Viral replicase points to potential cancer therapy

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Alpha viruses, such as Sindbis virus, carry their genetic information on a single strand of RNA. On infection they use a protein, replicase, to produce double stranded RNA (dsRNA) which is used as genetic material to make more viruses. However the body recognizes dsRNA as foreign, and infected cells initiate an immune response. New research published in BioMed Central's open access journal *BMC Cancer* demonstrates that an artificial plasmid coding for the replicase genes of Sindbis virus causes regression and destruction of lung cancer, or melanoma, cells in mice.

Previous attempts to use synthetic dsRNA to destroy tumor cells have met with problems, including side effects at an effective dose, but there are also concerns about using attenuated viruses, to deliver dsRNA inside cells. Researchers from the University of Texas at Austin have instead used a plasmid containing Sindbis replicase genes (nsp1-4) to force cells to produce dsRNA themselves.

For ten days mice were given daily injections of plasmid into the site of a tumor. After another 15 days most of the tumors had begun to regress, and by day 37 all of the tumors had either regressed or been destroyed. Professor Cui said, "The anti-cancer action of the plasmid seemed to be two-fold. Firstly accumulation of dsRNA resulted in cell death and secondly the presence of dsRNA, and the foreign, unmethylated, plasmid DNA, inside a cell activated both innate and adaptive immune responses."

Professor Cui continued, "In our study both highly immunogenic and poorly immunogenic tumors were receptive to treatment with an RNA replicase based plasmid. Our results suggested a novel approach to cancer molecular therapy."

More information: Replicase-based plasmid DNA shows anti-tumor activity, B. Leticia Rodriguez, Zhen Yu, Woon-Gye Chung, Richard Weiss and Zhengrong Cui, *BMC Cancer* (in press)

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