INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

Name of the Student	:	SUDHIR RAJAIAH MORLA
Roll Number	:	146106040
Programme of Study	:	Ph.D.

Thesis Title: **"**Characterization of virulent Newcastle disease virus isolate from India, its attenuation and exploration of its oncolytic potential"

Name of Thesis Supervisor(s)	:	Dr. SACHIN KUMAR
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SHORT ABSTRACT

Newcastle disease virus (NDV) is a causative agent of Newcastle disease (ND) of many avian species worldwide. ND is a serious problem in developing countries causing huge loss to the poultry industry. In India first NDV breakthrough was reported in the year 1928. Since then NDV is endemic for India. The present work were we have characterised six isolates of NDV reported from different outbreaks in India between the years 2006–2012. On pathogenicity test on 9 day old embryonated eggs and one day old chicks showed that the isolates were virulent. Later, complete genome sequence of an isolate from central India was determined from vaccinated chicken farms in India during outbreaks in 2010. The genome is 15,192 nucleotides (nt) in length and is classified as genotype XIII in class II. Deduced amino acid sequences of the F protein cleavage site showed a unique virulent cleavage site ^{112}RRQKR↓F^{117}. Reverse genetics system was constructed for the of virulent NDV strain Bareilly which belong to genotype XIII. To generate attenuated virus the F cleavage site was changed from ^{112}RRQKR↓F^{117} virulent to ^{112}GRQKGR↓L^{117} avirulent one. The pathogenicity was checked for the recovered virus by MDT assay which was >180 hours avirulent compared to <60 hours virulent. NDV strain Bareilly was characterized for its apoptotic potential and migration inhibition in human oral cancer cells. NDV decreased the mitochondrial membrane potential suggesting an intrinsic pathway of apoptosis in oral cancer cells. NDV infection in oral cancer cells results in migration inhibition by a reduction in levels of MMP-7. MMP-7 is one of the key target genes of β-catenin. The involvement of the Wnt/β-catenin pathway in NDV infection has never been reported. Our results showed that NDV dysregulates Wnt/β-catenin by down-regulation of p-Akt and p-GSK3β leading to degradation of β-catenin. The study will provide us with a better insight into the circulating genotype, probable vaccine candidate and the molecular mechanism of NDV mediated oncolysis.