

## 2009 AACR Annual Meeting

April 18-22, 2009

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**Abstract Number:** 4511  
**Session Title:** Clinical Trials 2  
**Presentation Title:** Clinical evidence of reovirus oncolysis in human prostate cancer  
**Presentation Start/End Time:** Tuesday, Apr 21, 2009, 1:00 PM - 5:00 PM  
**Location:** Hall B-F, Poster Section 29  
**Poster Section:** 29  
**Poster Board Number:** 18

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### Introduction:

Reovirus is a non-attenuated double stranded RNA virus that exploits aberrant signaling pathways allowing selective cytotoxicity against multiple cancer histologies.

Previously, we have shown the oncolytic potential of reovirus against prostate cancer cell lines *in vitro*, as well as in animal models (Proceedings of AACR, volume 41, Abs # 777). In the present study we investigated reovirus's potential as a cancer therapeutic in a small cohort of prostate cancer patients prior to prostatectomy.

### Methods:

Six prostate cancer patients (T2/T3, N0, M0) were recruited after local ethical IRB approval and informed patient consent at the Tom Baker Cancer Centre and Rockyview Hospital, Calgary, Canada. Pathology from initial transrectal ultrasound (TRUS) guided biopsies of organ confined disease, overall suitability and patient agreement for radical prostatectomy was confirmed. Normal hematological, hepatic and cardiac function was required, as well as the requirement for patients not to be on any systemic immunosuppression. After a single TRUS guided REOLYSIN injection ( $10^7$  plaque forming units in 1 ml of PBS) patients were followed for weekly X 3 for toxicity, evidence of viral shedding and PSA levels until prostatectomy after the third week. Immunohistochemical staining of resected prostate tumor was undertaken for evidence of apoptotic markers (caspases 3, 8), immune cell infiltration (CD8, CD4) and for reovirus proteins. Urine, stool and serum were analyzed for presence of REOLYSIN by viral culture and by extracting RNA for RT-PCR detection of virus. Reovirus neutralizing antibodies in patient's serum were assayed at baseline and until prostatectomy.

### Results/ Discussion:

Intralesional reovirus injections resulted in minimal side-effects (all toxicities  $\leq$  grade 2; NCI -CTG version 3) and evidence of anti-tumor activity. Histological analysis after prostatectomy of the injected lesions and other synchronous lesions demonstrated CD8 T-cell infiltration and evidence of caspase 3 activity within the reovirus injected areas. There was no evidence of viral spread to adjacent normal prostate epithelium. Interestingly, evidence of reovirus spread to other intraprostatic cancerous lesions was not observed; likely on the basis of systemic immune clearance.

**Conclusions:** These findings suggest that reovirus therapy may provide a novel treatment for prostate cancer. However, ongoing work to circumvent immune clearance of reovirus is required in order for it to be a viable systemic therapeutic for prostate cancer.

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