INTRODUCTION

Among mutants that were initially identified as "hyper rec", i.e., showing an abnormally high frequency of recombination between intrachromosomal duplications, one group was found in which the hyper rec phenotype coincided with the abnormal persistence of nascent DNA (Okazaki) fragments (1). The increased frequency of nicks and gaps in the chromosomes of such mutants might be expected to provide a corresponding increase in the number of sites at which recombination can occur and in this manner, generate the hyper rec phenotype (2). These hyper rec mutants fell into three classes. One consisted of mutants defective in DNA ligase (lig⁻), and the second consisted of mutants with a defect in DNA polymerase I (polA⁻). Both DNA ligase and DNA polymerase I have been implicated in the discontinuous replication of the E. coli chromosome (3,4), hence, isolation of mutants with defects in these enzymes was to be anticipated. However, the third class, that we have termed dnaS or sof⁻, was unanticipated and contained neither DNA ligase nor DNA polymerase I defectives. They could, however, be identified by the transient appearance of abnormally small (4-6S) Okazaki fragments (5) following brief pulses with (³H) thymidine. A comparison of the pulse labeling patterns observed in wild type, polA and sof⁻ mutants (designated as dut, see below) is shown in Fig. 1. Like the nascent fragments seen in wild type and polA strains, the small fragments observed in sof⁻ mutants appeared transiently and could be chased

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efficiently into high molecular DNA by the addition of an excess of unlabeled thymidine. Thus, with the exception of their relatively small size, Sof fragments were indistinguishable from Okazaki fragments. The sof mutants were subsequently shown to be identical to mutants (dut) defective in deoxyuridine triphosphate hydrolase (dUTPase) (6,7,8). This enzyme serves two crucial functions in pyrimidine nucleotide metabolism, (i) it removes dUTP as a substrate for DNA synthesis and thus prevents incorporation of uracil into DNA, and (ii) it provides the only known enzymatic route for the synthesis de novo of dTMP and hence dTTP.

![Graphs showing the role of dUTPase in the de novo synthesis of dTTP and in the elimination of dUTP for DNA synthesis.](image)

**Figure 1.** Role of dUTPase in the de novo synthesis of dTTP and in the elimination of dUTP for DNA synthesis.