4th day. The rate of thymidine incorporation peaks at 6–7 days and declines thereafter reaching a minimum (which is comparable with the levels observed at 2–3 days) by 10–11 days. The peak of rate of DNA replication is preceded by a period of increased rate of RNA synthesis and coincides with an approximate 2 fold increase in the rate of protein synthesis. The induction of DNA replication is accompanied by appearance of blasts in the culture as well as by induction of activities of DNA polymerase α and DNA topoisomerase II. The latter enzymes are known both to be required for eukaryotic DNA replication and be regulated during mitogenic activation of lymphocytes. A quantitative comparison shows that the number of cells replicating DNA in these cultures, as determined by the area under the peak of rate of thymidine incorporation, is equal to or sometimes greater than that observed after addition of concanavalin A despite the fact that former cultures contain about 20–30 % fewer cells due to cell death. These results demonstrate that the induction of DNA replication in lymphocytes can occur as a result of prolonged incubation in the medium in the absence of added mitogen and that the kinetics of induction and the proportion of cells that undergo replication are different from those observed in the presence of mitogen. Another interesting effect of incubation of lymphocytes in the culture is on the quantitative response to the added mitogen. Addition of concanavalin A after 24–48 hours of incubation of lymphocytes results in 2–4 fold greater mitogenic response, as measured by the rate of thymidine incorporation, than when the mitogen was added without any incubation. These results are indeed surprising and may be due to particular experimental conditions. However, they are not due to a factor in a specific batch of fetal calf serum since we have used several batches; furthermore the effect persists, but is lower, in presence of homologous human serum. We are systematically examining the experimental conditions in order to determine the cause of this effect. The explanation may be banal but might also be non-trivial.

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96. Induction of c-onc expression in polyclonally activated mouse lymphocytes

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Normal mouse splenic T and B lymphocytes were analyzed separately for the expression of cellular oncogenes. In LPS activated B cells and Con A activated T cells an increase in both myc and Ha-ras specific RNA was found as compared to unstimulated lymphocytes. So far no expression of abl, Blym, erb A and erb B, fes, fms, mos, myb, rel and sis was detected under these conditions. Kinetic studies with Con A activated T cells showed that c-myc expression is already maximal 3 hrs post stimulation while c-Ha-ras is maximally expressed around 20 hrs post stimulation. In either case the expression decreases thereafter. Different T cell subpopulations activated by the same mitogen seem to exhibit a different pattern of c-myc expression. Thus, Con A activated Lyt 2^+ cells express c-myc earlier and more strongly than the same cells do after stimulation with LA and IL-2. Similarly, one given subpopulation of T cells stimulated by different mitogens displays differences in c-onc expression. The differences in c-onc expression are not strictly correlated with the onset and intensity of proliferation. Also, both helper and cytotoxic long term T cells express considerably less of c-myc specific RNA than do freshly stimulated T cells. This again argues against a strict correlation between proliferation and c-myc expression.