A system of linear equations for the identification of DNA binding affinity of zinc fingers

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Jonghoon Kang[‡1] **and Albert M. Kang**[§]

From the [‡]*Department of Biology, Valdosta State University, Valdosta, Georgia 31698 and* [§]*Valdosta High School, Valdosta, Georgia 31601*

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In a recent article (1), the authors examined biophysical characteristics in the interaction between methylated DNA and ZBTB38 protein, which possesses five zinc finger domains (ZFs 6–10) in the C-terminal region. While the authors identified that ZFs 6–9 were minimal structural elements for high-affinity DNA binding, the role of ZF 10 remained inconclusive. Here, we show that the binding data shown in Fig. 1 of the paper can be used to predict the role of ZF 10 in regard to binding to methylated DNA with an algebraic technique of solving a system of linear equations (2).

Fig. 1 of the paper reports dissociation constants (K_D) of 5.3 nM, 5.0 nM, and 40.6 nM for ZFs 6–10, ZFs 6–9, and ZFs 7–10, respectively. From this information, a system of linear equations of binding affinity (ΔG^0) with three unknowns can be established using the thermodynamic relation, $\Delta G^0 = RT \times \ln K_D$ (3), with an assumption of additivity in the binding (4).

ZFs 6–10: ΔG^0(ZF 6) + ΔG^0(ZFs 7–9) + ΔG^0(ZF 10) = −46.7 kJ/mol

ZFs 6–9: ΔG^0(ZF 6) + ΔG^0(ZFs 7–9) = −46.9 kJ/mol

ZFs 7–10: ΔG^0(ZFs 7–9) + ΔG^0(ZF 10) = −41.7 kJ/mol

By solving the three equations, we obtained that ΔG^0(ZF 6) = −5.0 kJ/mol, ΔG^0(ZF 7–9) = −41.9 kJ/mol, and ΔG^0(ZF 10) = 0.2 kJ/mol. Our calculation clearly suggests that ZF 10 in ZBTB38 protein does not contribute to binding affinity in agreement with the speculation made in the paper (1).

These authors declare that they have no conflicts of interest with the contents of this article.

[1] To whom correspondence should be addressed. Tel.: 229-333-7140; Fax: 229-245-6585; E-mail: jkang@valdosta.edu.

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