



ScholarWorks

Search articles, posters, and other scholar works...

The influence of the Ku80 carboxy-terminus on activation of the DNA-dependent protein kinase and DNA repair is dependent on the structure of DNA cofactors

[Login \(/login\)](#)

- [IUPUI ScholarWorks Repository](#)
- [→](#)
- [Theses, Dissertations, and Doctoral Papers](#)
- [→](#)
- [Biochemistry & Molecular Biology Department Theses and Dissertations](#)
- [→](#)
- [View Item](#)

The influence of the Ku80 carboxy-terminus on activation of the DNA-dependent protein kinase and DNA repair is dependent on the structure of DNA cofactors

[Woods, Derek S.](#)



Name: Full Thesis Proquest ...

Size: 2.076Mb

Format: PDF

[View/Open](#)

Permanent Link: <http://hdl.handle.net/1805/4665>

Date: 2014-07-11

Committee Chair: [Turchi, John J.](#)

Committee: Harrington, Maureen A.

Members: Malkova, Anna L.

Takagi, Yuichiro

Degree: Ph.D.

Degree Year: 2013

Department: Department of Biochemistry & Molecular Biology

Grantor: Indiana University

Keywords: [DNA Repair](#); [NHEJ](#); [DNA-PK](#); [Ku70/80](#); [Ku80 Carboxy Terminus](#)

LC Subjects: [DNA -- Research -- Methodology](#); [DNA-protein interactions](#); [Protein-protein interactions](#); [DNA -- Synthesis](#); [Enzymes -- Analysis](#); [Protein kinases -- Research -- Evaluation](#); [DNA repair](#); [DNA damage](#); [DNA-binding proteins](#); [Cellular control mechanisms](#); [Nucleotide sequence](#); [Mutagenesis](#); [Biochemical genetics](#)

Abstract:

In mammalian cells DNA double strand breaks (DSBs) are highly variable with respect to sequence and structure all of which are recognized by the DNA- dependent protein kinase (DNA-PK), a critical component for the resolution of these breaks. Previously studies have shown that DNA-PK does not respond the same way to all DSBs but how DNA-PK senses differences in DNA substrate sequence and structure is unknown. Here we explore the enzymatic mechanism by which DNA-PK is activated by various DNA substrates. We provide evidence that recognition of DNA structural variations occur through distinct protein-protein interactions between the carboxy terminal (C-terminal) region of Ku80 and DNA-dependent protein kinase catalytic subunit (DNA-PKcs). Discrimination of terminal DNA sequences, on the other hand, occurs independently of Ku 80 C-terminal interactions and results exclusively from DNA-PKcs interactions with the DNA. We also show that sequence differences in DNA termini can drastically influence DNA repair through altered DNA-PK activation. Our results indicate that even subtle differences in DNA substrates influence DNA-PK activation and ultimately Non-homologous End Joining (NHEJ) efficiency.

Description:

Indiana University-Purdue University Indianapolis (IUPUI)

This item appears in the following Collection(s)

- [Biochemistry & Molecular Biology Department Theses and Dissertations \(/handle/1805/1663\)](/handle/1805/1663)



[Show Statistical Information \(#\)](#)

My Account

- [Login](#)
- [Register](#)

Statistics

- [Most Popular Items](#)
- [Statistics by Country](#)
- [Most Popular Authors](#)

[About Us \(/page/about\)](/page/about) | [Contact Us \(/contact\)](/contact) | [Send Feedback \(/feedback\)](/feedback)

[_\(/htmlmap\)](/htmlmap)

FULLFILLING *the* PROMISE

[Privacy Notice \(http://ulib.iupui.edu/privacy_notice\)](http://ulib.iupui.edu/privacy_notice)



Copyright (<http://www.iu.edu/copyright/index.shtml>) ©2015

The Trustees of Indiana University (<http://www.iu.edu/>),

Copyright Complaints (<http://www.iu.edu/copyright/complaints.shtml>)