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# DNAReplication: a database of information and resources for the eukaryotic DNA replication community

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## ABSTRACT

**DNAReplication (at http://www.dnareplication.net) has been set up as a freely available single resource to facilitate access to information on eukaryotic DNA replication. This database summarizes organism-sorted data on replication proteins in the categories of nomenclature, biochemical properties, motifs, interactions, modifications, structure, cell localization and expression, and general comments. Replication concepts are defined and a general model of the steps in DNA replication is presented. Links to relevant websites and homepages of replication labs are provided. The site also has an interactive section where links to recent replication papers are posted and readers are provided with the facility to post comments about each paper. The interactive and links pages are modified weekly and the whole site is updated annually.**

## INTRODUCTION

Over the last 20 years, there has been an explosion in our understanding of the mechanism of eukaryotic DNA replication. Currently, nearly 200 proteins have been identified that are involved in replicating the eukaryotic genome (1) and many other factors contribute to DNA synthesis in other situations, such as DNA repair. Studying eukaryotic DNA replication in a range of model organisms has shown that the basic set of proteins is highly conserved from yeast to humans (2), although mechanisms of control may be subject to species variation (3) and some proteins involved in DNA replication, such as geminin, show restricted phyletic distribution (4). The notion that the role of DNA replication is simply to duplicate the genetic material became outdated with the realization that replication factors are relevant to many other chromosomal processes. Proteins involved in genome replication may also influence DNA repair (5), recombination (6), chromatin structure (7), transcription (8) and chromosome cohesion (9), and as such the field is relevant to researchers interested in many aspects of chromosome biology. DNA replication is also relevant to human disease. Errors in DNA replication are likely to contribute to repeat instability that underlies disorders such as Huntington's disease (10). Defects in replication and/or associated checkpoint responses can lead to cancer via promotion of genome instability (11). Inhibitors of replication proteins have therapeutic importance, and detection of replication factors, such as Mcm2-7 promises to improve cancer screening (12).

Eukaryotic DNA replication is far from becoming a mature field. Although most of the proteins involved have been identified, there is considerable ignorance as to the biochemical function of individual proteins and how they are regulated. Although the regulation of DNA replication in the eukaryotic cell cycle can be explained in outline there are many uncertainties. To facilitate research and help access the increasing amount of information available on replication proteins in a flexible and readily updateable manner, we have launched a database at www.dnareplication.net, which we hope will be of value to researchers in the field, as well as to students and workers with more peripheral interests. All the data found in the database are 'hand curated' and as such should complement information on proteins available in genome sequence databases and automatically compiled resources.

## DATABASE ASSEMBLY

The main database pages were written in Microsoft Word, converted to HTML and exported to Rapidweaver (http://www.realmacsoftware.com/rapidweaver/). The list of proteins, with expandable short definitions, was constructed

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using Accordion. The search function uses Rapidsearch, and the interactive pages were constructed using Rapidblog. Sitemap is used to create and update a Robots file, which is picked up by internet search engines to maintain information about the site as current. Accordion, Rapidsearch, Rapidblog and Sitemap are all plug-in applications for Rapidweaver (available at the Rapidweaver website). The model pages were first written in Keynote (http://www.apple.com/iwork/keynote/), and exported into Quicktime. Browsers accessing the database require Quicktime to view the model pages.

## DATABASE DESCRIPTION

A menu of available pages is shown on most pages of the database and a search function is provided. Data are given in tabular form. The main sections of the database are summarized as follows.

### Model

The model pages present an attempt to integrate information on replication proteins into a cartoon showing the stepwise assembly of proteins at replication origins, and conversion to a replication fork. Important ambiguities and possible species-specific differences are highlighted in a commentary.

### Proteins

Proteins included in the database are either essential for DNA replication, show association with replication factors, or have been implicated in repair of damage resulting from replication defects. Some factors are included as they have been implicated in DNA replication from functional assays, colocalization studies, or from sequence similarity to known replication proteins. The introductory protein page presents a list of proteins (Figure 1A), which on clicking expands into a short description of the function of the protein (Figure 1B). Most entries are linked to a more extensive table presenting a summary of data from the relevant literature. These entries give alternative names for orthologues, molecular weights, biochemical properties, protein motifs, protein interactions and modifications, with citations to structure determinations, information on cellular localization and expression, and other miscellaneous data, sorted by taxonomic group. Relevant references are currently given as a flat list in each protein page. For all proteins the data are as extensive as possible; there has been no conscious selection of specific references. This reflects an attempt to provide an unbiased source of information. Errors or omissions can be emailed to info@dnareplication.net (available from a 'Contact us' button at the bottom of every page).

### Replication concepts and abbreviations

Definitions of important concepts and common abbreviations used in the replication community and in the database are presented as a flat listing.

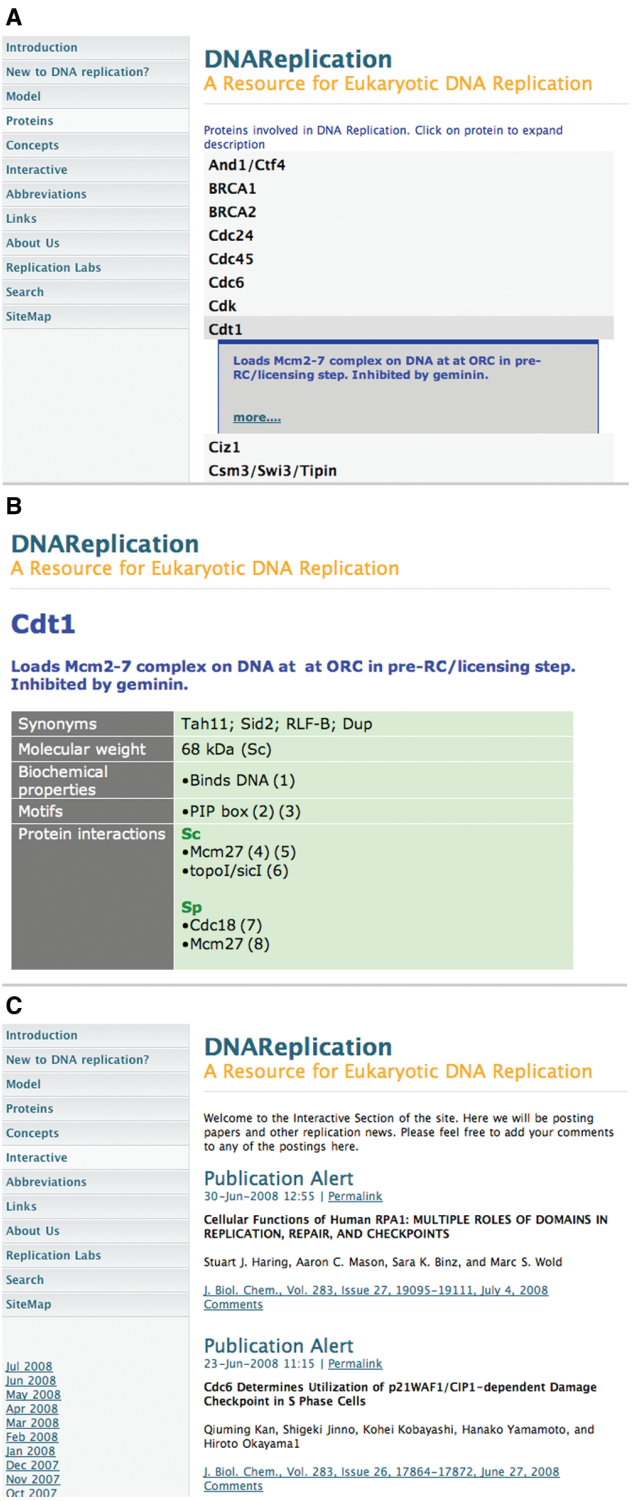


**Figure 1.** Screenshots of example database pages. (**A**) List of proteins. (**B**) Protein page entry for Cdt1. (**C**) Recent interactive page.

### Links

Links are provided to other relevant webpages and to labs involved in DNA replication; only labs that have given permission to be linked are included. Additional lab listings are welcome.

**Interactive**

Papers relevant to the replication community are posted here weekly (Figure 1C). A facility is available for posting comments on these papers. This can be done anonymously although the comments may be moderated before posting.

## FUTURE DEVELOPMENT

The website is under continuing development. In future iterations of the site, it is hoped to improve the ease of linking to references and the search function both within the site and externally. Protein pages will include sequence alignments. Protocols and reagents useful for DNA replication studies will be included (contributions welcome). We also hope to include brief descriptions of other processes relevant to DNA replication (e.g. summaries of repair pathways). The interactive section will be expanded to provide links for conferences and other postings for the community and possibly to include blog commentaries to highlight important advances. In addition, we welcome any comments and suggestions for improvements.

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