Abstract Submitted
for the MAR11 Meeting of
The American Physical Society

**Origin of using cisplatin over transplatin for cancer treatment: An ab initio study**[1] SA LI, PURU JENA, Virginia Commonwealth University, DEPARTMENT OF PHYSICS, VIRGINIA COMMONWEALTH UNIVERSITY TEAM — Eventhough cisplatin has been used as a chemotherapy anti-cancer drug for over 40 years the thermodynamics and kinetics of the reactions are still largely unknown. Cisplatin molecules are known to be attacked by water molecules before they react with DNA. As a result, two Cl atoms are eliminated. The active piece in the cell, therefore, is not cisplatin but $(NH_3)_2Pt^{2+}$. To explain why only cisplatin but not transplatin functions as anticancer drug, we used first principles method to study the dechlorination process in cis- and transplatin. Although transplatin molecule is more stable than cisplatin by 0.52 eV, we found cisplatin to be more favorable for reaction due to the following reasons: 1) the energy cost to remove a Cl atom is less from cisplatin than transplatin. 2) cis-form $(NH_3)_2Pt^{2+}$ derived from cisplatin with N-Pt-N angle of $97^\circ$ is lower in energy than trans-form derived from transplatin with N-Pt-N angle of $180^\circ$. The rotation barrier for N-Pt-N changing from $180^\circ$ to $97^\circ$ is about 1.0 eV. 3) When cis-form of $(NH_3)_2Pt^{2+}$ reacts with two Guanines in DNA, the two N atoms in Guanines can readily bind to the Pt atom in cisplatin. The transplatin due to steric reasons does not provide that opportunity.

[1]This work is supported by grants from the Department of Energy

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Date submitted: 18 Nov 2010 Electronic form version 1.4