

# **Supporting Information**

## **Synthesis of Sequence-Specific DNA-Protein Conjugates via a Reductive Amination Strategy**

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**Table S1.** Sites of reductive amination-mediated cross-linking between DHP-deaza-dG containing DNA and recombinant histone H4 protein as identified by nano HPLC-ESI<sup>+</sup>-MS/MS of tryptic digests.

<b>Amino acid positions</b>	<b>Amino acid sequence</b>	<b>Site of modification</b>
1 - 6	MSG <u>R</u> GK	R4
1 - 9	MSG <u>R</u> GKGGK	R4
10 - 17	GLG <u>K</u> GGAK	K13
10 - 18	GLG <u>K</u> GGAKR	K13
21 - 24	KV <u>L</u> R	R24
21 - 24	<u>K</u> VLR	K21
46 - 56	<u>R</u> ISGLIYEETR	R46

**Table S2.** Sites of reductive amination-mediated crosslinking between DHP-deaza-dG containing DNA and myoglobin as identified by nano HPLC-ESI<sup>+</sup>-MS/MS of tryptic digests.

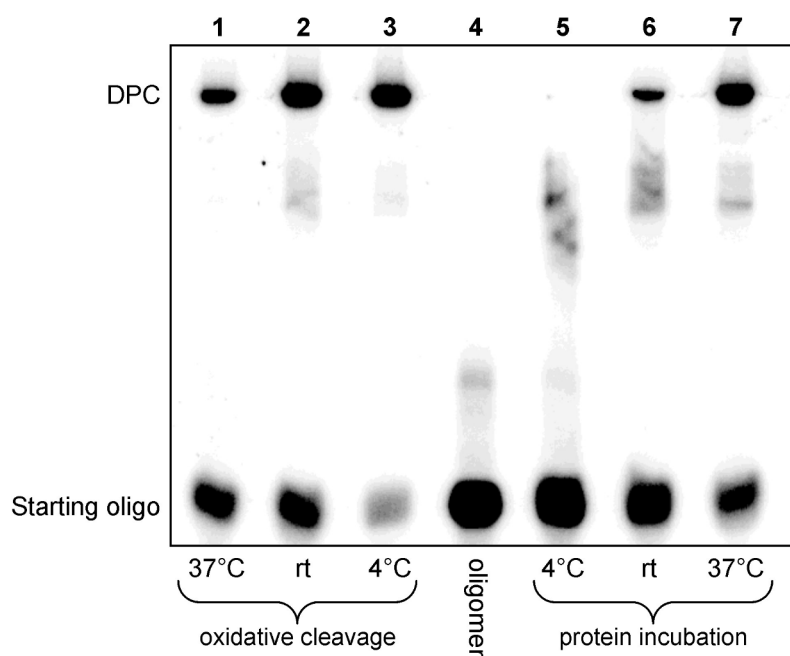
<b>Amino acid positions</b>	<b>Amino acid sequence</b>	<b>Site of modification</b>
46 - 56	FKHL <u>K</u> TEAEMK	K50
134 - 145	ALELF <u>R</u> NDIAAK	R139
134 - 145	ALELFRNDIAA <u>K</u>	K145
140 - 145	NDIAA <u>K</u>	K145
140 - 147	NDIAA <u>K</u> YK	K145

**Table S3.** Sites of reductive amination-mediated crosslinking between DHP-deaza-dG containing DNA and RNase I as identified by nano HPLC-ESI<sup>+</sup>-MS/MS sequencing of tryptic peptides.

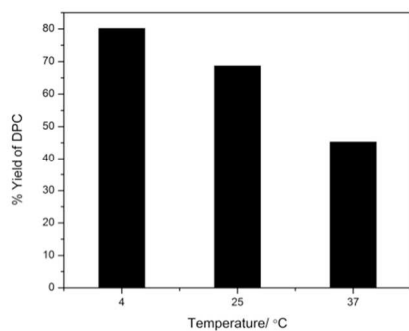
<b>Amino acid positions</b>	<b>Amino acid sequence</b>	<b>Site of modification</b>
1 - 7	<u><b>K</b></u> ETAAAK	K1
40 - 61	C <u><b>K</b></u> PVNTFVHESLADVQAVCSQK	K41
40 - 61	CKPVNTFVHESLADVQAVCSQ <u><b>K</b></u>	K61

**Figure S1.** Influence of reaction temperature on DPC yields from reductive amination-mediated crosslinking between DHP-deaza-dG containing DNA and the AlkB protein (A) Lane 1-3 and (B): Oxidative cleavage was most efficient at 4 °C; (A) Lane 5-7 and (C): Cross-linking reaction gave the highest yields at 37 °C.

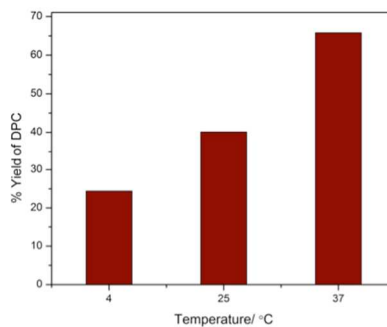
(A)



(B) Oxidative cleavage

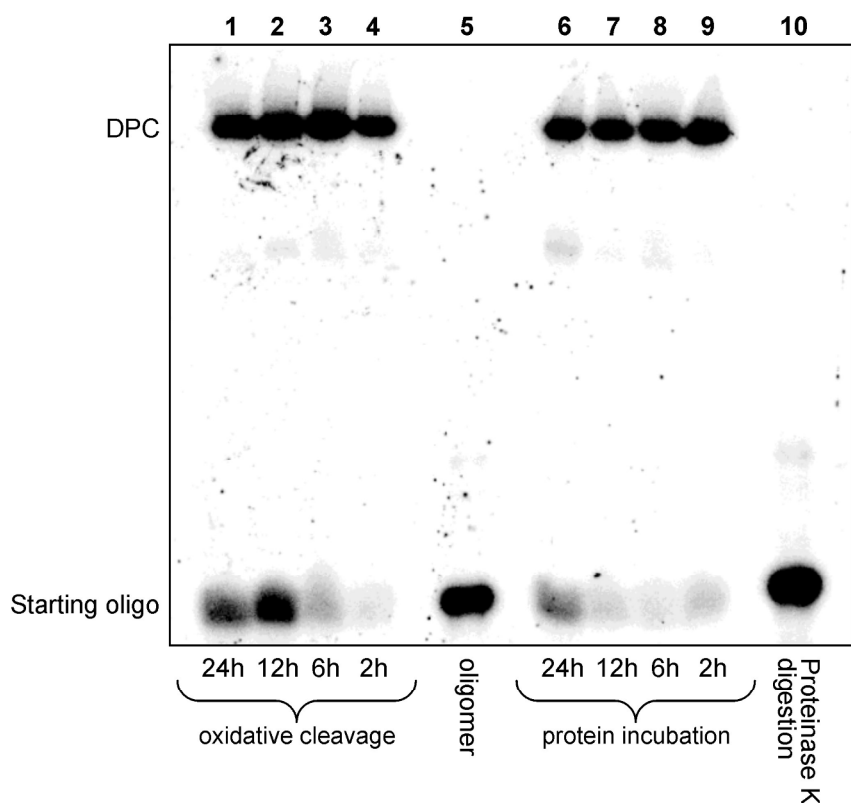


(C) Reductive amination

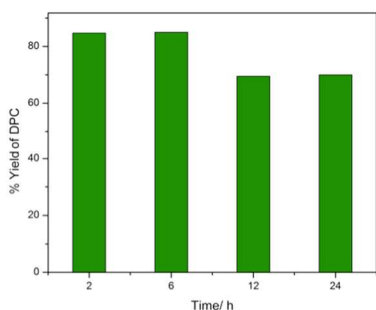


**Figure S2.** Influence of reaction time on DPC yields from reductive amination-mediated crosslinking between DHP-deaza-dG containing DNA and the AlkB protein. (A) Lane 1-4 and (B): Oxidative cleavage was high yielding at shorter reaction times (2-6 h); (A) Lane 6-9 and (C): Cross-linking reaction gave highest yields of DPCs when incubated for longer reaction times (12-24 h); Lane 10: Proteinase K digested reaction mixture did not show low mobility DPC band.

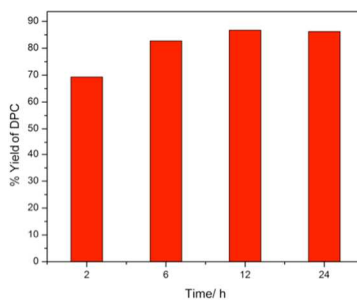
**A.**



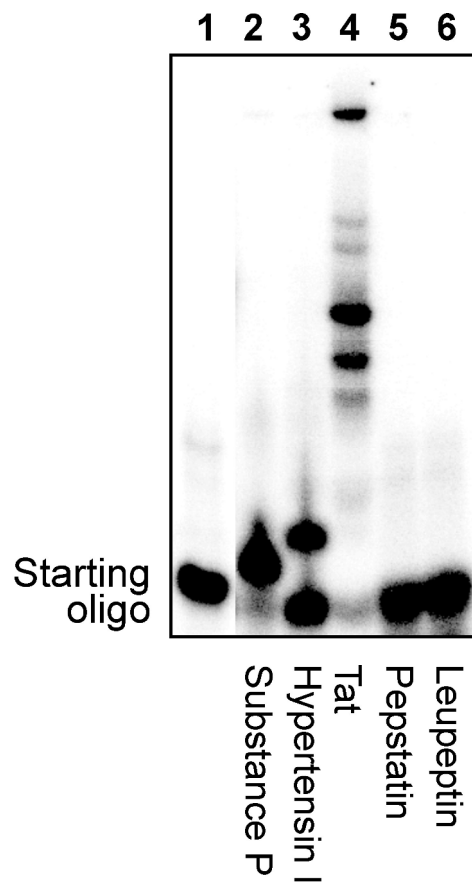
**B. oxidative cleavage time**



**C. reductive amination time**

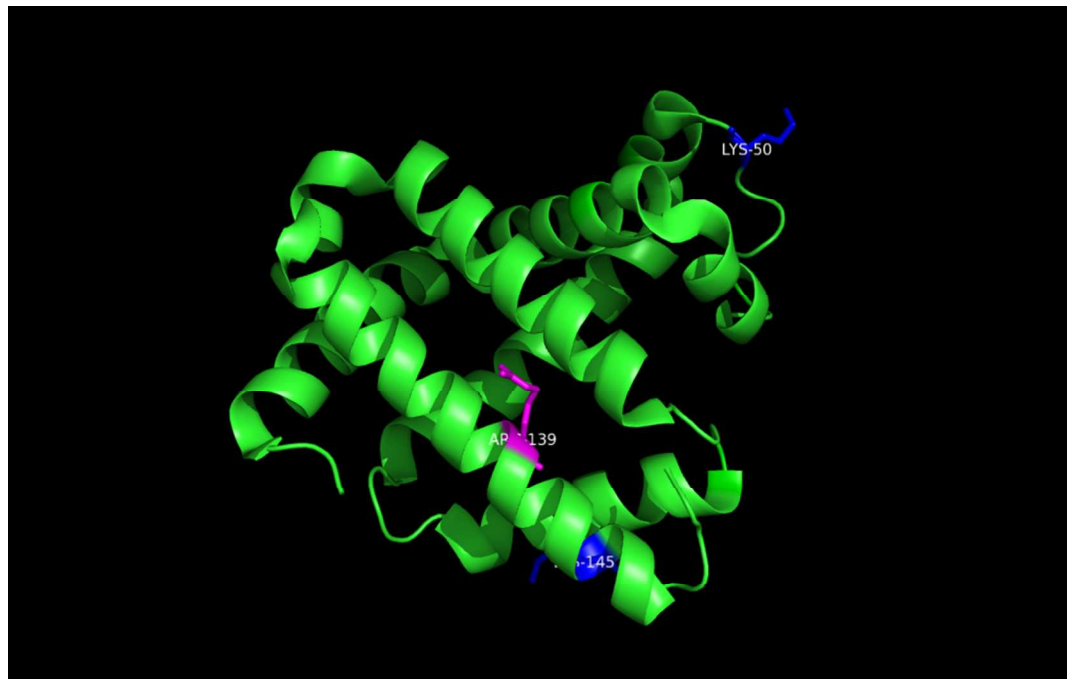


**Figure S3.** SDS-PAGE analysis of DPCs prepared using a set of different peptides that were visualized via  $^{32}\text{P}$ -end labeling of DNA. *Lane 1:* Aldehyde containing oligonucleotide in the presence of the reducing agent (negative control), *Lane 2:* Substance P produces DNA-peptide conjugate in very high yeilds, *Lane 3:* A single DPC band for Hypertensin I, which has only one arginine residue, but no lysine residues, proved that arginine is also involved in crosslinking to DNA; *Lane 4:* Multiple DPC bands observed with Tat peptide, which is highly rich in lysine and arginine residues suggesting the possibility of multiple DNA molecules binding to the same peptide/protein; *Lane 5:* No DPC bands are observed for pepstatin, which has no lysine or arginine residues suggesting that lysines and arginines are involved in cross-linking to DNA.

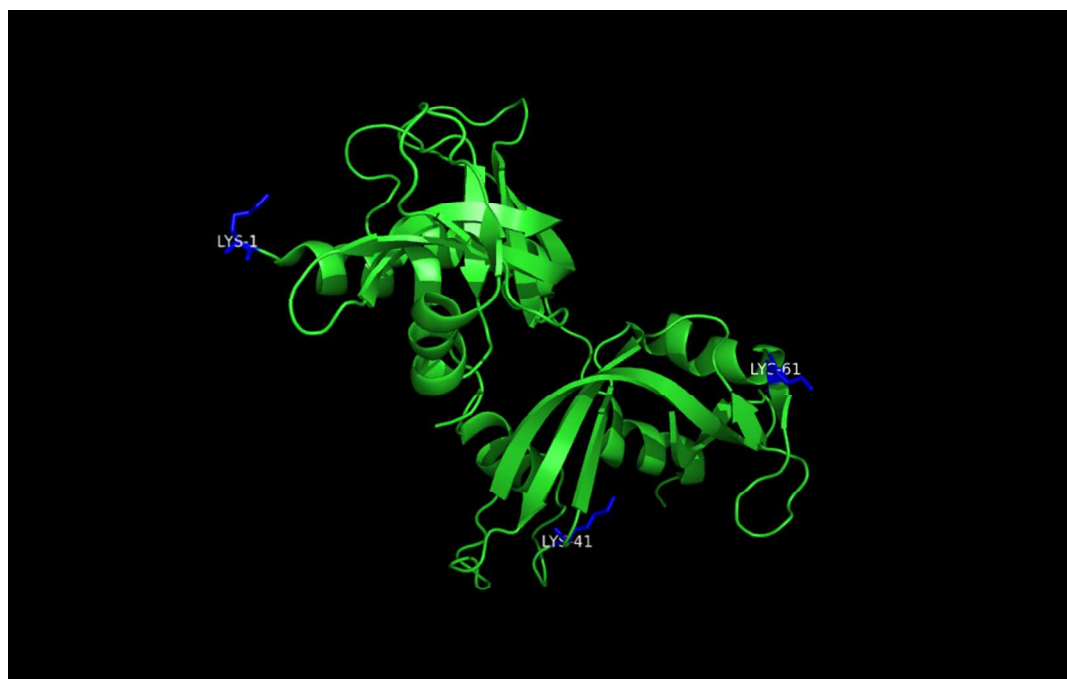


**Figure S4.** Amino acids side chains of myoglobin (A) and ribonuclease A (B) participating in reductive amination-mediated cross-linking to aldehyde-containing DNA.

(A)



(B)





**Figure S5.** HPLC-ESI<sup>+</sup>-MS/MS analysis of 7-deaza-7-(2-(N-acetylarginine)ethan-1-yl)-2'-deoxyguanosine.

