us with the means to penetrate in more depth the link between c-*myc* expression and cell proliferation.

MATERIALS AND METHODS

B-Cell Purification [illegible]

[illegible]

B-Cell Activation. [illegible]

[illegible]

Abbreviations: [illegible] B-cell growth factor [illegible]

[illegible]

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