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DISSERTATION SUMMARY

Characterization the enzymatic activities of the human base excision repair protein Ape2

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The base excision repair (BER) is a very high capacity repair pathway. A lot of DNA damage repaired via this way as miscoding bases, single strand breaks and abasic sites. Only from the abasic sites arise up to 10,000 spontaneously/cell /day.

Class II AP endonucleases are multifunctional enzymes that function in the removal of AP sites as well as 3'-blocking termini. Two families of class II AP endonuclease and repair diesterase enzymes have been identified. The endonuclease IV family contains endonuclease IV of *Escherichia coli* and the Apn1 protein, the major AP endonuclease of *Saccharomyces cerevisiae*. The exonuclease III (exoIII) family includes ExoIII, the major AP endonuclease of *E. coli*, the Apn2 protein of *S. cerevisiae*, the Ape1, the dominant AP endonuclease in human cells and the human Ape2, the newly identified member of this family. ExoIII displays, in addition to the AP endonuclease activity, strong 3'-5' exonuclease, 3'-phosphodiesterase, and 3'-phosphatase activities (Torres-Ramos et al. 2000). Human Ape1, however, has a strong AP endonuclease activity but weak 3'-5' exonuclease, 3'-phosphodiesterase, and 3'-phosphatase activities (Wilson DM 3rd et al. 1995; Suh et al. 1997).

Ape2 is an uncharacterized member of class II AP endonucleases, because it has not been purified yet. Only one recent study reported a weak AP endonucleas activity from partially purified Ape2 fraction. In this study we purified and characterized the Ape2 protein. We expressed the Ape2 protein in a yeast expression system in fusion with a GST-tag. After the purification of the Ape2 protein, we determined the activities of the protein. We were not able to detect any AP endonuclease activity, but we observed 3'-phosphatase activity.

From these experiments we conclude that Ape2 does not have an essential role in the repair of abasic sites, but has a role in the single strand breaks repair. Similar results were published for Apn2, the yeast homolog of the Ape2 (Unk et al. 2000; Unk et al. 2001).

In addition, we demonstrated an 3'-5' exonuclease activity of the Ape2. Our experiments indicated that the 3'-5' exonuclease activity is the major activity of the Ape2.

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