VEGF BINDING: A DYNAMICALLY DRIVEN PROCESS?

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The vascular endothelial growth factor (VEGF) seems to be the most important regulator of angiogenesis, that is, the growth of new blood vessels from pre-existing ones. VEGF is a member of the cystine knot superfamily of signaling molecules and its structure was determined by X-ray crystallography,[1] revealing that it is a homodimer in which the monomers are formed by ß-strands interconnected on the poles by three loops. In a recent work we have shown by the use of molecular dynamics (MD) simulations that the motions of the residues that form the same pole are strongly correlated and that between the residues of opposite poles the motions are strongly anti-correlated.[2] The results are well supported by several experimental evidences. In this work, we have used MD simulations in order to study the effects of binding (to receptor and inhibitor) on the structure and dynamics of VEGF. The results indicate that although binding to either receptor or inhibitor results on minor structural changes, the dynamical behavior is significantly affected.

1. Muller, Y. A.; Li, B.; Christinger, H. W.; Wells, J. A.; Cunningham, B. C.; DeVos, A. M. *PNAS* **1997,** 94, (14), 7192-7197.
2. Horta, B. A. C.; Cirino, J. J. V.; De Alencastro, R. B. *Proteins* **2007 (in press, DOI:** 10.1002/prot.21306**)**.