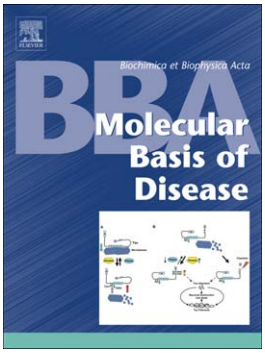

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Clusterin gene is predominantly regulated by histone modifications in human colon cancer and ectopic expression of the nuclear isoform induces cell death

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Running title: Epigenetic regulation and role of clusterin in cancer progression

ABSTRACT

Clusterin (CLU) is an important glycoprotein involved in various cellular functions. Different reports have mentioned that the two isoforms of CLU; secretary (sCLU) and nuclear (nCLU) have opposite (paradoxical) roles in cancer development. sCLU provides pro-survival signal, whereas nCLU is involved in pro-apoptotic signaling. However, the molecular mechanism of CLU gene regulation is not clear as of yet. We hypothesize that CLU gene is regulated by DNA methylation and histone modifications and clusterin play important role in colon cancer. To evaluate the hypothesis, we investigated CLU expression in colon cancer tissues and DNA methylation and histone modification status of CLU gene promoter. It is apparent from immonohistology data that both benign and cancerous (primary